APPENDIX-1

TREATMENT GUIDELINES

Treatment Guidelines followed in the National Disease Control Programmes of the Directorate General of Health Services, Government of the People's Republic of Bangladesh :

Appendix-1a

Treatment Guidelines for Acute Watery Diarrhoea

PLAN A: TREAT DIARRHEA AT HOME

Counsel the mother on the 4 Rules of Home treatment

1. Give extra fluid
2. Give zinc supplements (age 6 months up to 5 years)
3. Continue Feeding
4. When to return

1. GIVE EXTRA FLUID (as much as the child will take)

➢ ***Tell the mother***

- Breastfeed frequently and for longer at each feed
- If the child is exclusively breastfeed, give ORS or clean water in addition to breast milk
- If the child is not exclusively breastfeed, give one or more of the following ORS: ORS solution, food-based fluid (such as rice water, chira apni, yogurt drink) or clean water

It is especially important to give ORS at home when:

- The child has been treated with Plan B or Plan C during the visit
- The child cannot return to a clinic if the diarrhea get worse

➢ **TEACH THE MOTHER HOW TO MIX AND GIVE ORS. GIVE THE MOTHER 2 PACKETS OF ORS TO USE AT HOME**

➢ **SHOW THE MOTHER HOW MUCH FLUID TO GIVE IN ADDITION TO THE USUAL FLUID INTAKE**

Up to 2 years	50 to 100ml after each loose stool

2 years or more	100 to 200ml after each loose stool

➢ ***Tell the mother to***
- Give frequent small sips from a cup
- If the child vomits, wait 10 minutes. Then continue, but more slowly
- Continue giving extra fluid until the diarrhea stops

2. GIVE ZINC

➢ For acute diarrhea, persisting diarrhea and dysentery, give Zinc supplements for 10 days

AGE	ZINC TABLET (20mg)
2 months up to 6 months (Persistent diarrhea)	½
6 months up to 5 years	1

TELL THE MOTHER HOW MUCH ZINC TO GIVE
SHOW THE MOTHER HOW TO GIVE ZINC SUPPLEMENTS
- Infants –dissolve tablet in a small amount of expressed breast milk or ORS

3. CONTINUE FEEDING
4. WHEN TO RETURN

PLAN B: TREAT SOME DEHYDRATION WITH NEW ORS

In clinic, recommended amount of ORS over 4-hour period

➢ **DETERMINE AMOUNT OF ORS TO GIVE DURING FIRST 4 HOURS**

AGE*	Up to 4 months	4 months up to	12 months up to	2 years up to
WEIGHT	<6kg	6-<10kg	10-<12 kg	12-<20kg
Amount of Fluid (ml) over 4 hours	200-450	450-800	800-960	960-1600

Use the child's age only when you do not know the weight.* ***The approximate amount of ORS required (in ml) can also be calculated by multiplying the child's weight (in kg) times 75.*

- *If the child wants more ORS than shown, give more*

➢ **SHOW THE MOTHER HOW TO GIVE ORS SOLUTION**
- Give frequent small sips from a cup
- If the child vomits, wait 10 minutes. Then continue, but more slowly
- Continue breastfeeding whenever the child wants.

➢ **AFTER 4 HOURS**
- Release the child and classify the child for dehydration
- Select the appropriate plan to continue the treatment
- Begin feeding the child in clinic.

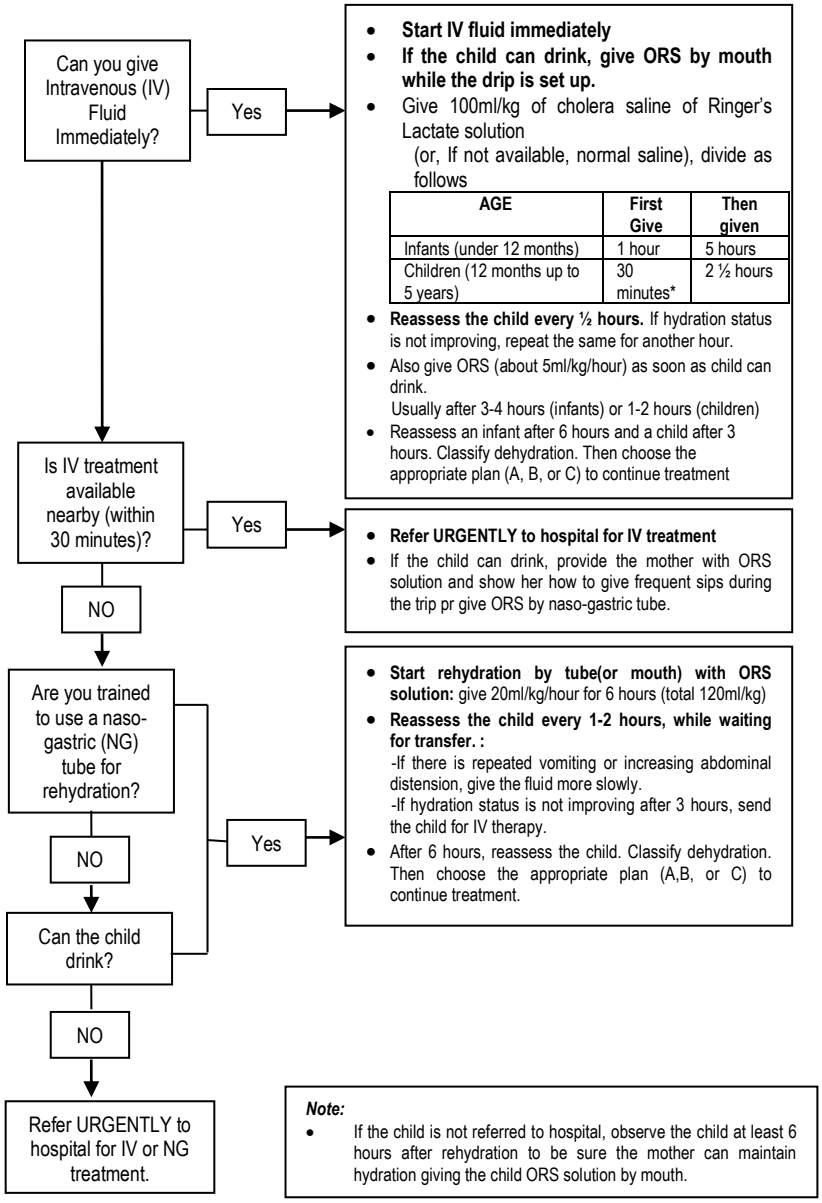
➢ **IF THE MOTHER MUST LEAVE BEFORE COMPLETING TREATMENT:**

- Show her how to prepare ORS solution at home.
- Show her how much ORS to give to finish 4 hours treatment at home
- Give her instruction how to prepare salt and sugar/gur solution at home (If ORS not available).
- Explain the 4 Rules of Home Treatment:

1. **GIVE EXTRA FLUID**
2. **GIVE ZINC (age 6 months up to 5 years)**
3. **CONTINUE FEEDING (exclusively breastfeeding if age less than 6 months)**
4. **WHEN TO RETURN**

Plan C: Treat Severe Dehydration Quickly

FOLLOW THE ARROWS, IF ANSWER IS "YES", GO ACROSS, IF "NO" GO DOWN



For dysentery: Give Ciprofloxacin for 3 days 15mg/kg/day-2 times a day for 3 days

Age or weight	**Ciprofloxacin** **Give two times daily for 3 days**
2 months up to 12 months (4 - <6kg)	1/4
4 months up to 3years (6 - <14kg)	1/2
3years up to 5years (14 - <20kg)	1

For CHOLERA: Give Tetracycline for 3 days

Age or weight	**TETRACYCLIN** **Give 4 times daily for 3 days**	**ERYTHROMYCIN** **Give 4 times daily for 3 days**
	CAPSULE 250mg	TABLET 250mg
2years up to 5years (10 - 19kg)	1	1

See also EPI Programme, DGHS, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix-1b
Treatment Guidelines for Tuberculosis

See also in section 1.1.9

Case Definition by previous treatment history

Case Classification	***Definition***
New	- A patient who has never received anti-TB drugs or - A patient who received anti-TB drugs for less than one month
Relapse	Relapse patients have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB cause by reinfection)
Treatment after failure	Treatment after failure patients are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment
Treatment after loss to follow up/default	Treatment after loss to follow up patients have previously been treated for TB and were declared to follow-up at the end of their most recent course of treatment. (These were previously known as treatment after default patients.)
Transfer in	A patient already registered for treatment in a DOTS centre and who is subsequently transferred to another register unit
Others(s)	Other previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

Standardized treatment regimen for each diagnostic category (Adults)

TB diagnostic Category	**Types of Patient**	**Treatment regimen**	
		Intensive Phase Daily)	**Continuation Phase (Daily)**
Cat. I	New smear-positive bacteriologically positive PTB patient New smear-negative PTB patient New extra pulmonary TB patient New concomitant /associated HIV/AIDS	2(HRZE) 2=First 2 months (HRZE)=4-FDC	4(HR) 4=Next 4months (HR)=2-FDC
Cat. II	Sputum smear-positive PTB with history of treatment of one month or more Relapse Treatment failure after Cat. I treatment After loss to follow up Others	2(HRZE)S/1(HRZE) 2=First 2 months, 1=Next 1 month (HRZE)=4-FDC S=Streptomycin	5(HRE) 5=Last 5 months (HRE)=3-FDC

Dosage of FDC Tablets

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FDC Tablets are composed as follows:

4FDC: rifampicin 150mg + isoniazid 75mg + pyrazinamide 400mg + ethambutol 275mg
2FDC: rifampicin 150mg + isoniazid 75mg
3FDC: rifampicin 150mg + isoniazid 75mg + ethambutol 275mg

The Dosage of FDC Tablets for adults are as follows:

Category I

Pre-treatment Weight (Kg)	Intensive Phase	Continuation Phase
	Daily First 2 Months	Daily Next 4 Months
	Number of 4FDC tablets	Number of 2FDC tablets
30-37	2	2
38-54	3	3
55-70	4	4
>70	5	5

Category II

Pre-treatment Weight (Kg)	Intensive Phase		Continuation Phase
	Daily First 3 Months	Daily First 2 Months	Daily Next 5 Months
	Number of 4FDC tablets	Injection Steptomycin	Number of 3FDC tablets
30-37	2	500mg	2
38-54	3	750mg	3
55-70	4	1gm	4
>70	5	1gm	5

Definition of Drug Resistance:

There are four different categories of drug resistance, namely:

Mono-resistance: resistance to one anti TB drug
Poly-resistance: resistance to more than one anti TB drug; other than isoniazid and rifampicin
Multidrug-resistance (MDR): resistance to at least isoniazid and rifampicin; two most potent anti-TB agents
Extensive drug-resistance (XDR): MDR-TB, plus resistance to at least one of the fluroquinolones, and al least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin)

The standard MDR-TB regimen:

The recommended standard MDR-TB regimen is as follows:

8{km-Z-Lfx(Ofx)-Eto-CS}/12{Lfx(Ofx)-Eto-CS-Z}

Length of the treatment for the standard MDR-TB Regimen:

Date of first sustained conversion	Length of the injectable agents	Length of total treatment for the standard MDR-TB Regimen
Between month 0 and 4	8 months	20-22 months
Between months 5 and 8	Add 4 months from conversion date	Add 18 months from conversion date

* Date of first negative smear and culture by two consecutive months

Adult dosage for second line anti- tuberculosis drugs

Drug	<33kg (mg/kg/day)	33-50kg (mg/kg/day)	51-70kg (mg/kg/day)	>70kg(nax) (mg/kg/day)
Pyrazinamide(Z) (500mg)	30-40mg	1000-1750mg	1750-2000mg	2000-2500mg
Kanamycin (Km) (1gm Vial)	15-20mg	500-750mg	1000mg	1000mg
Levofloxacin (Lfx) (250mg, 500mg)	7.5mg-10mg	750mg	750mg	750-1000mg
Ethionamide (Eto) (250mg)	15-20mg	500mg	750mg	750-1000mg
Cycloserine (CS) (250mg)	15-20mg	500mg	750mg	750-1000mg

See also section 1.1.9 and for more details NATIONAL GUIDELINES AND OPERATIONAL MANUAL FOR TUBERCULOSIS CONTROL (fifth edition), Published by National Tuberculosis Control Programme, DGHS, Ministry of Health & Family welfare, Govt. of Bangladesh

Appendix-1c
Treatment Guidelines for Leprosy

Leprosy (Hansen's disease) is a chronic disease caused by *Mycobactrium leprae*; it affects peripheral nervous system, skin and some other tissues, It is transmitted from person to person when bacilli shed from the nose and skin lesions of infected patients, but most individuals are naturally immune. Clinical leprosy manifests as a result of deficient cell mediated immunity in susceptible individuals. In Bangladesh, approximately 3 per 10,000 people are affected, with highest prevalence in the northern districts of Nilphamari, Dinajpur, Thakurgaon and Lalmonirhat.

For the purpose of grouping patients for chemotherapy, leprosy may be classified as multibacillary or paucibacillary.

Multibacillary leprosy occurs when cellular immunity is largely deficient and includes the subgroups lepromatous (LL), borderline lepromatous (BL) and other types giving positive skin smear for acid-fast bacilli, generally the lepromin test is negative.

Paucibacillay leprosy, results when cellular immunity is only partially deficient and includes subgroups like borderline tuberculoid (TB), tuberculoid (TT) and indeterminate (I) when skin smear is negative, generally lepromin test is positive.

Reactive episodes may be seen in leprosy patients undergoing treatment - the lepra reactions. Most reactions belong to one of two main types. Type 1 lepra reactions are delayed hypersensitivity reactions (type IV hypersensitivity) and respond to analgesics and corticosteriods.

Type 2 lepra reactions (also known erythema nodosum leprosum, ENL) represent a humoral antibody reaction (type III hypersensitivity) to dead bacteria, usually occurring in lepromatous type and respond to increasing dose of clofazamine, corticosteroid and analgesics.

Multidrugs treatment (MDT) for leprosy, as promoted by National TB and Leprosy Control Service of the Directorate General of Health Services, Government of the People's Republic of Bangladesh is shown in the *Table I* below.

Leprosy is a slowly progressive chronic infectious granulomatous disease caused by *Mycobacterium leprae* affecting mostly the skin and peripheral nerves resulting in anaesthetic hypopigmented patches in skin, and sometimes trophic changes producing deformities in certain other tissues notably oral/nasal mucosa, the eye, muscle and bone.

Leprosy can affect all ages and sexes. It is directly transmitted via droplets from nose and mouth, and by prolonged and/or close frequent contacts for many years. Rarely it may spread through fomites.

Table 1 : Multi-drugs treatment regimens for leprosy usually being practicing in Bangladesh

Type	Age Group	Supervised Doses	Self Administered Doses
PB with SINGLE lesion	ADULT > 15 years	Single one-time intake of Rifampicin 600 mg + Ofloxacin 400 mg + Minocycline 100 mg	Nil
	CHILD 5–15 years	Single one-time intake of Rifampicin 300mg + Ofloxacin 200 mg + Minocycline 50 mg	Nil
PB with 2–5 SKIN lesion Duration: 6 months	ADULT > 15	Rifampicin 600 mg + Dapsone 100 mg once in 28 days	Dapsone 100 mg daily
	CHILD 10–15 years	Rifampicin 450 mg + Dapsone 50 mg once in 28 days	Dapsone 50 mg daily
	CHILD 5–10 years	Rifampicin 300 mg + Dapsone 50 mg once in 28 days	Dapsone 25 mg daily
MB with 6 or more SKIN LESIONS or SKIN SMEAR +ve Duration: 12 months	ADULT > 15 years	Rifampicin 600 mg + Clofazimine 300 mg + + Dapsone 100 mg once in 28 days	Dapsone 100 mg + Clofazimine 50 mg daily
	CHILD 10–15 years	Rifampicin 450 mg + Clofazimine 150 mg + Dapsone 5o mg once in 28 days	Dapsone 50 mg daily + Clofazimine 50 mg alternate days.
	CHILD 5–10 years	Rifampicin 300 mg + Clofazimine 100 mg + Dapsone 5o mg once in 28 days	Dapsone 25 mg daily + Clofazimine 50 mg twice per week.

See also section 1.1.10 and for more details NATIONAL GUIDELINES AND TECHNICAL MANUAL FOR LEPROSY (3rd edition), Published by National leprosy Control Programme, DGHS, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix-1d
Treatment Guidelines for Dengue Infections

Dengue is the most important emerging tropical viral disease of humans in the world today. Over the last 10-15 years, dengue fever (DF) and dengue haemorrhagic fever (DHF) has become a leading cause of hospitalization and death among children in South-East Asian region, following diarrhoeal diseases and acute respiratory infections.

Manifestation of Dengue Infection

Asymptomatic Dengue Fever : Undifferentiated fever.
Without haemorrhage.

Symptomatic Dengue fever : With usual haemorrhage.
Dengue haemorrahagic fever (DHF).
Dengue haemorrhagic shock (DHS).

Chart-1: Clinical manifestation & Management of DHS Grades I and II
(The Manifestations & Management of DF & DHF during the febrile phase are the same)

Phase	Manifestations	Management
Febrile Duration: 2-7 days	• Temp 39-40°C (102-104°F) • Headache • Retro-orbital pain • Muscle pain • Joint bone pain • Flushed face • Rush • Skin hemorrhage, bleeding from nose, gums • Positive tourniquet test • Liver often enlarged • Leucopenia • Platelet/Hct normal	• At home • Bed rest • Keep the body temp. below 30°C • Paracetamol • No aspirin/NSAIDs • Oral fluids (fresh fruit juices) electrolyte therapy(ORS) • Follow-up for any change of platelet/Hct

Afebrile (critical) Duration: 2-7 days after febrile stage	• Same as during febrile phase • Improvement can be achieved with fluid therapy • Platelet /Hct reduced • Appetite regained slowly	• Bed rest • Check platelets /Hct • Fluids & electrolyte therapy (oral & intravenous) • The fluids if given intravenously should be started 1.5ml/kg/hr(18drops/min)for 6 hours,then3ml/kg/hrs(36 drops/min) for 6 hours, then 5ml/kg/hrs(60drop/min) for 6 hrs, then 7ml/kg/hrs(90drop/min) for 6 hrs. (the increment of fluid is important if patient is not responding with starting low dose) • After 24 hrs, the rate of IV fluid should be gradually reduced from 7 to 5, 5 to 3, 3 to 1.5 ml/kg/hr within next 24 hours.
Convalescence During 7-10 days after critical stages	• Further improvement in general condition & return of appetite • Bradycardia • Confluent petechial rash with white center/itching • weakness for 1or 2 weeks	• No special advise • No restriction • Normal diet

1. Patients & household members should be informed by the doctor that severe abdomen pain, passing of black stool, bleeding from other sites, no urine output in last 6 hrs, sweating & cold skin are warning signs & if any of these signs is noticed the patients should be taken to hospital immediately.
2. Paracetamol should be administered not more than 4 times in a 24-hr period. Paracetamol (250mg):<1 year-1/4 tablet,1-4 years $^{1}/_{2}$tablet,5yrs& above-one tablet. If syrup 50mg/kg/dose
3. 18drops/min (1.5ml/kg/hr) can be given in children as 72 micro drops/min through microburret set. Rest will be accordingly [1drop=4 micro drops in microburret set]

APPENDIX 1 : TREATMENT GUIDELINES

Chart-1: DHS Grades III and IV

Phase	Manifestations	Management
Afebrile (critical) Duration 2-3 days after febrile phase	In addition to the manifestations of DGF Grade II: -Circulatory failure evident by rapid and weak pulse, narrowing the pulse pressure (<20) or hypotension with the presence of cold clammy skin -CTR more than 2 seconds. Profound shock with unstable pulse and blood pressure	-Check Hct and total platelet count (TPL) -Initial IV therapy (0.9%NS) 10ml/kg/hr (125 drop/min) -Check vital signs , Hct, timed urine output - If improves, IV fluids should be reduced every hour from 10 (125 drop/min) To 7 (90 drop/min) and then from 7 to 5 (60 drop/min) and then 5 to 3 (36 drop/min) and lastly from 3 to 1.5ml/kg/hour(18 drop/min) that should be maintained up to 48 hours - If patient has already received 1 hour treatment of 10ml/kg/hour of IV fluids and vital signs are not stable check Hct again and - If Hct is increasing changed IV fluid to colloidal solution preferably Dextran or Plasma at 10ml/kg/hour - If Hct is decreasing from initial value give fresh hole blood transfusion 10ml/kg/hour and continue fluid therapy at 10ml/kg/hour and reducing it stepwise to 1.5ml/kg/hour and maintain it up to 48 hours - Initiate IV therapy (5%DNS) 10ml/kg/hour (125drops/minutes) as a bolus 1 or 2 times - Oxygen therapy - If continued shock colloid fluids (Dextran/Plasma) at 10-20ml/kg/hour to instituted - Persisting shock with declining Hct fresh whole blood 10ml/kg as bolus - Vital signs monitoring half hourly - If severe bleeding fresh whole blood bolus 20ml/kg - If TPL <500-1000mm3 Platelet rich plasma transfusion - After blood transfusion continue fluid therapy at 10ml/kg/hour and step wise reduce it to 1.5ml/kg/hour to be maintained up to 24-48 hours

Convalescence Duration: 2-3 days after recovery from critical stage	- 6-12 hours after critical/shock stage, some symptoms of respiratory distress (Pleural effusion, ascites) - 2-3 days after critical stage , strong pulse and normal blood pressure - Improved general condition with return of appetite - Good urine output - Stable Hct - TPL >50000 mm3 - Bradycardia/ arrhythmia - Eligible for discharge from hospital - Asthenia and depression continue for few weeks in adult.	- Rest for 1-2 days - Normal diet or no medication - Continued observation

See also for more details NATIONAL GUIDELINES AND FOR CLINICAL MANAGEMENT 0F DENGUE SYNDROME (3rd edition; 2013), Published by Disease Control Division, DGHS, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix-1e
Treatment Guidelines for Acute Respiratory Tract Infections (ARI)

FOR PNEUMONIA, ACUTE EAR INFECTION, VERY SEVER DISEASE OR SEVERE MALNUTRITION, IF INJECTABLE Drugs are not available

(Oral Amoxicillin can be given, in very severe disease; it is not possible to administer injectable Ampicillin, Gentamycin)

	Amoxicillin Give two times daily for 5 days		**COTRIMOXAZOLE (Trimethoprim + Sulphamethoxazole) Give two times daily for 5 days**		
Age or weight	**Tablet 250mg**	**Syrup 125mg/5ml**	**Adult tablet 80mg Trimethoprim + 400mg Sulphamethoxazole**	**Pediatric tablet 20mg Trimethoprim + 100mg Sulphamethoxazole**	**Syrup 40mg Trimethoprim + 200mg Sulphamethoxazole/5ml**
2months up to 12 months (4-<10kg)	3/4	7.5ml	1/2	2	5.0ml
12months up to 5years (10-<19kg)	1.5ml	15ml	1	3	7.5ml

See also EPI PROGRAMME, DGHS, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix-1f
Treatment Guidelines for Drug Addicts

Psychoactive Substance: A psychoactive substance is a substance that affects the body's central nervous system (CNS) and changes how people behave or perceive what is happening around them. Psychoactive substances include illicit/illegal drugs and some medications.

Psychoactive drugs are of the following types:

Stimulants	Opioids (Narcotics)	Depressants	Hallucinations	Others (Some drugs do not fit neatly into a category)
Cocaine	Heroin	**Alcohol**	LSD	Cannabinoids (marijuana, hashish)

Amphetamine	Morphine	Barbiturates	Mescaline Peyote	Khat/Miraa
Methampheta mine	Opium	Benzodiazepi nes	Ecstasy	Dissociative anesthetics (phencyclidine [PCP], ketamine)
Nicotine, Caffeine	Demerol	Gamma-Hydroxybutyr ate (GHB); Rohypnol	Mushrooms	Inhalants solvents, gases, nitrites

Nicotine, caffeine, and alcohol (in some countries), all of which are legal, are included in the chart of psychoactive substances. Just because a substance is legal does not mean it is safer than an illegal substance. The legality of a substance is generally more the result of traditions, culture, or political or religious factors than whether a substance is more or less harmful than another.

Substance Dependence: Also known as Drug Dependence. A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

(1) tolerance,
(2) Withdrawal,
(3) the substance is often taken in larger amounts or over a longer period than was intended
(4) there is a persistent desire or unsuccessful efforts to cut down or control substance use
(5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
(6) important social, occupational, or recreational activities are given up or reduced because of substance use
(7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption) (DSM-IV TR)

Addiction: Addiction is a chronic, relapsing brain disease that is characterized by compulsive substance seeking and use, despite harmful consequences.

Recovery: Recovery from alcohol and drug problems is a process of change through which an individual achieves abstinence and improved health, wellness, and quality of life. Recovery is defined as a process of continuous growth and improved functioning. It is not a goal that one achieves. It is instead a process of recovery management over a person's lifetime.

Relapse: A relapse is a complete return to using substances in the same way the person did before he or she quit.

Motivation

Treatment and recovery are ultimately about change. As we all know, change is not always easy for people. It is important to understand the concept of motivation because motivation for change is closely related to the level of probability that a person with a substance use disorder (or SUD) will enter treatment, continue in treatment and adhere to a specific change strategy.

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Motivation has been found to actually be dynamic rather than static and is: Purposeful, Intentional, Positive and Changeable.

Tolerance Tolerance, as defined by either of the following:

1. A need for markedly increased amounts of the substance to achieve intoxication or desired effect **or**
2. Markedly diminished effect with continued use of the same amount of the substance

Withdrawal: The unpleasant physical reaction that accompanies the process of ceasing to take an addictive drug:

- Withdrawal is the constellation of symptoms and a sign that a person experiences when, after a period of regular use, the quantity of available substance in the brain is reduced.

- Symptoms and signs of withdrawal are opposite to the main effect of the drug. For example:

    - Sedative withdrawal creates autonomic hyperactivity with dangerous medical complications.

    - Opioids withdrawal is accompanied by anxiety, powerful cravings and flu-like symptoms.

    - Stimulant withdrawal consists of depression, insomnia and cravings.

MANAGEMENT AND TREATMENT

Treatment of substance dependence patient refers to the whole range of services a client can receive directly from a treatment program or coordinated by the treatment program, the recovery oriented systems of care. These services or components, roughly in the order in which a client typically participates in them are as follows:

Components of Treatment

- ❖ Pre-treatment components
- ❖ Primary treatment
- ❖ Case management
- ❖ Continuing care, including ongoing recovery management

<u>Pretreatment Components</u>

- ■ **Outreach** - SUD program outreach includes organized efforts to identify and screen individuals who might have a problem with substance use, rather than wait for them to be referred to treatment programs or to decide to enroll in a program themselves
- ■ **Screening and brief intervention-**
    - ▪ Screening is the process of identifying individuals with possible SUDs. Screening provides an opportunity to initiate discussions with individuals about their substance use.
    - ▪ Brief intervention focuses on increasing a person's insight into and awareness of substance use and behavioral changes.
- ■ Assessment and treatment planning

- Assessment begins with engaging the client, obtaining the client's history, collecting data on the client, and observing the client during the first visit. It's important to remember that although it begins at the first visit, assessment is an ongoing process as the client's needs change over time.
- The treatment plan needs to be:
  - Individualized; Flexible; Realistic with behavioral objectives that are achievable, observable, and measurable;
  - Simple so that clients being served, their families, and staff members can understand them;
  - Focused on solutions and strengths and not on negative factors;
  - Clear in identifying the type and frequency of interventions; and Responsive to changes and progress.

■ Detoxification- Detoxification is the process of
- Stopping substance use;
- Clearing the substance from the body; and
- Managing the withdrawal syndrome.

Primary Treatment:

Primary treatments help patients engage in the treatment process, modify their attitudes and behaviors related to drug abuse, and increase healthy life skills. These treatments can also enhance the effectiveness of medications and help people stay in treatment longer. Treatment for drug abuse and addiction can be delivered in many different settings using a variety of behavioral approaches. It includes-

- Group Counseling
- Individual Counseling
- Other Components of primary treatment
  1. Testing for drug use
  2. Pharmacotherapy
  3. Orientation to mutual-help groups
  4. Medical treatment-symptomatic treatment during withdrawal period and any other physical illness
  5. Treatment for mental disorders
  6. General schooling for adolescents or young adults
  7. Employment skills training

Case Management: An integral part of treatment begins with screening and assessment and continues throughout a person's treatment and into ongoing recovery. It is the coordination of professional, social, and medical services to assist people with complex needs, often for long-term care and protection. Case management functions include: assessment, service planning, linkage and referral, monitoring and advocacy.

Continuing care, including ongoing recovery management

The continuing care process begins with discharge planning. Discharge planning leads to development of a continuing care plan. The plan contains written, treatment-related, and measurable objectives for the client to, for example: Sustain abstinence, Develop continuing recovery supports and Gain community living.

Appendix-1g
Treatment Guidelines for Burn Injury

Admission Criteria to NIBPS:

1. Burns greater than 10% of TBSA in paediatric {<12ears} and geriatric group(>60years)
2. >15% TBSA in adults (partial thickness)
3. Full thickness burns >5% of TBSA
4. burns of special areas-face, hands, feet, genitalia, perineum and major joints
5. Electrical burns, also lighting injury
6. Chemical burns
7. Burns with associated inhalation injury
8. Circumferential burns of the limbs or chest, neck
9. Burns in the very young or very old
10. Burns in people with pre existing medical or psychological disorders that could complicate management, prolong recovery or increase mortality
11. Burns with associated trauma
12. Burns with pregnancy
13. Burns in patients who will require special social, emotional, rehabilitative intervention.

Criteria's for Burn Patient to be called "Critical"

1. 15% in a child
   >30% in a adult partial thickness burns/full thickness burns
2. All Inhalation Burn
3. All Chemical Burn
4. Patients presenting late with inadequate resuscitation and or in a state of sepsis
5. All Electric Burn in First 24 hours

TRIAGE

On admission segregate the patients into groups and attach code to the file

A. Outpatient:
   <15% in adult<10% in children
B. Inpatient for routine care:
   15-30% in adult-10-25% in children
C. Critical but salvageable:
   >30%-50% in adult, >25%-50% in child
   (Need HDU or ICU care in course of time)
D. Critical but unpredictable outcome
   >50-70% (HDU)
E. Unsalvageable:
   >70%, comfort care

Out Patient Burn Management:

1. Take Clinical Picture
2. Wound lavage with normal saline, wash with mild soap
   Bister: if ruptured-debride if cause functional impairments-debride
3. Cover with moisture retaining no-adherent dressing/hydrocolloid dressing/Collagen/sufratulle/silver sulfadiazine
4. If contaminated wound, devitalized skin-topical antibiotic, silver sulhadiazine, Instruct-Change dressing daily. 24-48 hours after first dressing, check infection, give antibiotic, See at 2-3days interval, Heals within 2-3 weeks (if partial thickness). Report on admission day of same unit.
5. Face open-bacitracin ointment/collagen
6. Analgesic
7. Elevation of affected extremity
8. Injection T.T. ± TIG
9. Discharged patient will Come for weekly fixed follow up days for one month or till all the wounds have healed and advice pressure garments if there is tendency to develop hypertrophy
10. Refer patients to physiotherapy department and do the exercise explained
11. Follow up till 2 Years and may come at any time when they have difficulties. If the outpatients require surgery they are either admitted or grafted as outpatient in outdoor/Emergency OT.

Monitoring in first 24 hours

Clinical-
(Value in bracket, be alert, look for signs of shock or heart failure)

1. Pulse -4hourly(<60->100/min)
2. BP -4 hourly (<100mm of Hg systolic)
3. Urine output - hourly
   0.5ml/kg/hr adult
   1ml/kg/hour child
   2ml/kg/hour electric burn
   Maintain I/O Chart
4. Respiratory rate -4 hourly
5. Pulse oximetry - hourly in patients with suspected inhalation, shock, ventilated patient (<90% saturation)
6. Temp->105^0 (Mild fever expected secondary to hypermetobolic state)
7. Pain-

   VAS- utilize and document

   A) If severe pain- IV morphin 0.1-0.2mg/kg/dose children/2.5-10mg in adults/Oral/rectal. (titrate using patient response and respiratory rate) + diclofenac
   Or, ibuprofen+ paracetamol (in combination)

A narcotic infusion can be commenced once the initial treatments have stabilized the patient.

B) **Moderate pain – codeine 1mg/Kg + diclofenac 1mg/Kg/dose**
Or, Ibuprofen + Paracetamol

C) **Mild Pain-**Ibuprofen 10mg/Kg + paracetamol oral 20mg/Kg/dose, per-rectal 30mg/kg/dose

(Narcotic IM Inj. should not be administered as if >10% TBSA burn in adult, >15% in child as there is peripheral shutdown is present, so no absorption occurs. When circulation improves then overdose occurs.)

Monitoring after 24 hours
A daily progress note will include:

1. All vital sign (Pulse, BP, Temp, RR)
2. Level of consciousness
3. Systemic Exam-Chest, abdomen, lower limb for DVT, pressure areas
4. Intake output
5. Pain scoring
6. Notes on dressing change, wound condition/Color/Discharge/ odor
7. Nutritional adequacy
8. Physiotherapy-required or not
9. Psychological aspects
10. To communicate with family if parameter deterioriates
11. Patency of all channels

Lab Parameters:

1. Weight –on admission then quickly
2. Wound culture/biopsy on admission and weekly
3. CBC, sugar, urea, creatinine, Electrolyte daily if critical or until stable then weekly
4. FDP, D-Dimer, on admission & weekly
5. LFT, Albumin, CRP-weekly
6. CXR on admission and as required
7. PT/PTT (on admission and as required)
8. Ca, Mg, Phos (on admission and as required)
9. S.HBs. Ag/HIV/Urine Drug screening (on adm)
10. Beta-HCG (If female of reproductive age)

Drugs

1. Analgesic- adjust according to pain score
2. Antiemetic-Metachlorpromide/ondansetron
3. Antiulcer
4. Antihistamine
5. DVT Prophylaxis-Heparin 5000 IU s/c bd or Clexane 0.5mg/kg s/c
6. Nystatin (200,000I.U.) -3 times daily PO/NGT
7. Folate 1mg PO/NGT once daily
8. If %50% burn MgSO4 500ml once a week
9. Codeine 30mg PO 6 hours (for diarrhea)
10. Antibiotics

See also for more details CLINICAL PRACTICE GUIDELINES FOR BURN PATIENT MANAGEMENT, Published by National Institute of Burn & Plastic Surgery, Dhaka Medical College

Appendix-1h
Treatment Guidelines for Malaria

Uncomplicated Malaria (Falciparum): Fever or history of fever with high suspicion of malaria and positive BDT or Blood Slide Examination.
Treatment: Tablet artemether-lumefantrine, 20mg/120mg (6 doses over 3days) with single dose Tablet Primaqdine (0.75mg/kg) on day 0.

Virax Malaria: Fever or history of fever with high suspicion of malaria and positive BDT or Blood Slide Examination.

Treatment: Tablet Chloroquine over 3 days (1500mg for adult) and Tablet Primaquine 0.25mg/kg daily for 14 days.

Severe Malaria: Fever or history of fever with high suspicion of malaria and positive BDT or Blood Slide Examination with unconsciousness and/or confused and/or convulsion and/or prostration and/or jaundice and/or severe anemia and/or Acidosis and or ABDS.

Treatment: Injection artesunate (2.4mg/kg body weight). 1st dose instantly and then second dose at 12hrs. Subsequent dose once daily (Total depends on the condition of the patient's improvement). Injection artesunate will be follwed artemether-lumefantrine when patient can take orally (with single dose Primaquine)

Procedure for dilution of Injection artesunate:

- Inj. Artesunate 60mg/Vial should be mixed with 1ml 5% sodium bicarbonate solution and shaken for 2-3 min for better dissolution.
- For I/V: 5ml of 5% glucose or normal saline be added to make the concentration 10mg/ml for slow intravenous infusion.
- For I/M : 2ml 5% glucose or normal saline be added to make the concentration of Artesunate 20mg/ml for intramuscular injection.
- The total dose of intravenous infusion should be given within 3-4 minutes.

See also section 1.4.1 and for more details DIAGNOSIS AND MANAGEMENT OF SEVERE MALARIA, EARLY DIAGNOSIS AND PROMPT TREATMENT (EDPT), Learner's Guide, 2014; published by National Malaria Control Programme, Disease Control Division, DGHS, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix-1i
Treatment Guidelines for Kala-azar

The objective of treatment for Kala-azar is to cure the patient, prevent the complications of the disease and minimize side effects of medicines, restrain drug resistance and reduce the risk of spread of disease. Complications and concomitant disease(if any)should also be diagnosed and treated accordingly.

Drug treatment of Primary Kala-azar (PKA):

1st line treatment:

Following drugs are recommended as 1st line treatment for KA in Bangladesh:

Drug of Choice -
Liposomal Amphotericin B(10mg/kg single dose)
Alternative 1st line choices-(Depending on availability in our country)
• Miltefosine • Paromomycin • Combination treatment: Combination of Miltefosine & Paromomycin will be 1st choice Other alternative combinations will be Liposomal Amphotericin B* + Miltefosine Or Liposomal Amphotericin B* + Paromomycin. *LAmB5mg/kg body weight on alternate days for 3 doses

2nd line treatment:

The following drug is recommended as 2nd line treatment for PKA patients (if the 1st line drugs are not available or not tolerated):

1. Amphotericin B deoxycholate
2. Sodium Stibogluconate(SSG)

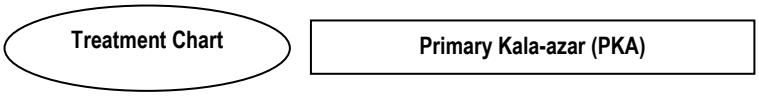
Indications of 2nd line drugs:

3. When the first line drugs are not available or not tolerated.

Description of 1st line drugs for KPA

Liposomal Amphotericin B (LAmB):

Figure-1: Treatment Chart for Kala-azar



1st line treatment for PKA

Drug of Choice

1. LiposomalAmphoterician B
(10mg/kg single dose)

Alternative 1st line choice – (Depending on availability in our country)

- Miltefosine
- Paromomycin
- Combination

Treatment : Combination of Miltefosine & Paromomycin will be 1st choice

Other alternative combination will be
Liposomal Amphoterician B*
+
Milterfosine
Or,
Liposomal Amphoterician B*
+
Paromomycin

*LamB 5mg/kg body weight on alternative days for 3 doses

2nd line treatment for PKA

Amphoterician -B deoxycholate
Dose: 1mg/kg body wt IV daily or alternative day (in 5% Dextrose solution 500ml)Duration: 15doses
Sodium stibogluconate(SSG)
Dose: 20mg/kg body wt IM daily.
Duration: 30 Days

Weight(kg)	SAG (ml)
up to 3	0.6
4-5	0.8-1
6-8	1.2-1.6
9-10	1.8-2
11-13	2.2-2.6
14-15	2.8-3.0
16-18	3.2-3.6
19-20	3.8-4.0
21-23	4.2-4.6
24-25	4.8-5.0
26-28	5.2-5.6
29-30	5.8-6.0
31-35	6.2-7.0
36-40	7.2-8.0
41-45	8.2-9.0
46-50	9.2-10
51-55	10.2-11
56-60	11.2-12

Treatment Chart of PKTF, PKDL and RKA

Treatment Chart | **KATF, PKDL & RKA**

When LAmB is not available or crontraindicatedor in KATF **1st line drugs :** **1. Miltefosine 28 days** a. Age more than 12 years & weighing? 25kg: 100mg. (cap. 50mg in morning & 50mg in evening with meal) b. Age more than 12 years but weighing < 25kg: 50mg. (Cap 50mg in the morning with meal) c. 2-12 years: 2.5mg/kg body weight in two divided does with meal, not exceeding 50mg/day) **2.Paromomycin:** Dose: 15mg/kg/day Paromomycin for 21 days IM **3**.Combination of 1st choice 2nd line drugs a. Amphtericin-B deoxycholate (1mg/kg daily or alternate day in IV for 15 doses) b. **Sodium stibogluconate** (SSG should be given at 20mg/kg daily IM for 30 days)	**Rx for RKA** 1. Combination 1st line drugs cap. Miltefosine (For adult dose:100mg daily in two divided doses for Children:2.5mg/kg body weight in two divided doses for10days) plus inj. Paromomycin at a dose 15mg/kg/day for 10 days.2.If fail then choose alternate combination- Inj.Liposomal Amphotericin B 5mg/kg body weight IV single dose on day 1 + **Cap.** Miltefosine following the above mention dose from day 2 to day 8 Or, **Inj.** Liposomal Amphotericin B 5mg/kg body weight IV single dose on day 1 + **Inj.** Paromomycin following the above mention dose from day 2 to day 11
Rx for PKDL **1st line-** **Miltefosine;** ADULT dose: 100mg daily in two divided doses for 12 wks. Children: 2.5mg/kg/day in two divided doses, not exceeding 50mg/day for 12 weeks 2nd line **a. Inj. Amphoterisin b Deoxycholate** Dose: 1 mg/kg body wt daily or alternate days IV for 15 doses per cycle with 6 cycle followed by 10days gap. **b. Inj. Sodium stibogluconate (SSG)** Dose: 20mg/kg body wt daily for 20days per cycle IM Duration : Six cycles with 10days interval between cycles	

PKTF : Primary Kala-azar Treatment failure
PKDL : Post Kala-azar Dermal leishmaniasis
RKA : Relapse Kala-azar
KATF : Kala-azar Treatment failure

See also for more detail in NATIONAL GUIDELINE FOR KALA-AZAR CASE MANAGEMENT, MAY, 2013; published by Kala-azar Elimination program, Directorate General of Health Services, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix-2

DRUG INTERACTIONS

One of the factors that can alter the response to drugs is the concurrent administration of other drugs. Two or more drugs given at the same time may exert their effects independently or may interact. The interaction may be potentiation or antagonism of one drug by another, or occasionally some other effects. There are several mechanisms by which drugs may interact, but most can be categorized as pharmacodynamic, pharmacokinetic (absorption, distribution, metabolism, excretion) or combined toxicity.

Pharmacodynamic interactions occur between drugs which have similar or antagonistic pharmacological effects or side-effects. The two drugs may or may not interact on the same recptor to produce addictive or synergistic effects. Conversely, drugs with opposing pharmacologic effects may reduce the response to one or both drugs. Pharmacodynamic interactions are usually predicatable from knowledge on pharmacology of the interacting drugs. They occur in a greater or lesser extent in most patients who receive the interacting drugs.

On the other hand, pharmacokinetic interactions occur when one drug alters the ADME (absorption, distribution, metabolism or excretion) of another, thus increasing or reducing the amount of drug available to produce its pharmacological effects. Reduction in the total amount of drug absorbed may result in infective therapy. Induction of the hepatic microsomal enzymes system by one drug can gradually increase the rate of metabolism of another, resulting in lower plasma concentrations and a reduced effect. Conversely inhibition of metabolism of one drug results in higher plasma concentrations and an increased effect with risk of toxicity. Drugs which share active transport mechanisms for elimination can delay excretion, resulting in toxicity of some drugs.

The combined use of two or more drugs, each of which has toxic effects on the same organ, can greatly increase the likelihood of organ damage.

Drug interactions are studied in Clinical Pharmacy. Clinical Pharmacists of the developed countries deal with the case of drug interactions. But in Bangladesh, the importance of drug interaction is not yet fully appreciated. Although most drug interactions are harmless, many of those, which are potentially harmful, occur in a small proportion of patients. Moreover, the severity of an interaction varies from one patient to another. Patients at increased risk from drug interactions include the elderly and those with impaired renal or liver function.

Drugs with a small therapeutic ratio (e.g. digoxin) and those which require careful control of dosage (e.g. anticoagulants, antihypertensives and antidiabetics) are most often involved in the drug interactions. Most of the potentially hazardous drug interactions are listed in the following chart. The combined administration of the drug listed in the chart should be avoided or only undertaken with caution and appropriate monitoring.

List of drug interactions :

The following is an alphabetical list of drugs and their interactions. To avoid excessive cross-referencing each drug or group is listed twice : in the alphabetical list and also against the drug or group with which it interacts. It is to be mentioned that in this compilation, (*****) has been placed against interactions that are potentially hazardous

and where combined administration of the drugs involved should be avoided (or undertaken with caution and appropriate monitoring).

Abacavir

Use of alcohol with abacavir may result in decreased elimination of abacavir and consequent increases in exposure.Abacavir increases the systemic clearance of oral methadone and patients should be monitored for signs of withdrawal symptoms. The dose of methadone may need to be increased in some patients.

Acarbose see Antidiabetics.

ACE inhibitors and Angiotensin-II antagonists

Alcohol: enhanced hypotensive effect.
Allopurinol: increased risk of toxicity with Captopril, especially in renal impairment.
* *Anesthetics:* enhanced hypotensive effect.
* *Analgesics:* antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with Ketorolac and possibly other NSAIDs .
Antacids: absorption of Captopril, Enalapril, fosinopril and possibly other ACE inhibitors reduced.
Anti-arrhythmics: Procainamide increases risk of toxicity with Captopril, especially in renal impairment.
Anticoagulant: increased risk of hyperkalaemia with Heparin.
Antidepressants: possibly enhanced hypotensive effect.
Antidiabetics: hypoglycemic effect possibly enhanced.
Other Antihypertensives: enhanced hypotensive effect.
Antipsychotics: enhanced hypotension effect.
An*xiolytics and Hypnotics:* enhanced hypotensive effect.
Beta-blockers: enhanced hypotensive effect.
Calcium-channel blockers: enhanced hypotensive effect.
* *Cardiac Glycosides:* plasma concentration of Digoxin possibly increased by Captopril.
* *Ciclosporin:* increased risk of hyperkalaemia.
Corticosteroids: antagonism of hypotensive effect.
Cytotoxics: Azathioprine increases risk of leucopoenia with Captopril.
* *Diuretics:* enhanced hypotensive effect (can be extreme); risk of severe hyperkalaemia with Potassium-sparing diuretics.
Dopaminergics: Levodopa enhances hypotensive effect.
Epoetin beta: antagonism of hypotensive effect: increased risk of hyperkalaemia.
* *Lithium:* ACE inhibitors and possibly Angiotensin-II antagonists reduce excretion of Lithium (increased plasma-lithium concentration).
Muscle Relaxants: Tizanidine enhance hypotensive effect.
Nitrates: enhance hypotensive effect.
Oestrogens and Progestogens: Oestrogens and combined oral contraceptives antagonize hypotensive effect.
* *Potassium Salts:* increased risk of hyperkalaemia.
Uricosurics: Probenecid reduces excretion of Captopril.

Acebutolol see Beta-blockers.
Aceclofenac see NSAIDs
Acetazolamide see Diuretics (Carbonic Anhydrase inhibitor).

Aciclovir

Note : Interactions do not apply to topical preparations.

Mycophenolate Mofetil: higher plasma concentrations of Aciclovir and of Mycophenolate Mofetil on concomitant administration.

Uricosurics: Probenecid reduces Aciclovir execration (increased plasma concentrations).

Acitretin see Retinoids.

Acrivastine see Antihistamines.

Adenosine Note Possibility of interaction with drugs tending to impair myocardial conduction

- Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with bupivacaine, levobupivacaine, prilocaine or ropivacaine
- Anti-arrhythmics: increased myocardial depression when anti-arrhythmics given with other antiarrhythmics
- Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with .antipsychotics that prolong the QT interval
- Beta-blockers: increased myocardial depression when anti-arrhythmics given with .beta-blockers
- Dipyridamole: effect of adenosine enhanced and extended by dipyridamole (important risk of toxicity)
- Nicotine: effects of adenosine possibly enhanced by nicotine
- Theophylline: anti-arrhythmic effect of adenosine antagonised by theophylline

Adrenaline see Sympathomimetics.

Aliskiren

- ACE Inhibitors: avoid concomitant use of aliskiren with ACE inhibitors
- Analgesics: hypotensive effect of aliskiren possibly antagonised by NSAIDs
- Angiotensin-II Receptor Antagonists: avoid concomitant use of aliskiren with angiotensin-II receptor antagonists; plasma concentration of aliskiren possibly reduced by irbesartan
- Antibacterials: plasma concentration of Aliskiren reduced by rifampicin
- Anticoagulants: increased risk of hyperkalaemia when aliskiren given with heparins
- Antifungals: plasma concentration of Aliskiren increased by itraconazole-avoid concomitant use
- Calcium-channel Blockers: plasma concentration of aliskiren increased by verapamil
- Ciclosporin: plasma concentration of Aliskiren increased by ciclosporin
- Diuretics: aliskiren reduces plasma concentration of furosemide; increased risk of hyperkalaemia when aliskiren given with potassium-sparing diuretics and aldosterone antagonists
- Potassium Salts: increased risk of Hyperkalaemia when aliskiren given with potassium salts

Alcohol

ACE Inhibitors and Angiotensin-II Antagonists: enhanced hypotensive effect.

Analgesics: sedative and hypotensive effect of opioid analgesics enhanced.

***** *Antibacterials:* Disulfiram-like reaction with Metronidazole, and possibly Tinidazole.

* *Anticoagulants:* see Warfarin.
* *Antidepressants:* sedative effect of Tricyclics (and related) enhanced; Tyramine (contained in some alcoholic and dealcoholised beverages) interacts with MAOIs (hypertensive crisis) - but if no Tyramine, enhanced hypotensive effect; effects of alcohol possibly enhanced by SSRIs.
Antidiabetics: enhanced hypoglycemic effect; flushing with chlorpropamide (in susceptible subjects); increased risk of lactic acidosis with Metformin.
Antiepileptics: CNS side-effects of Carbamazepine possibly enhanced.
Antihistamines: enhanced sedative effect.
Antihypertensives: enhanced hypotensive effect.
Antimuscarinics: sedative effect of Hyoscine enhanced.
Antipsychotics: enhanced sedative effect.
Anxiolytics and Hypnotics: enhanced sedative effect.
Barbiturates: enhanced sedative effect.
Beta-blockers: enhanced hypotensive effect.
Calcium-channel Blockers: enhanced hypotensive effect; plasma-alcohol concentration possibly increased by Verapamil.
Cytotoxics: disulfiram-like reaction with procarbazine.
Muscle Relaxants: Tizanidine enhanced sedative effect.
Nitrates: enhanced hypotensive effect.
Retinoids: Etretinate formed form Acitretin in presence of alcohol.

Albendazole
*Anthelmintics: The plasma concentration of albendazole sulfoxide has been increased by praziquantel.
*Antiepileptics: Phenytoin, carbamazepine, andphenobarbital appear to induce the oxidative metabolism ofalbendazole via the cytochrome P450 isoenzyme CYP3A by roughly the same extent, resulting in significantly reduced concentrations of albendazolesulfoxide.
*Corticosteroids: lasma concentrations of the active metabolite of albendazole (albendazole sulfoxide) were reported to be raised by about 50% in a study in 8 patients receivingdexamethasone.
*Gastrointestinal drugs: Concentrations of albendazole sulfoxide have been found to be raised in bile and hydatid cyst fluid when albendazole was given withcimetidine, which may increase efficacy in the treatment of echinococcosis.

Alendronate Sodium see Bisphosphonates.

Allopurinol
ACE Inhibitors and Angiotensin-II Antagonists: increased risk of toxicity with Captopril, especially in renal impairment.
Antibacterials: increased risk of rash with concomitant ampicillin and amoxicillin.
Anticoagulants: effects of Warfarin possibly enhanced.
Ciclosporin: plasma-ciclosporin concentration possibly increased (risk of nephrotoxicity).
* *Cytotoxics:* effects of Azathioprine and Mercaptopurine enhanced with increased toxicity (reduce dose when given with Allopurinol).
Theophylline: plasma-theophylline concentration possibly increased

Alpha-Blockers
ACE Inhibitors and Angiotensin-II Antagonists: enhanced hypotensive effect.
* *Anaesthetics:* enhanced hypotensive effect.
Analgesics: NSAIDs antagonize hypotensive effect.
* *Antidepressants:* enhanced hypotensive effect.

Other Antihypertensives: additive hypotensive effect.
Antipsychotics: enhanced hypotensive effect.
Anxiolytics and Hypnotics: enhanced hypotensive and sedative effect.

* *Beta-blockers:* enhanced hypotensive effect; increased risk of first-dose hypotensive effect of past-synaptic alpha-blockers such as Prazosin.
* *Calcium-channel Blockers:* enhanced hypotensive effect; increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers such as Prazosin.
Corticosteroids; antagonism of hypotensive effect of post-synaptic alpha-blockers such as Prazosin.
* *Diuretics:* enhanced hypotensive effect; increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers such as Prazosin.
Dopaminergics: Levodopa enhances hypotensive effect.
Muscle Relaxants: Tizanidine enhance hypotensive effect.
Nitrates: enhanced hypotensive effect.
Oestrogens and Progestogens: Oestrogens and combined oral contraceptive antagonize hypotensive effect.

Alprazolam see Anxiolytics and Hypnotics.
Aluminium Hydroxide see Antacids.

Ambrisentan

- *Antibacterials: plasma concentration of ambrisentan possibly increased by rifampicin*
- *Ciclosporin: plasma concentration of ambrisentan increased by closporin*

Amikacin see Aminoglycosides.
Amiloride see Diuretics (potassium-sparing).

Aminoglycosides

Analgesics: Indomethacin possibly increases plasma concentration of Gentamicin and Amikacin in neonates.
Other Antibacterials: increased risk of ototoxicity and nephrotoxicity with Vancomycin; Neomycin reduces absorption of Phenoxymethyl Penicillin.

* *Anticoagulants:* see Phenindione and Warfarin.
Antidiabeti7cs: Neomycin possibly enhances hypoglycemic effect of Acarbose and increases severity of gastro-intestinal effects.
Antifungals: increased risk of nephrotoxicity with Amphotericin.
* *Botulinum Toxin:* neuromuscular block enhanced (risk of toxicity).
* *Ciclosporin:* increased risk of nephrotoxicity.
Cardiac Glycosides: Neomycin reduces absorption of Digoxin.
* *Cytotoxics:* increased risk of nephrotoxicity and possibly of ototoxicity with Cisplatin.
* *Diuretics:* increased risk of ototoxicity with loop diuretics.
* *Muscle Relaxants:* effect of non-depolarizing muscle relaxants enhanced.
* *Parasympathomimetics:* antagonism of effect of Neostigmine and Pyridostigmine.

Aminophylline see Theophylline.

Amiodarone

Note : Amiodarone has a long half-life; there is a potential for drug interactions to occur for several weeks (or even months) after treatment with it has been stopped.

* O*ther Anti-arrhythmics:* additive effect with Disopyramide, Flecainide, Procainamide, and Quinidine (increased risk of ventricular arrhythmias - avoid concomitant use); increased plasma concentration of Flecainide, Procainamide and Quinidine; increased myocardial depression with any anti-arrhythmic.

* *Antibacterials:* increased risk of ventricular arrhythmias with Erythromycin (parenteral) Co-trimoxazole and moxifloxacin (avoid concomitant use).
* *Anticoagulants:* metabolism of Warfarin inhibited (enhanced anticoagulant effect).
* *Antidepressants:* increased risk of ventricular arrhythmias with Tricyclics (avoid concomitant use).
* *Antiepileptics:* metabolism of Phenytoin inhibited (increased plasma concentration).
* *Antimalarials:* increased risk of ventricular arrhythmias with Chloroquine, Hydroxychloroquine, Mefloquine and Quinine (avoid concomitant use); manufacturer of artemether with lumefantrine advises avoid concomitant use (risk of ventricular arrhythmias)
* *Antipsychotics:* increased risk of ventricular arrhythmias with Phenothiazines and Haloperiodol (avoid concomitant use).
* *Beta-blockers:* increased risk of bradycardia, AV block, and myocardial depression (avoid concomitant use).
* *Calcium-channel Blockers:* Diltiazem and Verapamil increase risk of bradycardia, AV block, and myocardial depression.
* *Cardiac Glycosides:* increased plasma concentration of Digoxin (halve Digoxin maintenance dose).
  Ciclosporin: plasma concentration of Ciclosporin possibly increased.
  Diuretics: cardiac toxicity increased if hypokalaemia occurs with Acetazolamide, loop diuretics, and Thiazides.
  Lithium: increased risk of hypothyroidism.
  Ulcer-healing Drugs: Cimetidine increases plasma concentrations of Amiodarone.

Amitriptyline see Tricyclic Antidepressants.
Amlodipine see Calcium-Channel Blockers.
Amoxycillin see Penicillins.
Ampicillin see Penicillins.

Anabolic Steroids
* *Anticoagulants:* anticoagulant effect of Warfarin enhanced.
  Antidiabetics: hypoglycaemic effect possibly enhanced.

Anaesthetics, General
* *ACE Inhibitors and Angiotensin-II antagonist:* enhanced hypotensive effect.
  Antibacterials: possible potentiation of Isoniazid hepatotoxicity; effect of Thiopental enhanced by Sulphonamides; hypersensitivity-like reactions can occur with concomitant intravenous Vancomycin.
  Antidepressants: risk of arrhythmias and hypotension increased with Tricyclics: MAOIs.
* *Antihypertensives:* enhanced hypotensive effect.
* *Antipsychotics:* enhanced hypotensive effect.
  Anxiolytics and Hypnotics: enhanced sedative effect.
* *Beta-blockers:* enhanced hypotensive effect.
* Calcium-channel Blockers: enhanced hypotensive effect and AV delay with Verapamil; hypotensive effect of Dihydropyridines enhanced by Isoflurane.
* *Dopaminergics:* risk of arrhythmias if volatile liquid anaesthetics such as Halothane given with Levodopa.
  Oxytocin: oxytocic effect possibly reduced by volatile anaesthetics (also enhanced hypotensive effect and risk of arrhythmias).
* *Sympathomimetics:* risk of arrhythmias if adrenaline or Isoprenaline given with volatile liquid anaesthetics such as Halothane.
  Theophylline: increased risk of arrhythmias with halothane.

Anaesthetics, Local see Bupivacaine, Lignocaine.
Analgesics see Aspirin, NSAIDs, Opioid Analgesics, and Paracetamol.

Antacids

ACE Inhibitors: reduced absorption of captopril, enalapril, fosinopril and possibly other ACE inhibitors.
Analgesics: excretion Aspirin increased in alkaline urine.
Anti-arrhythmics: excretion of Quinidine reduced in alkaline urine (may occasionally increase plasma concentration).
Antibacterials: reduced absorption of Azithromycin, Cefaclor, Cefpodoxime, Ciprofloxacin, Isoniazid, Levofloxacin, Moxifloxacin, Nitrofurantoin, Norfloxacin, Ofloxacin, Rifampicin and most Tetracyclines.
Antiepileptics: reduced absorption of Gabapentin and Phenytoin.
Antifungals: reduced absorption of Itraconazole and Ketoconazole.
Antihistamines: reduced absorption of Fexofenadine
Antiplatelet Drugs: Dipyridamole patient information leaflet advises avoidance of antacids.
Antimalarials: reduce absorption of Chloroquine and Hydroxychloroquine; Magnesium trisilicate reduces absorption of Proguanil.
Antipsychotics: reduced absorption of Phenothiazines and of Sulpiride
Antivirals: reduced absorption of Zalcitabine.
Bisphosphonates: reduced absorption.
Cardiac Glycosides: possibly reduced absorption of Digoxin.
Iron: Magnesium trisilicate reduces absorption of oral iron.
Lithium: sodium bicarbonate increases excretion (reduced plasma-lithium concentration).
Penicillamine: reduced absorption.
Ulcer-healing Drugs: possibly reduced absorption of Lansoprazole.

Antazoline see Antihistamines.
Anthranol see **dithranol**

- Minoxidil: Absorption of minoxidil may be increased by the concurrent use of topical dithranol.

Anti-arrhythmics see Adenosine; Amiodarone; Disopyramide; Lignocaine; Procainamide; Quinidine.
Anticholinergics see Antimuscarinics.
Anticholinesterases see Parasympathomimetics.
Anticoagulants see Heparin, and Warfarin.

Antidepressants, SSRI

Alcohol: effects possibly enhanced.

* *Analgesics:* risk of CNS toxicity increased with Tramadol; increased risk of bleeding with aspirin and NSAIDs.
* *Anticoagulants:* effect of Warfarin possibly enhanced.
* O*ther Antidepressant:* CNS effects of SSRIs increased by MAOIs (risk of serious toxicity), plasma concentration of some Tricyclics increased; agitation and nausea with Tryptophan; Fluoxetine increases plasma concentration of Nefazodone.
* *Antiepileptics:* antagonism (convulsive threshold lowered); plasma concentration of Carbamazepine lowered by Fluoxetine; plasma concentration of Phenytoin increased by Fluoxetine; Phenytoin and possibly other antiepileptics reduce plasma concentration of Paroxetine.

* *Antimalarials*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use.
* *Antipsychotics:* plasma concentration of Clozapine increased by Fluoxetine, Paroxetine and Sertraline; plasma concentration of Haloperidol increased by Fluoxetine; plasma concentration of Thioridazine increased by Paroxetine (risk of ventricular arrhythmias – avoid concomitant use); plasma concentration of Risperidone increased by Fluoxetine.
* *Antivirals:* plasma concentration possibly increased by Ritonavir.
* *Dopaminergics:* hypertension and CNS excitation with Fluoxetine, Paroxetine or Sertraline and Selegiline (Selegiline should not be started until 5 weeks after discontinuation of Fluoxetine for 2 weeks after stopping Selegiline).
* *Lithium:* increased risk of CNS effects (lithium toxicity reported).
  Opioid Analgesics: Tramadol possibly increases risk of convulsions.
* *Theophylline:* plasma-theophylline concentration increased (concomitant use should usually be avoided, but where not possible halve Theophylline dose and monitor plasma-theophylline concentration).

Antidepressants, Tricyclic

* *Alcohol:* enhanced sedative effect.
* Anaesthetics: risk of arrhythmias and hypotension increased.
* *Analgesics:* risk of CNS toxicity increased with Tramadol; possibly increased sedation with opioid analgesics.
* *Anti-arrhythmics:* increased risk of ventricular arrhythmias with drugs that prolong QT interval, including Amiodarone (avoid concomitant use), Disopyramide, Procainamide and Quinidine.
  Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin (avoid concomitant use); plasma concentrations of some tricyclics reduced by Rifampicin (reduced antidepressant effect).
* *other Antidepressants:* CNS excitation and hypertension with MAOIs; Tricyclic or related antidepressant should not be started until 2 weeks after stopping MAOI; conversely, MAOI should not be started until at least 1 week after Tricyclic or related antidepressant has been stopped; plasma concentrations of some Tricyclics increased by SSRIs.
* *Antiepileptics:* antagonism (convulsive threshold lowered); plasma concentration of some Tricyclics reduced (reduced antidepressant effect).
* *Antihypertensives:* in general, hypotensive effect enhanced, but antagonism of effect of adrenergic neurone blockers and of Clonidine (and increased risk of hypertension on Clonidine withdrawal).
  Antimuscarinics: increased antimuscarinic side-effects.
* *Antipsychotics:* increased risks of ventricular arrhythmias- avoid concomitant use with Pimozide; increased plasma concentrations of Tricyclic antidepressants and increased antimuscarinic side-effects with Phenothiazines.
  Anxiolytics and Hypnotics: enhanced sedative effect.
* *Barbiturates:* see under Antiepileptics, above.
  Calcium-channel Blockers: Diltiazem and Verapamil increase plasma concentration Imipramine and possibly other Tricyclics.
  Diuretics: increased risk of postural hypotension.
* *Dopaminergics:* CNS toxicity reported with Selegiline.
  Muscle Relaxant: enhanced muscle relaxant effect.
  Nitrates: reduced effect of sublingual nitrates (owing to dry mouth).
  Oestrogens and Progestogens: oral contraceptives antagonize antidepressant effect (but side-effects may be increased due to increased plasma concentrations of Tricyclics).

* *Sympathomimetics:* hypertension and arrhythmias with adrenaline (but local anaesthetics with adrenaline appear to be safe); hypertension with Noradrenaline.
  Ulcer-healing Drugs: plasma concentrations of Amitriptyline, and probably other Tricyclics increased by Cimetidine (inhibition of metabolism).

Antidiabetics

Note : Includes Acarbose; Insulin; Metformin; Nateglinide; Repaglinide, Sulphonylureas.
ACE Inhibitors: possibly enhance hypoglycemic effect.
Alcohol: enhanced hypoglycemic effect; flushing with Chlorpropamide (in susceptible subjects); risk of lactic acidosis with Metformin.
Anabolic Steroids: possibly enhance hypoglycemic effect.

* *Analgesics:* possibly NSAIDs enhance effect of Sulphonylureas.
* *Antibacterials:* Chloramphenicol, Co-trimoxazole, and Sulphonamides enhance effect of Sulphonylureas; Ciprofloxacin possibly enhances effect of Glibenclamide; Neomycin possibly enhances hypoglycemic effect of Acarbose and increases severity of gastrointestinal effects; Clarithromycin enchances effect of repaglinide; Rifampicin reduces effect of Chlorpropamide, Tolbutamide and possibly other Sulphonylureas (accelerate metabolism); Rifampicin reduces plasma concentration of Repaglinide.
  Anticoagulants: possibly enhanced hypoglycemic effects of Sulphonylureas and changes to anticoagulant effects of Warfarin and other Coumarins.
  Antidepressants: MAOIs enhance hypoglycemic effect of Insulin, Metformin, Sulphonylureas and possibly other antidiabetics.
  Antifungals: Fluconazole and Miconazole increase plasma concentrations of Sulphonylureas- avoid concomitant use Miconazole with Gliclazide or Glipizide.
  Antihistamines: depressed thrombocyte count with concomitant use of Biguanides and Ketotifen.
  Antihypertensives: hypoglycemic effect antagonized by Diazoxide.
  Antipsychotics: Phenothiazines possibly antagonize hypoglycemic effect of Sulphonylureas.
  Beta-blockers: enhanced hypoglycemic effect and masking of warning signs of hypoglycemia such as tremor.
  Calcium-channel Blockers: Nifedipine may occasionally impair glucose tolerance
  Corticosteroids: antagonism of hypoglycemic effect.
  Diuretics: hypoglycemic effect antagonized by loop and Thaizide diuretics; Chlorpropamide increases risk of hyponatraemia with Thiazides in combination with potassium-sparing diuretics.
  Hormone Antagonists: manufacturer advises metabolism of oral Antidiabetics possibly accelerated by Aminoglutethimide.
  Lipid-regulating drugs: Fibrates may improve glucose tolerance and have an additive effect; increased risk of severe hypoglycaemia with Repaglinide and Gemfibrozil (avoid concomitant use)
  Lithium: may occasionally impair glucose tolerance.
  Oestrogens and Progestogens: oral contraceptives antagonize hypoglycemic effect.
  Orlistat: manufacturer advises avoid concomitant use with Acarbose or Metformin.
  Pancreatin: hypoglycemic effect of Acarbose reduced by Pancreatin.
  Testosterone: hypoglycemic effect possibly enhanced.
  Ulcer-healing Drugs: Cimetidine inhibits renal excretions of Metformin (increased plasma Metformin concentration); Cimetidine enhances hypoglycemic effect of Sulphonylureas.

Antiepileptics see Carbamazepine; Clonazepam; Ethosuximide; Gabapentin; Lamotrigine; Phenytoin; Valproate.
Antifungals see Amphotericin; Imidazole, Triazole, Griseofulvin, Terbinafine.

Antifungals, Imidazole and Triazole
Note : Imidazole antifungals include Clotrimazole, Ketoconazole and Miconazole; Triazoles include Fluconazole and Itraconazole. In general, interactions relate to multiple-dose treatment.

Analgesics: metabolism of Alfentanil inhibited by Ketoconazole (risk of prolonged or delayed respiratory depression); plasma concentration of Celecoxib increased by Fluconazole (halve Celecoxib dose).

Antacids: Antacids reduce absorption of Itraconazole and Ketoconazole.

* *Antibacterials:* Rifampicin accelerates metabolism of Fluconazole, Itraconazole and Ketoconazole (reduced plasma concentrations); plasma concentration of Rifampicin may be reduced by Ketoconazole; plasma concentration of Rifabutin increased by Fluconazole and possibly other Triazoles (risk of uveitis-reduce Rifabutin dose); plasma concentration of Ketoconazole may be reduced by Isoniazid.
* *Anticoagulants:* effect of Warfarin enhanced by Fluconazole, Itraconazole, Ketoconazole, and Miconazole (note: oral gel and vaginal formulations absorbed).
* *Antidiabetics:* plasma concentrations of Sulphonylureas increased by Fluconazole and Miconazole; Fluconazole, Itraconazole, and Ketoconazole possibly increase plasma concentration Repaglinide (manufacturer advises avoid concomitant use); avoid concomitant use of Miconazole with Glipizide.
* *Antiepileptics:* effect of Phenytoin enhanced by Fluconazole and Miconazole; plasma concentrations of Itraconazole and Ketoconazole reduced by Phenytoin.

Other Antifungals: Imidazoles and Triazoles possibly antagonize effect of Amphotericin.

* *Antihistamines:* manufacturer advises possibility of increased plasma-loratadine concentration with Ketoconazole; metabolism of Mizolastine inhibited by Ketoconazole and possibly other Imidazoles (avoid concomitant use).

Antimuscarinics: reduced absorption of Ketoconazole.

* *Antipsychotics:* risk of ventricular arrhythmias if Imidazoles or Traizoles given with Pimozide (avoid concomitant use).
* *Anxiolytics and Hypnotics:* plasma concentration of Midazolam increase by Itraconazole, Ketoconazole, and possibly Fluconazole (prolonged sedative effect).
* *Calcium-channel Blockers:* Itraconazole inhibits metabolism of dihydropyridines (increased plasma concentration).
* *Cardiac Glycosides:* plasma concentration of Digoxin increased by Itraconazole.
* *Ciclosporin:* metabolism inhibited by Itraconazole, Ketoconazole and possibly Fluconazole and Miconazole (increased plasma-Ciclosporin concentration).

Corticosteroids: Ketoconazole inhibits metabolism of Methylprednisolone and possibly other Corticosteroids; Itraconazole possibly inhibits metabolism of Methylprednisolone.

Cytotoxics: Itraconazole may inhibit metabolism of Vincristine (increased risk of neurotoxicity); in vitro studies suggest possible interaction between Ketoconazole

Diuretics: plasma concentration of Fluconazole increased by Hydrochlorothiazide

* *Lipid-regulating Drugs:* Itraconazole, Ketoconazole, and possibly other Imidazoles and Triazoles increase risk of myopathy with Simvastatin - avoid concomitant use of Itraconazole, Ketoconazole with Simvastatin, Itraconazole

and possibly other Imidazole and Triazoles may increase risk of myopathy with Atorvastatin; Itraconazole increases plasma concentration of Cervistatin.

Oestrogens and Progestogens: anecdotal reports of contraceptive failure with Fluconazole, Itraconazole, Ketoconazole and possibly others.

* *Theophylline:* plasma-theophylline concentration possibly increased by Fluconazole and possibly Ketoconazole.

Ulcer-healing Drugs: histamine H_2- antagonists reduce absorption of Itraconazole and Ketoconazole; proton-pump inhibitors reduce absorption of Ketoconazole and possibly Itraconazole; Sucralfate reduces absorption of Ketoconazole.

Antihistamines

Note : Sedative interactions apply to a lesser extent to the non-sedating antihistamines, and they do not appear to potentiate the effects of alcohol. Interactions do not generally apply to antihistamines used for topical action (including inhalation).

Alcohol: enhanced sedative effect.

* *Anti-arrhythmics:* increased risk of ventricular arrhythmias with Mizolastine (avoid concomitant use with Amiodarone, Disopyramide, Procainamide and Quinidine).
* *Antibacterials:* manufacturer advises possibility of increased plasma-loratadine concentration with Erythromycin.

Antidepressants: MAOIs and Tricyclics increase antimuscarinic and sedative effects.

* *Antidiabetics:* depressed thrombocyte count with concomitant use of Biguanides and Ketotifen.
* *Antifungals:* manufacturer advises possibility of increased plasma-loratadine concentration with Ketoconazole (avoid concomitant use).

Antimuscarinics: increased antimuscarinic side-effects.

Antivirals: plasma concentration of non-sedating antihistamines possibly increased by Ritonavir.

Anxiolytics and Hypnotics: enhanced sedative effect.

* *Beta-blockers:* Sotalol increases risk of ventricular arrhythmias with Mizolastine.

Betahistine: antagonism (theoretical).

Ulcer-healing Drugs: manufacturer advises possibility of increased plasma-loratadine concentration with Cimetidine.

Antihypertensives see individual drugs or groups.
Antimalarials see individual drugs.

Antimuscarinics

Note : Many drugs have antimuscarinic effects; concomitant use of two or more such drugs can increase side effects such as dry mouth, urine retention, and constipation; concomitant use can also lead to confusion in the elderly; interactions do not generally apply to antimuscarinics used by inhalation.

Alcohol: sedative effect of Hyoscine enhanced.

Analgesics: increased antimuscarinic effects.

Anti-arrhythmics: increased antimuscarinic effects with Disopyramide; Atropine delays absorption of Mexiletine.

Antidepressants: increased antimuscarinic side-effects with Tricyclics and MAOIs.

Antidepressants: increased antimuscarinic side-effects with Tricyclics and MAOIs.

Antifungals: reduced absorption of Ketoconazole.

Antihistamines: increased antimuscarinic side-effects of Phenothiazines (but reduced plasma concentrations).

Antipsychotics: increased antimuscarinic side-effects of Phenothiazines (but reduced plasma concentrations); increased side effects of Clozapine.
Dopaminergics: increased antimuscarinic side-effects with Amantadine; absorption of Levodopa possibly reduced.
Metoclopramide and Domperidone: antimuscarinics antagonize gastro-intestinal effects.
Nitrates: reduced effect of sublingual nitrates (failure to dissolve under tongue owing to dry mouth).
Parasympathomimetics: antagonism of effect.

Antiplatelet Drugs see Aspirin, Clopidogrel, Dipyridamole and Ticlopidine.

Antipsychotics
Note : Increased risk of toxicity with myelosuppressive drugs- Clozapine in particular should not be used concurrently with drugs associated with a substantial potential for causing agranulocytosis, such as Carbamazepine, Co-trimoxazole, Chloramphenicol, Sulphonamides, Pyrazolone analgesics such as Azapropazone, Penicillamine or Cytotoxics also avoid Clozapine with long-acting depot antipsychotics (have myelosuppressive potential).

ACE Inhibitors and Angiotensin-II antagonist: severe postural hypotension with Chlorpromazine and possibly other Phenothiazines.
Alcohol: enhanced sedative effect.
* *Anaesthetics:* enhanced hypotensive effect.
* *Analgesics:* enhanced sedative and hypotensive effect with opioid analgesics; severe drowsiness possible if Indomethacin given with Haloperidol; risk of ventricular arrhythmias if Levacetylmethadol given with Chlorpromazine, Haloperidol, Pimozide or Thioridazine (avoid concomitant use).
Antacids and Adsorbents: reduced absorption of Phenothiazines with antacids and possibly with Kaolin.
* *Anti-arrhythmics:* increased risk of ventricular arrhythmias with drugs that prolong QT interval – avoid concomitant use of Pimozide or Thioridazine with Amiodarone, Disopyramide, Procainamide or Quinidine (also avoid Haloperidol with Amiodarone).
* *Antibacterials:* risk of arrhythmias if Clarithromycin and possibly Erythromycin given with Pimozide (avoid concomitant use); Erythromycin possibly increases plasma concentration Clozapine (possible increased risk of convulsions); Rifampicin accelerates metabolism of Haloperidol (reduced plasma-Haloperidol concentration).
* *Antidepressants:* increased risk of arrhythmias with Tricyclic antidepressants- avoid concomitant use of Pimozide with Tricyclics; increased plasma concentrations and increased antimuscarinic effects notably on administration of Tricyclics with Phenothiazines; Fluoxetine possibly increase plasma concentration of Clozapine; Fluoxetine increases plasma concentration of Haloperidol; Clozapine possibly enhances central effects of MAOIs.
Antidiabetics: hypoglycemic effect of Sulphonylureas possibly antagonized by Phenothiazines.
* *Antiepileptics:* antagonism (convulsive threshold lowered); Carbamazepine accelerates metabolism of Clozapine and Haloperidol (reduced plasma concentrations); Phenytoin accelerates metabolism of Clozapine
* *Antifungals:* risk of ventricular arrhythmias if Imidazoles or Triazoles given with Pimozide (avoid concomitant use).

Antihypertensives: enhanced hypotensive effect; increased risk of extrapyramidal effects on administration Methyldopa.

* *Antimalarials:* avoid concomitant use of Pimozide with Mefloquine and Quinine.

Antimuscarinics: antimuscarinic side-effects of Phenothiazines increased (but reduced plasma concentrations).

* Antivirals: Protease inhibitors possibly increase plasma concentration of Pimozide (risk of ventricular arrhythmias- avoid concomitant use); Ritonavir increases plasma concentration of Clozapine (risk of toxicity – avoid concomitant use); Ritonavir possibly increases plasma concentration of other antipsychotics.
* *Anxiolytics and Hypnotics:* enhanced sedative effect; Diazepam increases plasma concentration of Zotepine; Buspirone increases plasma concentration of Haloperidol.
* *Beta-blockers:* Phenothiazines increase risk of ventricular arrhythmias with Sotalol; concomitant administration of Propranolol and Chlorpromazine may increase plasma concentration of both drugs.

Calcium-channel Blockers: enhanced hypotensive effect.

* *Desferrioxamine:* manufacturer advises avoid Prochlorperazine (also Levomepromazine on theoretical grounds).
* *Diuretics:* hypokalaemia increased risk of ventricular arrhythmias with Pimozide (avoid concomitant use).

Dopaminergics: antagonism of hypoprolactinaemic and ant antiparkinsonian effects of Bromocriptine; antagonism of effect of Apomorphine, Levodopa and Pergolide.

Lithium: increased risk of extrapyramidal effects and possibility of neurotoxicity with Clozapine, Haloperidol and Phenothiazines.

Metoclopramide and Domperidone: increased risk of extrapyramidal effects with Metoclopramide.

Sympathomimetics: antagonize pressor action.

Ulcer-healing Drugs: Cimetidine may enhance effects of Chlorpromazine, Clozapine, and possibly other antipsychotics.

Antivirals see Aciclovir; Saquinavir; Zalcitabine; Zidovudine.

Anxiolytics and Hypnotics

Alcohol: enhanced sedative effect.

Anaesthetics: enhanced sedative effect.

Analgesics: opioid analgesics enhance sedative effect.

* *Antibacterials:* erythromycin inhibits metabolism of Midazolam (increased plasma-Midazolam concentration, with profound sedation) and Zopiclone; Isoniazid inhibits metabolism of Diazepam; Rifampicin increased metabolism of diazepam and possibly other Benzodiazepines.

Anticoagulants: Chloral Hydrate may transiently enhance anticoagulant effect of Warfarin.

Antidepressants: enhanced sedative effect; manufacturer contra-indicates Buspirone with MAOIs.

Antiepileptics: metabolism of Clonazepam accelerated (reduced effect); plasma-Phenytoin concentrations increased or decreased by Diazepam and possibly other Benzodiazepines.

* *Antifungals:* Itraconazole, Ketoconazole, and possibly Fluconazole increase plasma concentration of Midazolam (prolonged sedative effect)

Antihistamines: enhanced sedative effect.

Antihypertensives: enhanced hypotensive effect; enhanced sedative effect with alpha-blockers.

Antipsychotics: enhanced sedative effects; Diazepam increases plasma concentration of Zotepine.
Calcium-channel Blockers: Diltiazem and Verapamil inhibit metabolism of Midazolam (increased plasma-midazolam concentration, with increased sedation)
Disulfiram: metabolism of Benzodiazepines inhibited, with enhanced sedative effect.
Dopaminergics: Benzodiazepines occasionally antagonize effect of Levodopa.
Muscle Relaxants: Tizanidine enhance sedative effect.
Ulcer-healing Drugs: Cimetidine inhibits metabolism of Benzodiazepines and Chlormethiazole and Zaleplon (increased plasma concentrations); Omeprazole inhibits metabolism of Diazepam (increased plasma concentration).

Artemether with Lumefantrine
Note: Grapefruit juice possibly inhibits metabolism Artemether and Lumefantrine (manufacturer advises avoid)

- *Antiarrhythmics*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use with Amiodarone, Disopyramide, Procainamide and Quinidine (risk of ventricular arrhythmias)
- *Antibacterials*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use with Macrolides and Quinolones.
- *Antidepressants*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use.
- *Antifungals*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use with imidazoles and triazoles
- *Other Antimalarials*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use.
- *Antipsychotics*: manufacturer of Artemether with Lumefantrine advises avoid concomitant use.
- Beta-blockers: manufacturer of Artemether with Lumefantrine advises avoid concomitant use with metoprolol.

Artesunate as of artemisinin
Use of artemisinin derivatives with drugs that prolong the QT interval should be avoided if possible; caution is advised when artemisinin derivatives are given with other antimalarials that have this propensity.Artemisinin has been reported to be a potent inhibitor of the cytochrome P450 isoenzyme CYP1A2, and might interact with drugs metabolised via this enzyme (such as theophylline). In contrast it is said to be an inducer of CYP2A6, although the clinical implications of this are unclear.

Aspirin

* *Other Analgesics:* avoid concomitant administration of other NSAIDs (increased side-effects).
Antacids and Adsorbents: excretion of aspirin increased in alkaline urine; Kaolin possibly reduces absorption.
* *Anticoagulants:* increased risk of bleeding due to Antiplatelet effect.
Antiepileptics: enhancement of effect of Phenytoin and Valproate.
Corticosteroids: increased risk of gastro-intestinal bleeding and ulceration; Corticosteroids reduce plasma-salicylate concentration.
* *Cytotoxics:* reduced excretion of Methotrexate (increased toxicity).
Diuretics: antagonism of diuretic effect of Spironolactone; reduced excretion of Acetazolamide (risk of toxicity).
Leukotriene Antagonists: Aspirin increases plasma concentration Zafirlukast.
Metoclopramide and Domperidone: Metoclopramide enhances effect of Aspirin (increased rate of absorption).
Uricosurics: effect of Probenecid and Sulphinpyrazone reduced.

Atenolol see Beta-blockers.
Atorvastatin see Statins.
Atracurium see Muscle Relaxants (non-depolarizing).
Atropine see Antimuscarinics.
Azathioprine

* *Allopurinol:* enhancement of effect with increased toxicity (reduce dose of Azathioprine when given with Allopurinol).
* *Antibacterials:* manufacturer reports interaction with Rifampicin (transplants possibly rejected).

Azithromycin see Erythromycin and other Macrolides.
Aztreonam

Caution is recommended in patients receiving aztreonam and oral anticoagulants because of the possibility of increased prothrombin time.

Barbiturates

Alcohol: enhanced sedative effect.
Anti-arrhythmics: metabolism of Disopyramide and Quinidine increased (reduced plasma concentrations).
Antibacterials: metabolism of Chloramphenicol, Doxycycline, and Metronidazole accelerated (reduced effect); Sulphonamides enhance effect of Thiopental

* *Anticoagulants:* metabolism of Warfarin accelerated (reduced anticoagulant effect).
* *Antidepressants:* antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of Mianserin and some Tricyclics accelerated (reduced plasma concentrations).
* *Antiepileptics:* concomitant administration Phenobarbital with other antiepileptics may enhance toxicity without a corresponding increase in antiepileptics effect; moreover interactions can complicate monitoring of treatment; interactions include enhanced effects, increased sedation, and reductions in plasma concentrations.

Antifungals: Phenobarbital reduces absorption of Griseofulvin (reduced effect).

* *Antipsychotics:* antagonism of anticonvulsant effect (convulsive threshold lowered); Phenobarbital accelerates metabolism of Haloperidol (reduced plasma concentration).
* *Antivirals:* plasma concentration of Saquinavir possibly reduced.
* *Calcium-channel Blockers:* effect of Felodipine and probably Nifedipine and other Dihydropyridines, Diltiazem, and Verapamil reduced.

Cardiac Glycosides: metabolism of Digitoxin only accelerated (reduced effect).

* *Ciclosporin:* metabolism of Ciclosporin accelerated (reduced effect).
* *Corticosteroids:* metabolism of Corticosteroids accelerated (reduced effect).
* *Folic Acid and Folinic Acid:* plasma concentration of Phenobarbital possibly reduced by Folic acid and Folinic acid.

Leukotriene Antagonists: plasma concentration of Montelukast reduced by Phenobarbital.

* *Oestrogens and Progestogens:* metabolism of oral contraceptives accelerated (reduced contraceptive effect).

Theophylline: metabolism of Theophylline accelerated (reduced effect).
Thyroxine: metabolism of Thyroxine accelerated (may increase Thyroxine requirements in hypothyroidism).
Vitamins: vitamin D requirements possibly increased.

Beclomethasone see Corticosteroids.
Bendrofluazide see Diuretics (thiazide).

Benzodiazepines see Anxiolytics and Hypnotics.
Benzoic acid There are no interaction messages
Benzoylperoxide There are no interaction messages
Benzylpenicillin see Penicillins.

Beta-Blockers
Note : Since systemic absorption may follow topical application of beta-blockers to the eye the possibility of interactions, in particular, with drugs such as Verapamil should be borne in mind.

ACE Inhibitors: enhanced hypotensive effect.
Alcohol: enhanced hypotensive effect.
* *Anaesthetics:* enhanced hypotensive effect; increased risk of Bupivacaine toxicity with Propranolol.
Analgesics: NSAIDs antagonize hypotensive effect.
* *Anti-arrhythmics:* increased risk of myocardial depression and bradycardia; with Amiodarone increased risk of bradycardia and AV block; increased risk of Lignocaine toxicity with Propranolol; Propafenone increases plasma concentration of Metoprolol and Propranolol; risk of ventricular arrhythmias associated with Sotalol increased by Amiodarone, Disopyramide, Procainamide, and Quinidine (avoid concomitant use).
* *Antibacterials:* increased risk of arrhythmias with Sotalol and Fluroquinolones (avoid concomitant use); Rifampicin accelerates metabolism of Propranolol (significantly reduced plasma concentration).
* *Antidepressants:* risk of ventricular arrhythmias associated with Sotalol increased by Tricyclics.
Antidiabetics: enhanced hypoglycemic effect and masking of warning signs of hypoglycemia such as tremor.
* *Antihypertensives:* enhanced hypotensive effect; increased risk of withdrawal hypertension with Clonidine (withdraw beta-blocker several days before slowly withdrawing Clonidine); increased risk of first-dose hypotensive effect with post-synaptic alpha-blockers such as Prazosin.
* *Antimalarials:* risk of ventricular arrhythmias associated with Sotalol increased by Phenothiazines; concomitant administration of Propranolol and Chlorpromazine may increase plasma concentration of both drugs.
Anxiolytics and Hypnotics: enhanced hypotensive effect.
* *Calcium-channel Blockers:* increased risk of bradycardia and AV block with Diltiazem; severe hypotension and heart failure occasionally with Nifedipine and possibly other Dihydropyridines; asystole, severe hypotension, and heart failure with Verapamil.
Cardiac Glycosides: increased AV block and bradycardia.
Corticosteroids: antagonism of hypotensive effect.
Diuretics: enhanced hypotensive effect; risk of ventricular arrhythmias associated with Sotalol increased by hypocalcaemia.
Ergotamine: increased peripheral vasoconstriction.
Muscle Relaxants: Propranolol enhances effect; possible enhanced hypotensive effect and bradycardia with Tizanidine.
Oestrogens and Progestogens: oestrogens and combined oral contraceptives antagonize hypotensive effect.
Parasympathomimetics: risk of arrhythmias possibly increased by Pilocarpine; Propranolol antagonizes effect of Neostigmine and Pyridostigmine.
* *Sympathomimetics:* severe hypertension with Adrenaline and Noradrenaline and possibly with Dobutamine (especially with non-selective beta-blockers).
Theophylline: beta-blockers should be avoided on pharmacological grounds (bronchospasm).

Thyroxine: metabolism of Propranolol accelerated (reduced effect).
Ulcer-healing Drugs: plasma concentrations of Labetalol, Metoprolol and Propranolol increased by Cimetidine; hypotensive effect antagonized by Carbenoxolone.

Betahistine
Antihistamines: antagonism (theoretical).

Betamethasone see Corticosteroids.
Betaxolol see Beta-blockers
Bile Acids
Antacids: may reduce absorption of bile acids.
* *Clofibrate group:* Clofibrate increases elimination of cholesterol in bile.
* *Oestrogens and Progestogens:* oestrogens increase elimination of cholesterol in bile.

Bismuth Chelate see Tripotassium Dicitratobismuthate.
Bisoprolol see beta blockers
Bisphosphonates
Analgesics: bioavailability of Tiludronic acid increased by Indomethacin.
Antacids: reduced absorption.
Antibacterials: increased risk of hypocalcaemia with Aminoglycosides.
Calcium salts: reduced absorption.
Iron: reduced absorption.
Bosentan
- Antibacterials: plasma concentration of bosentan reduced by rifampicin
- Antidiabetics: increased risk of hepatotoxicity when bosentan given with glibenclamide
- Antifungals: plasma concentration of bosentan possibly increased by fluconazole; plasma concentration of bosentan possibly increased by itraconazole
- Antivirals: bosentan possibly reduces plasma concentration of indinavir; plasma concentration of bosentan increased by lopinavir ritonavir (consider reducing of bosentan); bosentan possibly reduces plasma concentration of telaprevir, also concentration of bosentan possibly increased; avoidance of bosentan advised by manufacturer of tipranavir
- Ciclosporin: plasma concentration of bosentan increased by ciclosporin (also plasma concentration of iclosporin reduced
- Cytotoxics: bosentan possibly reduces plasma concentration of bosutinib
- Lipid-regulating Drugs: bosentan reduces plasma concentration of simvastatin
- Oestrogens: bosentan possibly causes contraceptive failure of hormonal contraceptives containing oestrogens (alternative contraception recommended)
- Progestogens: bosentan possibly causes Contraceptive failure of hormonal contraceptives containing progestogens (alternative contraception recommended)
- Sildenafil: bosentan reduces plasma concentration of sildenafil
- Tadalafil: bosentan reduces plasma concentration of tadalafil

Brinzolamide see diuretics (Carbonic anhydrase inhibitor)
Bromazepam see Anxiolytics and Hypnotics.
Bromocriptine
Alcohol: reduced tolerance to Bromocriptine.
Antibacterials: Erythromycin and possibly other Macrolides increase plasma concentration (increased risk of toxicity).
Antipsychotics: antagonism of hypoprolactinaemic and antiparkinsonian effects.

Metoclopramide and Domperidone: antagonize hypoprolactinaemic effect.

* *Sympathomimetics:* increased risk of toxicity with Bromocriptine and Phenylproponolamine.

Budesonide see Corticosteroids.
Bumetanide see Diuretics
Bupivacaine

Anti-arrhythmics: increased myocardial depression.
Beta-blockers: increased risk of Bupivacaine toxicity with Propranolol.

Butenafine there are no interaction messages
Butobarbitone see Barbiturates and Primidone.
Calcipotriol see vitamin D derivative
Calcium Salts

Antibacterials: reduced absorption of Ciprofloxacin and Tetracyclines.
Cardiac Glycosides: large intravenous doses of calcium can precipitate arrhythmias.
Diuretics: increased risk of hypocalcaemia with Thiazides.

Calcium-Channel Blockers
Note : Grapefruit juice increases plasma concentration of dihydropyridine calcium-channel blockers (except Amlodipine) and Verapamil; Dihydropyridine calcium-channel blockers include Amlodipine, Felodipine, Lacidipine, Nifedipine and Nimodipine.

ACE Inhibitors: enhanced hypotensive effect.

* *Anaesthetics:* Verapamil increases hypotensive effect of general anaesthetics and risk of AV delay; Isoflurane enhances hypotensive effect of Dihydropyridines
* *Anti-arrhythmics:* Amiodarone-induced risk of bradycardia, AV block, and myocardial depression increased by Diltiazem and Verapamil; plasma-concentration of Quinidine reduced by Nifedipine; increased risk of myocardial depression and asystole if Verapamil given with Disopyramide; with Verapamil raised plasma concentration Quinidine (extreme hypotension may occur).
* *Antibacterials:* Erythromycin possibly inhibits metabolism of Felodipine (increased plasma concentration); Rifampicin increases metabolism of Diltiazem, Nifedipine, Verapamil and possibly Nisoldipine (plasma concentrations significantly reduced).

Antidepressants: Diltiazem and Verapamil increase plasma concentration of Imipramine and possibly other Tricyclics.
Antidiabetics: Nifedipine may occasionally impair glucose tolerance.

* *Antiepileptics:* effect of Carbamazepine enhanced by Diltiazem and Verapamil; Diltiazem and Nifedipine increase plasma concentration of Phenytoin; effect of Felodipine and probably Nifedipine and other Dihydropyridines reduced by Carbamazepine, Phenobarbitone, Phenytoin; effect of Diltiazem and Verapamil reduced by Phenobarbital and Phenytoin.
* *Antifungals:* Itraconazole inhibits metabolism of Felodipine (increased plasma concentration).
* *Antihypertensives:* enhanced hypotensive effect, increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers such as Prazosin

Antimalarials: possible increased risk of bradycardia with some calcium-channel blockers and Mefloquine.
Antipsychotics: enhanced hypotensive effect.
Anxiolytics and Hypnotics: Diltiazem and Verapamil inhibit metabolism of Midazolam (increased plasma-midazolam concentration, with increased sedation)

* *Barbiturates:* see under Antiepileptics, above.

* *Beta-blockers:* increased risk of bradycardia and AV block with Diltiazem; occasionally severe hypotension and heart failure with Nifedipine and possibly other dihydropyridines; asystole, severe hypotension, and heart failure with Verapamil.
* *Other Calcium-channel Blockers:* clearance of Nifedipine reduced by Diltiazem (increased plasma Nifedipine concentration).
* *Cardiac Glycosides:* plasma concentration of Digoxin increased by Diltiazem, Verapamil and possibly Nifedipine; increased AV block and bradycardia with Verapamil.
* *Ciclosporin:* plasma-ciclosporin concentrations increased by Diltiazem and Verapamil; possibly increases plasma concentration of Nifedipine.
  Diuretics: enhanced hypotensive effect.
  Lithium: neurotoxicity may occur without increased plasma-lithium concentrations in patients given Diltiazem and Verapamil.
  Muscle Relaxants: Nifedipine and Verapamil enhance effect of non-depolarizing muscle relaxants, hypotension, myocardial depression, and hyperkalaemia with Verapamil and intravenous Dantrolene; risk of arrhythmias with Diltiazem and intravenous Dantrolene; enhanced hypotensive effect with Tizanidine.
* *Theophylline:* Diltiazem, Verapamil and possibly other calcium-channel blockers enhance effect (increased plasma-theophylline concentration).
  Ulcer-healing Drugs: Cimetidine inhibits metabolism of some calcium-channel blockers (increased plasma concentration).

Candesartan see ACE Inhibitors and Angiotensin-II Antagonists.
Capecitabine see Fluorouracil (prodrug of fluorouracil)
Capreomycin care should be taken when capreomycin is used with other drugs that have neuromuscular blocking activity. It should not be given with other drugs that are ototoxic or nephrotoxic.
Captopril see ACE Inhibitors.

Carbamazepine
Alcohol: CNS side-effects of Carbamazepine possibly enhanced.
* *Analgesics:* Dextropropoxyphene enhances effect of Carbamazepine; effect of Methadone and Tramadol decreased by Carbamazepine.
* *Antibacterials:* metabolism of Doxycycline accelerated (reduced effect); plasma-Carbamazepine concentration increased by Clarithromycin, Erythromycin and Isoniazid (also Isoniazid hepatotoxicity possibly increased).
* *Anticoagulants:* metabolism of Warfarin accelerated (reduced anticoagulant effect).
* *Antidepressants:* antagonism of anticonvulsant effect (convulsive threshold lowered); plasma concentration of Carbamazepine increased by Fluoxetine; metabolism of Mianserin and Tricyclics accelerated (reduced plasma concentrations); manufacturer advises avoid with MAOIs or within 2 weeks of MAOIs.
* *Other Antiepileptics:* concomitant administration of two or more antiepileptics may enhance toxicity without a corresponding increase in antiepileptic effect; moreover interactions between individual antiepileptics can complicate monitoring of treatment; interactions include enhanced effects, increased sedation, and reductions in plasma concentrations.
* *Antimalarials:* Chloroquine and Mefloquine antagonize anticonvulsant effect
* *Antipsychotics:* antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of Clozapine, Haloperidol and Olanzapine accelerated (reduced plasma concentrations).
* *Antivirals:* plasma concentration of Saquinavir possibly reduced.

* *Calcium-channel Blockers:* Diltiazem and Verapamil enhance effect of Carbamazepine; effect of Felodipine and probably Nifedipine and other Dihydropyridines reduced.
* *Corticosteroids:* metabolism accelerated (reduced plasma-ciclosporin concentration).
* *Diuretics:* increased risk of hyponatraemia; Acetazolamide increases plasma-Carbamazepine concentration.
* *Hormone Antagonists:* Danazol inhibits metabolism of Carbamazepine (enhanced effect).

Lithium: neurotoxicity may occur without increased plasma-lithium concentration.
Muscle Relaxants: effect of non-depolarizing muscle relaxants antagonized (recovery from neuromuscular blockade accelerated).
Oestrogens and Progestogens: Carbamazepine accelerates metabolism of oral contraceptives (reduced contraceptive effect).
Retinoids: plasma concentration possibly reduced by Isotretinoin.
Theophylline: metabolism of theophylline accelerated (reduced effect).
Thyroxine: metabolism accelerated (may increase Thyroxine requirements in hypothyroidism).

* *Ulcer-healing Drugs:* metabolism inhibited by Cimetidine (increased plasma-Carbamazepine concentration).

Vitamins: Carbamazepine possibly increases vitamin D requirements.

Carbonic Anhydrase Inhibitors see Diuretics.

Cardiac Glycosides

ACE Inhibitors: Captopril possibly increases plasma concentration Digoxin.
Analgesics: NSAIDs may exacerbate heart failure reduce GFR and increase plasma-cardiac glycoside concentrations.
Antacids and Adsorbents: Antacids and Kaolin possibly reduce absorption of Digoxin.

* *Anti-arrhythmics:* plasma concentration of Digoxin increased by Amiodarone, Propafenone, and Quinidine (halve maintenance dose of Digoxin).

Antibacterials: Erythromycin and possibly other Macrolides enhance effect of Digoxin.

* *Antifungals:* plasma concentration Digoxin increased by Itraconazole.
* *Antimalarials:* quinine (includes use of quinine for cramp), hydroxychloroquine and possibly Chloroquine raise plasma concentration of Digoxin; possible increased risk of bradycardia with Mefloquine.

Barbiturate: see under Antiepileptics, above.
Beta-blockers: increased AV block and bradycardia.

* *Calcium Salts:* large intravenous doses of calcium can precipitate arrhythmias.
* *Calcium-channel Blockers:* plasma concentration Digoxin increased by Diltiazem, Verapamil and possibly Nifedipine; increased AV block and bradycardia with Verapamil.

Corticosteroids: increased risk of hypokalaemia.

* *Diuretics:* increased toxicity if hypokalaemia occurs with Acetazolamide, loop diuretics, and Thiazides; effects of Digoxin enhanced by Canrenoate and Spironolactone.
* *Lipid-regulating Drugs:* plasma concentration of Digoxin possibly increased by Atorvastatin.
* *Muscle Relaxants:* arrhythmias with Suxamethonium.
* *Sulphasalazine:* absorption of Digoxin possibly reduced.
* *Ulcer-healing Drugs:* plasma concentration of Digoxin possibly increased by proton pump inhibitors; absorption possibly reduced by Sucralfate.

Carteolol see Beta-blockers
Carvedilol see Beta-blockers.
Cefaclor see Cephalosporins.
Cefazoline see Cephalosporins.
Cefdinir see Cephalosporins.

Absorption of cefdinir is decreased by antacids or iron supplements and doses should be separated by an interval of at least 2 hours. Probenecid reduces the renal excretion of cefdinir.

Cefditoren see Cephalosporins.

Absorption of cefditoren after oral doses is decreased by antacids or histamine H2-receptor antagonists. Probenecid reduces the renal excretion of cefditoren.

see Cephalosporins.
Cefetamet see Cephalosporins.
Cefixime see Cephalosporins.
Cefoperazone see Cephalosporins.

Unlike many other cephalosporins, the renal clearance of cefoperazone is not affected by probenecid.

Cefotaxime see Cephalosporins.
cefpirome Cephalosporins.

Probenecid reduces the renal clearance of cefpirome.

Cefpodoxime see Cephalosporins.
Ceftazidime see Cephalosporins.
Ceftibuten see Cephalosporins.
Ceftriaxone see Cephalosporins.
Cefuroxime see Cephalosporins.
Celecoxib see NSAIDs.
Cephalosporins

* *Anticoagulants:* anticoagulant effect of Warfarin enhanced by Cephamandole and possibly others.
  Diuretics: Loop diuretics may increase nephrotoxicity of Cephalosporines.
  Uricosurics: excretion of Cephalosporins reduced by Probenecid (increased plasma concentrations).

Cephalexin see Cephalosporins.
Cephradine see Cephalosporins.
Cetirizine see Antihistamines.

Chloramphenicol

Other Antibacterials: Rifampicin accelerates metabolism (reduced Chloramphenicol-plasma concentration).

* *Anticoagulants:* anticoagulant effect of Warfarin enhanced.
* *Antidiabetics:* effect of Sulphonylureas enhanced.
* *Antiepileptics:* metabolism accelerated by Phenobarbital (reduced Chloramphenicol-plasma concentration); increased plasma concentration of Phenytoin (risk of toxicity).
* *Barbiturates:* see under Antiepileptics, above.

Chloroquine and Hydroxychloroquine

* *Analgesics:* Chloroquine and Hydroxychloroquine increase risk of ventricular arrhythmia with Levacetylmethadol (avoid concomitant use).
  Antacids and Adsorbents: antacids reduce absorption of Chloroquine and Hydroxychloroquine; Kaolin educes absorption of Chloroquine.

* *Antiarrhythmics:* Chloroquine and Hydroxychloroquine increase risk of ventricular arrhythmias with Amiodarone (avoid concomitant use).
* *Antiepileptics:* antagonism of anticonvulsant effect of other Antimalarials; increased risk of convulsions with Mefloquine; increased risk of arrhythmias with Halofantrine.
* *Cardiac Glycosides:* Hydroxychloroquine and possibly Chloroquine increase plasma concentration of Digoxin.
* *Ciclosporin:* Chloroquine increases plasma-Ciclosporin concentration (increased risk of toxicity).

  Parasympathomimetics: Chloroquine and Hydroxychloroquine have potential to increase symptoms of myasthenia gravis and thus diminish effect of Neostigmine and Pyridostigmine.

  Ulcer-healing Drugs: Cimetidine inhibits metabolism of Chloroquine (increased plasma concentration).

Chlorpheniramine see Antihistamines.
Chlorpromazine see Antipsychotics.
Chlorpropamide see Antidiabetics (Sulphonylureas).
Cilazapril see ACE Inhibitors.
Cilostazol
Cilostazol is extensively metabolised to active and inactive metabolites by cytochrome P450 isoenzymes, mainly CYP3A4 and to a lesser extent CYP2C19. Therefore use with other drugs that inhibit or are metabolised by these hepatic enzymes may result in changes in plasma concentrations of either drug and, possibly, adverse effects.Cilostazol should therefore be used with caution in patients taking drugs metabolised by these enzymes; in patients taking enzyme inhibitors it should be avoided or a reduced dose should be considered.
The risk of bleeding is increased if cilostazol is given with clopidogrel and aspirin; its use, therefore, is contra-indicated in patients receiving two or more other antiplatelet or anticoagulant drugs.
Cimetidine see Histamine H_2-antagonists.
Cinnarizine see Antihistamines.
Ciprofloxacin see Quinolones.
Cisatracurium see Muscle Relaxants (non-depolarizing).

Cisplatin
* *Antibacterials:* Aminoglycosides increased risk of nephrotoxicity and possibly of ototoxicity.

  Diuretics: increased risk of nephrotoxicity and ototoxicity.

Citalopram see Antidepressants, SSRI
Clarithromycin see Erythromycin and other Macrolides.

Clindamycin

Muscle Relaxants: enhancement of effect of non-depolarizing muscle relaxants.
Parasympathomimetics: antagonism of effect of Neostigmine and Pyridostigmine.

Clobazam see Anxiolytics and Hypnotics.
Clofazimine
Some preliminary data have suggested that the anti-inflammatory action of clofazimine in Type 2 lepra reactions may be reduced by dapsone, although US licensed product information (Lamprene; Novartis, USA) states that these findings have not been confirmed; the antimycobacterial effect was not affected.

Elevated plasma and urine concentrations of clofazimine have been detected in patients receiving high doses of clofazimine with isoniazid, although skin concentrations were found to be lower.
For a report of the effect of clofazimine on rifampicin absorption.

Clomipramine see Antidepressants, Tricycles.
Clonidine

- ACE Inhibitors: enhanced hypotensive effect when clonidine given with ACE inhibitors;
- Adrenergic Neurone Blockers: enhanced hypotensive
- Alcohol: enhanced hypotensive effect
- Aldesleukin: enhanced hypotensive effect
- Alpha-blockers: enhanced hypotensive effect
- Anaesthetics, General: enhanced hypotensive effect
- Analgesics: hypotensive effect
- Angiotensin-II Receptor Antagonists: enhanced hypotensive effect
- Antidepressants: enhanced hypotensive effect when clonidine given with MAOIs; hypotensive effect of clonidine possibly antagonised by mirtazapine, tricyclics, also increased risk of hypertension on clonidine withdrawal
- Antipsychotics: enhanced hypotensive effect when clonidine given with phenothiazines
- Anxiolytics and Hypnotics: enhanced hypotensive effect when clonidine given with anxiolytics and hypnotics
- Beta-blockers: increased risk withdrawal hypertension when clonidine given with beta-blockers
- Calcium-channel Blockers: enhanced hypotensive effect
- Corticosteroids: hypotensive effect of clonidine antagonized by corticosteroids
- Cytotoxics: possible increased risk of bradycardia when clonidine given with crizotinib
- Diazoxide: enhanced hypotensive effect when clonidine given with diazoxide
- Diuretics: enhanced hypotensive effect when clonidine given with diuretics
- Dopaminergics: enhanced hypotensive effect when clonidine given with levodopa
- Histamine: avoidance of clonidine advised by manufacturer of histamine
- Methyldopa: enhanced hypotensive effect when clonidine given with methyldopa
- Moxisylyte: enhanced hypotensive effect when clonidine given with moxisylyte
- Moxonidine: enhanced hypotensive effect when clonidine given with moxonidine
- Muscle Relaxants: enhanced hypotensive effect when clonidine given with baclofen or tizanidine
- Nitrates: enhanced hypotensive effect when clonidine given with nitrates
- Oestrogens: hypotensive effect of clonidine antagonized by oestrogens
- Prostaglandins: enhanced hypotensive effect when clonidine given with alprostadil.
- Sympathomimetics: possible risk of hypertension when clonidine given with adrenaline (epinephrine) or noradrenaline (norepinephrine); serious adverse events reported with concomitant use of clonidine and methylphenidate (causality not established)
- Vasodilator Antihypertensives: enhanced hypotensive effect when clonidine given with hydralazine, minoxidil or sodium nitroprusside

Clonazepam (general sedative interactions as for Anxiolytics and Hypnotics).
Clopidogrel

Analgesics: increased risk of bleeding with NSAIDs (including aspirin)

- *Anticoagulants*: enhanced effect due to antiplatelet action of Clopidogrel; manufacturer advises avoid concomitant use of Warfarin.
- *Other Antiplatelet drugs*: increased risk of bleeding.

Clotrimazole see Antifungals, Imidazole and Triazole.
Clozapine see Antipsychotics.
Co-amoxiclav see Penicillins.
Codeine see Opioid Analgesics.
Cold and Cough Remedies see Antihistamines and Sympathomimetics.
Colestipol as for Colestyramine
Contraceptives, Oral
Note : Also covers Oestrogens taken alone; interactions unlikely with low dose hormone replacement therapy.

ACE Inhibitors: Oestrogens and combined oral contraceptives antagonize hypotensive effect.

* *Antibacterials:* Rifampicin accelerate metabolism of both combined and Progestogen-only oral contraceptives (reduced contraceptive effect); when broad-spectrum antibiotics such as Ampicillin and Tetracycline given with combined oral contraceptives possibility have reduced contraceptive effect (risk probably small).

* *Anticoagulants:* antagonism of anticoagulant effect of Nicoumalone, Phenindione, and Warfarin.

Antidepressants: antagonism of antidepressant effect has been reported, but side-effects of Tricyclics may be increased due to higher plasma concentration.

Antidiabetics: antagonism of hypoglycemic effect.

* *Antiepileptics:* Carbamazepine, Phenobarbital and Phenytoin accelerate metabolism (reduce effect of both combined and Progestogen-only contraceptives).

* *Antifungals:* Griseofulvin accelerates metabolism (reduced contraceptive effect) anecdotal reports of contraceptive failure with Fluconazole, Itraconazole, Ketoconazole and possibly others.

Antihypertensives: combined oral contraceptives antagonize hypotensive effect

* *Barbiturates:* see under Antiepileptics, above.

Beta-blockers: Oestrogens and combined oral contraceptives antagonize hypotensive effect.

* *Bile Acids:* Oestrogens increase elimination of cholesterol in bile.

* *Ciclosporin:* increased plasma Ciclosporin concentration.

Corticosteroids: oral contraceptives increase plasma concentration of Corticosteroids.

Diuretics: combined oral contraceptives antagonize diuretic effect.

* *Retinoids:* oral Tretinoin reduces efficacy of Progestogen-only and possibly combined oral contraceptives.

Tacrolimus: efficacy of oral contraceptives possibly decreased.

Theophylline: combined oral contraceptives delay excretion (increased plasma-theophylline concentration).

Ulcer-healing drugs: manufacturer advises Lansoprazole possibly accelerates metabolism.

Corticosteroids
Note : Do not generally apply to Corticosteroids used for topical action (including inhalalation).

Analgesics: increased risk of gastro-intestinal bleeding and ulceration with aspirin and NSAIDs. Corticosteroids reduce plasma-salicylate concentration.

* *Antibacterials:* Rifampicin accelerate metabolism of Corticosteroids (reduced effect); Erythromycin inhibits metabolism of Methylprednisolone and possibly other Corticosteroids.
  Antihypertensives: antagonism of hypoglycemic effect.
  Antivirals: plasma concentration of Saquinavir possibly reduced by Dexamethasone.
* *Barbiturates:* see under Antiepileptics, above.
* *Cardiac Glycosides:* increased toxicity if hypokalaemia occurs with Corticosteroids.
* *Ciclosporin:* plasma-Ciclosporin concentration increased by high-dose of Methylprednisolone (risk of convulsions); Ciclosporin increases plasma concentration of Prednisolone.
  Diuretics: antagonism of diuretic effect; Acetazolamide, loop diuretics, and Thiazides increase risk of hypokalaemia.
  Hormone Antagonists: Aminoglutethimide accelerates metabolism of Corticosteroids (reduced effect).
  Oestrogens and Progestogens: oral contraceptives increase plasma concentration Corticosteroids.
  Somatropin: growth promoting effect may be inhibited.
  Sympathomimetics: increased risk of hypokalaemia if high does of Corticosteroids given with high doses of Ritodrine, Salbutamol, Salmeterol and Terbutaline; Ephedrine accelerates metabolism of Dexamethasone.
  Ulcer-healing Drugs: Carbenoxolone increases risk of hypocalcaemia.

Co-Trimoxazole and Sulphonamides

Note : For interactions with co-trimoxazole see also under Trimethoprim.

Anesthetics: effect of Thiopental enhanced.
* *Anti-arrhythmics:* Co-trimoxazole increases risk of ventricular arrhythmias with Amiodarone (avoid concomitant use).
* *Anticoagulants:* effect of Warfarin enhanced.
* *Antidiabetics:* effect of Sulphonylureas enhanced.
* *Antiepileptics:* antifolate effect and plasma concentration of Phenytoin increased by Co-trimoxazole and possibly other Sulphonamides.
* *Antimalarials:* increased risk of antifolate effect with Pyrimethamine (includes Fansidar and Maloprim).
* *Ciclosporin:* increased risk of nephrotoxicity; plasma Ciclosporin concentration possibly reduced by Sulphadiazine.
* *Cytotoxics:* antifolate effect of Methotrexate increased by Co-trimoxazole; risk of Methotrexate toxicity increased by Sulphonamides.

Cyclophosphamide

* *Anticoagulants:* possibly enhances effect of Warfarin.
* *Muscle Relaxants:* Cyclophosphamide enhances effect of Suxamethonium.

Cycloserine

Patients receiving cycloserine and taking alcohol are at increased risk of convulsions; for reference to increased blood-alcohol concentrations in patients receiving cycloserine. Neurotoxic effects may be potentiated by use of cycloserine with ethionamide, and concurrent use ofcycloserine and isoniazid may result in increased CNS toxicity, such as dizziness and drowsiness.

Cyclosporin

Note : Grapefruit juice increases plasma-Ciclosporin concentration (risk of toxicity).

* *ACE Inhibitors:* increased risk of hyperkalaemia.
  Allopurinol: possibly increases plasma-ciclosporin concentration (risk of toxicity).

* *Analgesics:* increased risk of nephrotoxicity with NSAIDs; Ciclosporin increases plasma concentration of Diclofenac (halve diclofenac dose).
* *Anti-arrhythmics:* Amiodarone and Propafenon possibly increase plasma-Ciclosporin concentration.
* *Antibacterials:* Aminoglycosides, Co-trimoxazole (and Trimethoprim alone), and Quinolones increase risk of nephrotoxicity; Doxycycline possibly increases plasma-Ciclosporin concentration; Erythromycin, Clarithromycin and possibly other Macrolides increase plasma-Ciclosporin concentration; Erythromycin; Clarithromycin and possibly other Macrolides increase plasma-Ciclosporin concentration; Rifampicin, intravenous Trimethoprim (and possibly Sulphadiazine) reduce plasma-ciclosporin concentration.
* *Antiepileptics:* Carbamazepine, Phenobarbitone, Phenytoin, and Primidone accelerate metabolism (reduced plasma-Ciclosporin concentration).
* *Antifungals:* Griseofulvin possibly reduces plasma-Ciclosporin concentration; Itraconazole, Ketoconazole, and possibly Fluconazole and Miconazole inhibit metabolism (increased plasma-Ciclosporin concentration).
* *Antimalarials:* Chloroquine increases plasma-Ciclosporin concentration (risk of toxicity).

  Barbiturates: see under Antiepileptics, above.
* *Calcium-channel Blockers:* Diltiazem and Verapamil increase plasma-Ciclosporin concentration; Ciclosporin possibly increases plasma concentration of Nifedipine.
* *Corticosteroids:* high-dose Methylprednisolone increases plasma-Ciclosporin concentration (risk of convulsions); Ciclosporin increases plasma concentration Prednisolone.
* *Cytotoxics:* increased risk of neurotoxicity with Doxorubicin, increased toxicity with Methotrexate; in vitro studies suggest possible interaction with Docetaxel-consult product literature.
* *Diuretics:* potassium-sparing diuretics increase risk of hyperkalaemia.
* *Hormone Antagonists:* Danazol inhibits metabolism (increased plasma-Ciclosporin concentration).
* *Lipid-regulating Drugs:* increased risk of myopathy with statins.
* *Oestrogens and Progestogens:* Progestogens inhibit metabolism (increased plasma-Ciclosporin concentration).
* *Potassium Salts:* increased risk of hyperkalaemia.
* *Tacrolimus:* plasma-Ciclosporin half-life prolonged (increased risk of toxicity).
* *Ulcer-healing Drugs:* Cimetidine possible increased plasma-Ciclosporin concentration.

Cytarabine
Flucytosine: plasma-flucytosine concentration possibly reduced.

Cytotoxics see under individual drugs.
Dalteparin see Heparin.

Danazol
* *Anticoagulants:* effect of Warfarin enhanced (inhibits metabolism).
* *Antiepileptics:* inhibits metabolism of Carbamazepine (increased plasma-Carbamazepine concentration).
* *Ciclosporin:* inhibits metabolism (increased plasma-ciclosporin concentration).

Dantrolene see Muscle Relaxants.

Dapsone
Antibacterials: plasma concentration reduced by Rifampicin.

Probenecid: Dapsone excretion reduced (increased risk of side-effects).

Desferrioxamine

Antipsychotics: manufacturer advises avoid Prochlorperazine (also Methotrimeprazine of theoretical grounds).

Desloratadine see Antihistamines

Desmopressin

Analgesics: effect of Desmopressin potentiated by Indomethacin.

Desogestrel see Progestogens.

Dexamethasone see Corticosteroids.

Diazepam see Anxiolytics and Hypnotics.

Diclofenac see NSAIDs.

Diethylcarbamazine

* Ammonium chloride: Making the urine acidic with ammonium chloride appears to markedly increase the excretion of diethylcarbamazine.

***** Sodium bicarbonate: Making the urine alkaline with sodium bicarbonate appears to markedly increase the retention of diethylcarbamazine.

Digoxin see Cardiac Glycosides.

Diltiazem see Calcium-channel Blockers.

Dimenhydrinate see Antihistamines.

Diphenydramine see Antihistamines.

Dipivefrine see Sympathomimetics (as for adrenaline).

Dipyridamole

Antacids: patient information leaflet advises avoidance of antacids.

***** *Anti-arrhythmics:* effect of adenosine enhanced and extended (important risk of toxicity).

***** *Anticoagulants:* enhanced effect due to antiplatelet action of Dipyridamole.

Cytotoxics: efficacy of Fludarabine possibly reduced.

Disopyramide

***** *Other Anti-arrhythmics:* Amiodarone increases risk of ventricular arrhythmias (avoid concomitant use); increased myocardial depression with any antiarrhythmic.

***** *Antibacterials:* plasma concentration of Disopyramide reduced by Rifampicin but increased by erythromycin and possibly Clarithromycin (risk of toxicity).

***** *Antidepressants:* increased risk of ventricular arrhythmics with Tricyclics.

Antiepileptics: plasma concentration of Disopyramide reduced by Phenobarbital, Phenytoin.

Antihistamines: increased risk of ventricular arrhythmias with Mizolastine (avoid concomitant use).

***** *Antimuscarinics:* increased antimuscarinic side-effects.

***** *Antipsychotics:* increased risk of ventricular arrhythmias –avoid concomitant use with Pimozide or Thioridazine.

Barbiturates: see under Antiepileptics, above.

***** *Beta-blockers:* increased myocardial depression; increased risk of ventricular arrhythmias associated with Sotalol (avoid concomitant use).

***** *Calcium-channel blockers:* increased myocardial depression with Verapamil.

***** *Diuretics:* cardiac toxicity of Disopyramide increased if hypokalaemia occurs with Acetazolamide, Loop diuretics, and Thiazides.

***** *Nitrates:* reduced effect of sublingual nitrates (failure to dissolve under tongue owing to dry mouth).

Diuretics

* *ACE Inhibitors:* enhanced hypotensive effect (can be extreme) risk of severe hyperkalaemia with potassium-risk of severe hyperkalaemia with potassium-sparing diuretics.
* *Analgesics:* diuretics increase risk of nephrotoxicity of NSAIDs; NSAIDs notably Indomethacin and Ketorolac antagonize diuretic effect; Indomethacin and possibly other NSAIDs increase risk of hyperkalaemia with potassium-sparing diuretics; occasional reports of decreased renal function when Indomethacin given with Triamterene; diuretic effect of Spironolactone antagonized by Aspirin; Aspirin reduces excretion of Acetazolamide (risk of toxicity).
* *Anti-arrhythmics:* cardiac toxicity of Amiodarone, Disopyramide and Quinidine increased if hypokalaemia occurs; action of Lignocaine and Mexiletine antagonized by hypokalaemia; Acetazolamide reduces excretion of Quinidine (increased plasma concentration).
* *Antibacterials:* loop diuretics increase ototoxicity of Aminoglycosides and Vancomycin.
* *Antidepressants:* increased risk of postural hypotension with Tricyclics.
  Antidiabetics: hypoglycemic effect antagonized by Loop and Thiazide diuretics; Chlorpropamide increases risk of hyponatraemia associated with Thiazides in combination with potassium-sparing diuretics.
* *Antiepileptics:* increased risk of hyponatraemia with Carbamazepine; Acetazolamide increases plasma concentration of Carbamazepine; carbonic anhydrase inhibitors possibly increase risk of osteomalacia with antiepileptics such as Phenytoin.
  Antifungals: Hydrochlorothiazide increases plasma concentration Fluconazole.
* *Antihypertensives:* enhance hypotensive effect; increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers such as Prazosin.
* *Antimalarials:* electrolyte disturbances increase risk of ventricular arrhythmias with Halofantrine.
* *Antipsychotics:* in hypokalaemia increased risk of ventricular arrhythmias with Pimozide (avoid concomitant use).
  Beta-blockers: enhanced hypotensive effect: in hypokalaemia increased risk of ventricular arrhythmias with Sotalol.
  Calcium Salts: increased risk of hypercalcaemia with Thiazides.
  Calcium-channel Blockers: enhanced hypotensive effect.
* *Cardiac Glycosides:* increased toxicity if hypokalaemia occurs with Acetazolamide, Loop diuretics, and Thiazides; effect enhanced by Canrenoate and Spironolactone.
  Corticosteroids: increased risk of hypokalaemia with Acetazolamide, Loop diuretics, and Thiazides, antagonism of diuretic effect.
* *Ciclosporin:* increased risk of hyperkalaemia with potassium-sparing diuretics.
  Cytotoxics: increased risk of nephrotoxicity and ototoxicity with Cisplatin.
  Other Diuretics: increased risk of hypokalaemia if Acetazolamide, Loop diuretics or Thiazides given together; profound diuresis possible if Metolazone given with Frusemide.
  Hormone Antagonists: increased risk of hyponatraemia with Aminoglutethimide.
* *Lithium:* Lithium excretion reduced by Loop diuretics, potassium-sparing diuretics and Thiazides (increased plasma-lithium concentration and risk of toxicity-loop diuretics safer than Thiazides); lithium excretion increased by Acetazolamide.
* *Oestrogens and Progestogens:* Oestrogens and combined oral contraceptive antagonize diuretic effect.
* *Potassium Salts:* hyperkalaemia with potassium-sparing diuretics.
  Sympathomimetics: increased risk of hypokalaemia if Acetazolamide, Loop diuretics, and Thiazides given with high does of Ritodrine, Salbutamol, Salmeterol and Terbutaline.

Ulcer-healing Drugs: increased risk of hypokalaemia if Acetazolamide, Loop diuretics, and Thiazides given with Carbenoxolone; Carbenoxolone antagonizes diuretic effect; Amiloride and Spironolactone antagonize ulcer-healing effect of Carbenoxolone.
Vitamins: increased risk of hypercalcaemia if Thiazides given with vitamin D.

Dobutamine see Sympathomimetics.

Docetaxel Trihydrate
Antibacterials: in-vitro studies suggest possible interaction with erythromycin-consult product literature.
Antifungals: in-vitro studies suggest possible interaction with Ketoconazole-consult product literature.
Ciclosporin: in-vitro studies suggest possible interaction with Ciclosporin.

Domperidone
Analgesics: opioid analgesics antagonize effect on gastro-intestinal activity; absorption of Paracetamol accelerated (enhanced effect).
Antimuscarinics: antagonism of effect on gastrointestinal activity.
Dopaminergics: possible antagonism of hypoprolactinaemic effect of Bromocriptine.
Dopamine see sympathomimetics
Dopaminergics see Bromocriptine and Levodopa.
Doxazosin see Alpha blockers (post-synaptic).
Doxorubicin
Note : Antivirals may inhibit effect of Stavudine.
***** *Ciclosporin:* increased risk of neurotoxicity.

Doxycycline see Tetracycline.
Econazole
Econazole is a known inhibitor of CYP3A4/2C9. Due to the limited systemic availability clinically relevant interactions are unlikely to occur but have been reported with oral anticoagulants. In patients taking oral anticoagulants, such as warfarin or acenocoumarol, caution should be exercised and the anticoagulant effect should be monitored more frequently.
Adjustment of the oral anticoagulant dosage may be necessary during and after the treatment with econazole.
Ecothiophate see Parasympathomimetics.
Efavirenz
Efavirenz is metabolised mainly by cytochrome P450 isoenzymes including CYP3A4. Consequently, it may compete with other drugs metabolised by this system, potentially resulting in mutually increased plasma concentrations and toxicity. Enzyme inducers may decrease plasma concentrations of efavirenz; efavirenz itself acts as an enzyme inducer and can reduce plasma concentrations of other drugs. Inhibition of some P450 isoenzymes has also been found in vitro.
Efavirenz is contra-indicated with drugs that are highly dependent on CYP3A4 for clearance and for which elevated plasma concentrations are associated with serious or life-threatening events. These drugs include antihistamines (astemizole and terfenadine), calcium-channel blockers (bepridil), ergot derivatives (dihydroergotamine, ergometrine, ergotamine, methylergometrine), gastrointestinal prokinetics (cisapride), antipsychotics (pimozide), and sedatives and hypnotics (midazolam and triazolam). St John's wort decreases the concentration of efavirenz; use with the antiretroviral is not recommended due to the possible loss of its activity and development of resistance.
Enalapril see ACE Inhibitors.

Fnfuvirtide no clinical data is available
Enoxaparin see Heparin.
Entacapone
Antidepressants: manufacturer advises avoid concomitant use of MAOIs, Tricyclics or Maprotiline.
Antihypertensives: effect of Methyldopa possibly enhanced.
Iron: absorption of Entacapone reduced.
Sympathomimetics: effect of Adrenaline, Dobutamine, Dopamine, Isoprenaline and Noradrenaline possibly enhanced.
Entecavir

Ephedrine see Sympathomimetics.
Caution should be exercised when entecavir is given with other drugs eliminated by active tubular secretion as competition for the elimination pathway may increase the serum concentrations of either drug.
Eplerenone see Diuretics
Epoetin Beta
ACE Inhibitors and Angiotensin-II Antagonists: antagonism of hypotensive effect; increased risk of hyperkalaemia.
Eptifibatide
*Warfarin and dipyridamole: Eptifibatide did not appear to increase the risk of major and minor bleeding associated with concomitant use of warfarin and dipyridamole. Eptifibatide -treated patients who had a prothrombin time (PT) > 14.5 seconds and received warfarin concomitantly did not appear to be at an increased risk of bleeding.
*Eptifibatide and thrombolytic agents: Data are limited on the use of eptifibatide in patients receiving thrombolytic agents. There was no consistent evidence that eptifibatide increased the risk of major or minor bleeding associated with tissue plasminogen activator in either a PCI or an acute myocardial infarction study; Eptifibatide appeared to increase the risk of bleeding when administered with streptokinase in an acute myocardial infarction study. The combination of reduced dose tenecteplase and eptifibatide compared to placebo and eptifibatide significantly increased the risk of both major and minor bleeding when administered concomitantly in an acute ST-elevation myocardial infarction study.
In an acute myocardial infarction study involving 181 patients, eptifibatide (in regimens up to a bolus injection of 180 microgram/kg, followed by an infusion up to 2 microgram/kg/min for up to 72 hours) was administered concomitantly with streptokinase (1.5 million units over 60 minutes). At the highest infusion rates (1.3 microgram/kg/min and 2.0 microgram/kg/min) studied, eptifibatide was associated with an increased incidence of bleeding and transfusions compared to the incidence seen when streptokinase was given alone.

Ergometrine see Ergotamine and Ergometrine
Ergotamine and Ergometrine
* Anaesthetics: Halothane reduces effect of ergometrine on the parturient uterus
* *Antibacterials:* increased risk of ergotism with Azithromycin, Clarithromycin and Erythromycin – avoid concomitant use; increased risk of ergotism with Tetracyclines.
* *Antivirals:* risk of ergotism with Nelfinavir and Ritonavir-avoid concomitant use
Beta-blockers: increased peripheral vasoconstriction.
Ertapenem
Probenecid inhibits the renal excretion of ertapenemthereby increasing its plasma concentrations and prolonging its elimination half-life.
Erythromycin and Other Macrolides
Note : Interactions do not apply to small amounts used topically.

Antacids: antacids reduce absorption of Azithromycin.

* *Anti-arrhythmics:* plasma concentration of Disopyramide increased by erythromycin and possibly Clarithromycin (risk of toxicity);erythromycin (parenteral) increases risk of ventricular arrhythmias with Amiodarone (avoid concomitant use).
* *Other Antibacterials:* Clarithromycin and possibly other Macrolides increase plasma concentration of Rifabutin (risk of uveitis-reduce Rifabutin dose).
* *Anticoagulants:* effect of Warfarin enhanced by Erythromycin and possibly enhanced by Clarithromycin and some other Macrolides.

Antidiabetics: Erythromycin possibly increase plasma concentration of Repaglinide (manufacturer advises avoid concomitant use).

* *Antihistamines:* manufacturer advises possibility of increased plasma-loratadine concentration with erythromycin and possibly other Macrolides (avoid concomitant use).
* *Antipsychotics:* risk of arrhythmias if Clarithromycin and possibly erythromycin given with Pimozide (avoid concomitant use); Erythromycin possibly increases plasma concentration Clozapine (possible increased risk of convulsions).
* *Antivirals:* Clarithromycin tablets reduce absorption of Zidovudine; Ritonavir possibly increases plasma concentration Macrolides.
* *Anxiolytics and Hypnotics:* Erythromycin inhibits metabolism of Midazolam (increased plasma-Midazolam concentration, with profound sedation) and Zopiclone.

Calcium-channel Blockers: erythromycin possibly inhibits metabolism of Felodipine (increased plasma concentration).

Cardiac Glycosides: effect of Digoxin enhanced by Erythromycin and possibly enhanced by other Macrolides.

Corticosteroids: Erythromycin inhibits metabolism of Methylprednisolone and possibly other Corticosteroids.

* *Ciclosporin:* Erythromycin, Clarithromycin and possibly other Macrolides inhibit metabolism (increased plasma-ciclosporin concentration).

Cytotoxics: in-vitro studies suggest possible interaction between Erythromycin and Docetaxel- consult product literature.

Dopaminergics: plasma concentration of Bromocriptine increased by Erythromycin and possibly other Macrolides.

* *Ergotamine:* ergotism reported.

Leukotriene Antagonists: erythromycin reduces plasma concentration of Zafirlukast.

Lipid-regulating Drugs: Clarithromycin and erythromycin increase risk of myopathy with Simvastatin.

* *Tacrolimus:* Clarithromycin and Erythromycin increase plasma-tacrolimus concentration.
* *Theophylline:* Clarithromycin and Erythromycin inhibit metabolism (increased plasma-Theophylline concentration (if Erythromycin given by mouth also decreased plasma-erythromycin concentration).

Ulcer-healing Drugs: Cimetidine increases plasma-erythromycin concentration (increased risk of toxicity, including deafness).

Erythropoietin see Epoetin.
Escitalopram see Antidepressants, SSRI.
Esomeprazole see Proton pump Inhibitors.
Estradiol see Contraceptives, Oral
Ethacrynic Acid see Diuretics (loop).
Ethinyloestradiol see Contraceptives, Oral.
Ethambutol none

Ethionamide

The adverse effects of other antimycobacterials may be increased when ethionamide is used see Effects on the Liver, and under Cycloserine, Interactions.

Etidronate Disodium see Bisphosphonates.

Ezetimibe

- Anticoagulants: ezetimibe possibly enhances Anticoagulant effect of coumarins
- Ciclosporin: plasma concentration of both drugs may increase when ezetimibe given with ciclosporin
- Lipid-regulating Drugs: increased risk of cholelithiasis and gallbladder disease when ezetimibe given with fibrates - discontinue if suspected

Famotidine see Histamine H_2-antagonists.

Felodipine see Calcium-channel Blockers.

Fenofibrate see Fibrates.

Fentanyl see Opioid Analgesics.

Ferrous Salts see Iron.

Fexofenadine See Antihistamines

Fibrates

* *Anticoagulants:* enhancement of effect of Nicoumalone, Phenindione, and Warfarin.
  Antidiabetics: may improve glucose tolerance and have additive effect; increased risk of severe hypoglycaemia with gemfibrozil (avoid concomitant use)
* *Cyclosporin:* possible increased risk of renal impairment with fenofibrate.
* *Other Lipid-regulating Drugs:* increased risk of myopathy with statins (preferably avoid concomitant use of gemfibrozil with statins)

Filgrastim

Note : Use not recommended in period form 24 hours before to 24 hours after chemotherapy - for further details consult product literature.

Cytotoxics: possible exacerbation of neutropenia with Fluorouracil.

Finasteride

Note: No clinically important interactions reported.

Flucloxacillin see Penicillins.

Fluconazole see Antifungals, Imidazole and Triazole.

Flucytosine

Flucytosine is commonly used with amphotericin B. Amphotericin B can cause a deterioration in renal function, which can result in raised flucytosine blood concentrations and increased toxicity. However, the two drugs are generally regarded as having synergistic antifungal activity. Cytarabine has been claimed to reduce blood concentrations of flucytosine and to antagonise its antifungal activity, although the evidence is limited.

Fluorouracil

Antibacterials: Metronidazole inhibits metabolism (increased toxicity

Filgrastim: possible exacerbation of neutropenia.

Ulcer-healing Drugs: Cimetidine inhibits metabolism (increased plasma-fluorouracil concentration).

Fluoxetine see Antidepressants, SSRI.

Flupenthixol see Antipsychotics.

Fluphenazine see Antipsychotics.

Flurazepam see Anxiolytics and Hypnotics.

Flutamide

* *Anticoagulants:* effect of Warfarin enhanced.

Fluticasone see Corticosteroids.
Fluvastatin see Statins.
Folic Acid and Folinic Acid
* *Antiepileptics:* plasma concentrations of Phenobarbital and Phenytoin possibly reduced.

Formoterol See Sympathomimetics, $Beta_2$
Fosinopril see ACE inhibitors.
Frusemide see Diuretics, Loop.
Gabapentin
- *Antacids:* reduced Gabapentin absorption.
- *Antidepressants:* antagonism of anticonvulsive effect (convulsive threshold lowered)

  Other Antiepileptics: none demonstrated with Carbamazepine, Phenobarbital, Phenytoin, or Valproate.

  Antimalarials: Mefloquine antagonises anticonvulsant effect; Chloroquine occasionally reduces convulsive threshold.

Gallamine see Muscle Relaxant (non-depolarizing).
Gemfibrozil see Fibrates.
Gemifloxacin as for Ciprofloxacin
Gentamicin see Aminoglycosides.
Gestrinone

Antibacterials: Rifampicin accelerates metabolism (reduced plasma concentration)

Antiepieptics: Carbamazepine, Phenobarbital, and Phenytoin accelarate metabolism (reduced plasma concentration)

Glibenclamide see Antidiabetics (Sulphonylureas).
Gliclazide see Antidiabetics (sulphonylurea).
Glimepride see Antidiabetics (sulphonylurea).
Glipizide see Antidiabetics (sulphonylurea).
Glyceryl Trinitrate
Note : General hypotensive interactions as for Hydralazine.

Anti-arrhythmics: Disopyramide may reduce effect of sublingual nitrates (owning to dry mouth).

* *Anticoagulants:* excretion of heparin increase by Glyceryl Trinitrate infusion (reduced anticoagulant effect).

Antidepressants: Tricyclics may reduce effect of sublingual nitrates (owing to dry mouth).

Antimuscarinics: Antimuscarinics such as Atropine and Propantheline may reduce effect of sublingual nitrates (owing to dry mouth).

Griseofulvin
* *Anticoagulants:* metabolism of Nicoumalone and Warfarin accelerated (reduced anticoagulant effect).

Antiepileptics: absorption reduced by Phenobarbital (reduced effect).

Barbiturates: see under Antiepileptics above.

Ciclosporin: plasma-ciclosporin concentration possibly reduced.

* *Oestrogens and Progestogens:* metabolism of oral contraceptives accelerated (reduced contraceptive effect.

Halofantrine
* *Anti-arrhythmics:* increased risk of ventricular arrhythmias with drugs that prolong QT interval (including Amiodarone, Disopyramide, Flecainide, Procainamide and Quinidine).
* *Antidepressants:* increased risk of ventricular arrhythmias with Tricycles.

* *Other Antimalarials:* increased risk of arrhythmias with Chloroquine, Mefloquine and Quinine (important: see also advice under Halofantrine).
* *Antipsychotics:* increased risk of ventricular arrhythmias with Phenothiazines.
* *Beta-blockers:* increased risk of ventricular arrhythmias with Sotalol.
* *Diuretics:* increased risk of ventricular arrhythmias if electrolyte disturbances occur.

Haloperidol see Antipsychotics.
Halothane see Anaesthetics, General (volatile liquid).

Heparin

ACE Inhibitors and Angiotensin–II Antagonists: Increased risk of hyperkalaemia

* *Analgesics:* aspirin enhances anticoagulant effect; increased risk of hemorrhage with parenteral Diclofenac and Ketorolac (avoid concomitant use, including low-dose Heparin).

Antiplatelet Drugs: Aspirin, Dipyridamole and possibly Clopidogrel enhance anticoagulant effect.

* *Nitrates:* Glyceryl Trinitrate infusion increases excretion (reduced anticoagulant effect).

Histamine H_1-Antagonists see Antihistamines.

Histamine H_2-Antagonists

Analgesics: Cimetidine inhibits metabolism of opioid analgesics notably Pethidine (increased plasma concentrations) Cimetidine possibly increases plasma concentration of Azapropozone.

Anthelmintics: Cimetidine possibly inhibits metabolism of Mebendazole (increased plasma concentration).

* *Anti-arrhythmics:* Cimetidine increases plasma concentrations of Amiodarone, Flecainide, Lignocaine, Procainamide, Propafenone, Quinidine, and possibly Moracizine.

Antibacterials: Cimetidine increases plasma-erythromycin concentration (increased risk of toxicity, including deafness); Rifampicin accelerates metabolism of Cimetidine (reduced plasma-cimetidine concentration); Cimetidine inhibits metabolism of Metronidazole (increased plasma-metronidazole concentration).

Anticoagulants: Cimetidine enhances anticoagulant effect.

Antidepressants: Cimetidine inhibits metabolism of Amitriptyline, Doxepin, Imipramine, Moclobemide, Nortriptyline and Sertraline (increased plasma concentration).

Antidiabetics: Cimetidine inhibits real excretion of Metformin (increased plasma concentration; Cimetidine enhances hypoglycemic effect of Sulphonylureas.

Antiepileptics: Cimetidine inhibits metabolism of Carbamazepine, Phenytoin, and Valproate (increased plasma concentration).

Antifungals: absorption of Itraconazole and Ketoconazole reduced; plasma concentration of Terbinafine increased by Cimetidine.

Antihistamines: manufacturer advises possibility of increased plasma-loratadine concentration with Cimetidine.

Antimalarials: Cimetidine inhibits metabolism of Chloroquine and Quinine (increased plasma concentration).

Antipsychotics: Cimetidine possibly enhance effect of chlorpromazine, Clozapine, and possibly other antipsychotics.

Antivirals: plasma concentration of Zalcitabine possibly increased by Cimetidine.

Anxiolytics and Hypnotics: Cimetidine inhibits metabolism of Benzodiazepines and Chlormethiazole and Zaleplon (increased plasma concentration).
Beta-blockers: Cimetidine inhibits metabolism of beta-blockers such as Labetalol, Metoprolol and Propranolol (increased plasma concentrations).
Calcium-channel Blockers: Cimetidine inhibits metabolism of some calcium-channel blockers (increased plasma concentration).
* *Ciclosporin:* Cimetidine possibly increases plasma-ciclosporin concentration.
Cytotoxics: Cimetidine increases plasma concentration of Fluorouracil.
Hormone Antagonists: Octreotide possibly delays absorption of Cimetidine.
$5HT_1$- Agonists: Cimetidine inhibits metabolism of Zolmitriptan (reduce dose of Zolmitriptan).
* *Theophylline:* Cimetidine inhibits metabolism (increased plasma-theophylline concentration).

Homatropine see Antimuscarinics.
Hormone Antagonists see Aminoglutethimide; Bicalutamide; Danazol; Finasteride; Flutamide; Gestfrinone; Octeotide; Tamoxifen; Toremifene; Trilostane.

$5HT_1$ -Agonists
Note : There are currently no recognized drug interaction with Naratriptan.
Antibacterials: Quinolones possibly inhibit metabolism of Zolmitriptan (reduce dose of Zolmitriptan).
* *Antidepressants:* risk of CNS toxicity with MAOIs including Lobemide (avoid Rizatriptan or Sumatriptan for 2 weeks after MAOI, reduce dose of Zolmitriptan when given with Moclobemide); Sumatriptan increases risk of CNS toxicity with SSRIs (avoid concomitant use); Fluvoxamine possibly inhibits metabolism of Zolmitriptan (reduce dose of Zolmitriptan).
Beta-blockers: Propranolol may increase plasma concentration of Rizatriptan (reduce Rizatriptan dose).
* *Ergotamine:* increased risk of vasospasm (avoid Ergotamine for 6 hours after Rizatriptan, Sumatriptan or Zolmitriptan, avoid Rizatriptan or Sumatriptan for 24 hours and Zolmitriptan for 6 hours after Ergotamine).
* *Lithium:* Sumatriptan increases risk of CNS toxicity (avoid concomitant use)
Ulcer-healing Drugs: Cimetidine inhibits metabolism of Zolmitriptan (reduce dose of Zolmitriptan (reduce dose of Zolmitriptan).

Hydralazine
ACE Inhibitors: enhanced hypotensive effect.
Alcohol: enhanced hypotensive effect.
* *Anaesthetics:* enhanced hypotensive effect.
Analgesics: NSAIDs antagonize hypotensive effect.
Antidepressants: enhanced hypotensive effect.
Other Antihypertensives: additive hypotensive effect.
Antipsychotics: enhanced hypotensive effect.
Anxiolytics and Hypnotics: enhanced hypotensive effect.
Beta-blockers: enhanced hypotensive effect.
Calcium-channel Blockers: enhanced hypotensive effect.
Corticosteroids: antagonism of hypotensive effect.
Diuretics: enhanced hypotensive effect.
Dopaminergics: Levodopa enhanced hypotensive effect.
Muscle Relaxant: Baclofen and Tizanidine enhances hypotensive effect.
Nitrates: enhanced hypotensive effect.
Oestrogens and Progestogens: Oestrogens and combined oral contraceptives antagonize hypotensive effect.

Thymoxamine: enhanced hypotensive effect.

Hydrochlorathiazide see Diuretics (Thiazide).
Hydrocortisone see Corticosteroids.
Hydroxychloroquine see Chloroquine and Hydroxychloroquine.
Hydroxyprogesterone see Progestogens.
Hyoscine see Antimuscarinics (for general sedative interactions see also Antihistamines).
Hypnotics see Anxiolytics and Hypnotics.
Ibuprofen see NSAIDs.
Ifosfamide see Cyclophosphamide.
Imatinib

- *Analgesics*: manufacturer of imatinib advises restriction or avoidance of concomitant regular paracetamol.
  Anticoagulants: manufacturer of imatinib advises replacement of Warfarin with a Heparin (possibility of enhanced Warfarin effect)
  Antiepileptics: plasma concentration of Imatinib reduced by Phenytoin.
  Antifungals: plasma concentration of Imatinib increased by Ketoconazole.
  Lipid-regulating Drugs: plasma concentration of Simvastatin increased by Imatinib.

Imidapril see ACE Inhibitors and Angiotensin-II Antagonists.
Imipramine see Antidepressants, Tricyclic.
IMMUNOGLOBULINS
Note : for advice on Immunoglobulins and live virus vaccines, see under Normal Immunoglobulin section.
Indapamide see Diuretics (thiazide-related).
Indinavir
Indinavir is metabolised mainly by the cytochrome P450 isoenzyme CYP3A4. It may compete for the same metabolic pathways with many drugs that are metabolised similarly, often resulting in mutually increased plasma concentrations. A drug that is a significant inducer of microsomal enzymes, particularly CYP3A4, may reduce plasma concentrations of indinavir. HIV-protease inhibitors may themselves induce metabolism and may reduce plasma concentrations of other drugs.
Although specific guidance varies between licensing authorities, licensed product information generally contra-indicates the use of HIV-protease inhibitors, includingindinavir with drugs that are highly dependent on CYP3A4 for clearance and for which elevated plasma concentrations are associated with serious or life-threatening events. These include

-the alpha1-adrenoceptor antagonist alfuzosin
-antiarrhythmics (amiodarone)
-antihistamines (astemizole and terfenadine)
-antipsychotics (pimozide)
-ergot derivatives (dihydroergotamine, ergometrine, ergotamine, and methylergometrine)
-gastrointestinal prokinetics (cisapride)
-sedatives and hypnotics (alprazolam, oral midazolam, and triazolam)
-statins (lovastatin and simvastatin)

When indinavir is boosted with ritonavir, use with bepridil, clozapine, dextropropoxyphene, fusidic acid, diazepam, estazolam, flurazepam, quinidine, pethidine, and piroxicam should also be avoided. Similarly, ritonavir-boosted indinavir should not be used with drugs having narrow therapeutic windows that are highly dependent on CYP2D6 for clearance, such as the antiarrhythmics encainide, flecainide, and propafenone. Owing to the potential for increased serum concentrations of sildenafil,indinavir should be avoided with sildenafil when given at

the doses needed for the treatment of pulmonary hypertension. Similarly, indinavir may increase serum concentrations of inhaled salmeterol and the combination is not recommended. Use of indinavir with rosuvastatin should also be avoided. Rifampicin and St John's wort decrease the concentration ofindinavir; use with the antiretroviral is contra-indicated due to the possible loss of its activity and development of resistance. Use of indinavir with atazanavir is contra-indicated as both drugs have been associated with indirect hyperbilirubinaemia.

Indomethacin see NSAIDs.

Inositol no interaction of clinical significance is available.

Insulin see Antidiabetics

Interferons

Note : Consult product literature for interactions of interferon beta and gamma.

Theophylline: interferon alpha inhibits metabolism of Theophylline (enhanced effect).

Ipratropium see Antimuscarinics.

Irbesartan see ACE Inhibitors and Angiotensin-II Antagonists.

Iron

Antacids: Magnesium Trisilicate reduces absorption of oral iron.

Antibacterials: Tetracyclines reduce absorption of oral iron (and vice versa); absorption of Ciprofloxacin, Norfloxacin, and Ofloxacin reduced by oral iron

Bisphosphonates: reduced absorption.

Dopaminergics: absorption of Entacapone and Levodopa may be reduced.

Penicillamine: reduced absorption of Penicillamine.

Trientine: reduced absorption of oral iron.

Zinc: reduced absorption of oral iron (and vice versa).

Isoflurane see Anaesthetics, General (volatile liquid).

Isoniazid

Anaesthetics: hepatotoxicity possibly potentiated by Isoflurane.

Antacids and Adsorbents: antacids reduce absorption.

Other Antibacterials: increased CNS toxicity with Cycloserine.

***** *Antiepileptics:* metabolism of Carbamazepine, Ethosuximide, and Phenytoin inhibited (enhanced effect); also, with Carbamazepine, Isoniazid hepatotoxicity possibly increased.

Antifungals: plasma concentration of Ketoconazole may be reduced.

Anxiolytics and hypnotics: metabolism of diazepam inhibited.

Theophylline: Isoniazid possibly increases plasma-theophylline concentration.

Isoprenaline see Sympathomimetics.

Isosorbide Dinitrate see Glyceryl Trinitrate.

Isosorbide Mononitrate see Glyceryl Trinitrate.

Isotretinoin see Retinoids.

Isradipine see Calcium-Channel Blockers.

Itraconazole see Antifungals, Imidazole and Triazole.

Ivabradine

- Anti-arrhythmics: increased risk of ventricular arrhythmias when ivabradine given with amiodarone or disopyramide
- Antibacterials: plasma concentration of Ivabradine possibly increased by clarithromycin and telithromycin — avoid concomitant use; increased risk of ventricular arrhythmias when ivabradine given with erythromycin—avoid concomitant use

- Antidepressants: plasma concentration of Ivabradine reduced by St John's wort
- Antifungals: plasma concentration of ivabradine increased by fluconazole—reduce initial dose of vabradine; plasma concentration of ivabradine possibly increased by itraconazole
- Antimalarials: increased risk of ventricular arrhythmias when ivabradine given with mefloquine
- Antipsychotics: increased risk of ventricular arrhythmias when ivabradine given with pimozide
- Antivirals: plasma concentration of ivabradine possibly increased by ritonavir
- Beta-blockers: increased risk of ventricular arrhythmias when ivabradine given with sotalol
- Calcium-channel Blockers: plasma concentration of ivabradine increased by diltiazem and verapamil
- Grapefruit Juice: plasma concentration of ivabradine increased by grapefruit juice
- Pentamidine Isetionate: increased risk of ventricular arrhythmias when ivabradine given with pentamidine isetionate

Ivermectin

* Levamisole: Levamisole appears to increase the exposure to ivermectin. Ivermectin does not alter the pharmacokinetics of levamisole.
* Acenocoumarol: A patient showed a marked increase in his response to acenocoumarol when exposed to insecticides containing ivermectin and methidathion.
* Warfarin: The US manufacturer notes that cases of raised INRs have been rarely reported with ivermectin and warfarin.
* Alcohol: Alcohol may increase the bioavailability of ivermectin, which could increase adverse effects such as postural hypotension.

Kanamycin as for Gentamicin Sulfate

Kaolin

Analgesics: absorption of aspirin possibly reduced.
Anti-arrhythmics: absorption of Quinidine possibly reduced (possibly reduced plasma concentration).
Antibacterials: absorption of Tetracyclines possibly reduced.
Antimalarials: absorption of Chloroquine reduced.
Antipsychotics: absorption of Phenothiazines possibly reduced.
Cardiac Glycosides: absorption of Digoxin possibly reduced.

Ketamine see Anaesthetics, General.
Ketoconazole see Antifungals, Imidazole and Triazole.
Ketoprofen see NSAIDs.
Ketorolac see NSAIDs.
Ketotifen see Antihistamines.
Lacidipine see Calcium-channel Blocker.
Labetalol see Beta-blockers

Lamivudine

Antibacterials: Trimethoprim increases plasma concentration.- avoid concomitant use of high-dose co-trimoxazole.

Lamotrigine

* *Other Antiepileptics:* concomitant administration of two or more Antiepileptics may enhance toxicity without a corresponding increase in antiepileptic effect; moreover interactions between individual antiepileptics can complicate monitoring

of treatment; interactions include enhanced effects, increased sedation, and reductions in plasma concentrations.

Lansoprazole see Proton Pump Inhibitors.

Leflunomide

Note: Increased risk of toxicity with other haematotoxic and hepatotoxic drugs.

Lenograstim

Note : Use not recommended from 24 hours before until 24 hours after chemotherapy; for further details consult product literature.

Lercarnidipine see Calcium channel Blockers

Leukotriene Antagonists

Analgesics: aspirin increases plasma concentration of Zafirlukast.
Antibacterials: Erythromycin reduces plasma concentration of Zafirlukast.
Anticoagulants: anticoagulant effect of Warfarin enhanced by Zafirlukast.
Barbiturates: plasma concentration of Montelukast reduced by Phenobarbital.
Theophylline: Zafirlukast possibly increases plasma-theophylline concentration; plasma-Zafirlukast concentration reduced.

Levamisole

*Alcohol: US licensed product information states that levamisole can produce a disulfiram-like reaction withalcohol.
*Anticoagulants: Increase in the activity of warfarin when given with levamisole and fluorouracil.
*Antiepileptics: Increased phenytoin concentrations when given with levamisole and fluorouracil.

Levocetirizine see Antihistamines

Levodopa

* *Antidepressants:* hypertensive crisis with MAOIs (including Moclobemide)- avoid for at least 2 weeks after stopping MAOI.
* *Antihypertensives:* enhanced hypotensive effect.
* *Antipsychotics:* antagonism of effect.

Anxiolytics and Hypnotics: occasional antagonism of effect by Chlordiazepoxide, Diazepam, Lorazepam and possibly other Benzodiazepines.
Iron: absorption of Levodopa may be reduced.
Metoclopramide and Domperidone: Levodopa-plasma concentrations increased by Metoclopramide.
Vitamins: effect of Levodopa antagonized by pyridoxine unless a dopa-decarboxylase inhibitor also given.

Levofloxacin see Quinolones

Levonorgestrel see Progestogens.

Lignocaine

Other Anti-arrhythmics: increased myocardial depression.
Beta-blockers: increased risk of myocardial depression; increased risk of Lignocaine toxicity with Propranolol.
Diuretics: effect of Lignocaine antagonized by hypokalaemia with Acetazolamide, loop diuretics, and Thiazides.
Muscle Relaxants: action of Suxamethonium prolonged.
Ulcer-healing Drugs: Cimetidine inhibits metabolism of Lignocaine (increased risk of toxicity).

Linezolide see MAOIs

Note: Linezolide is a reversible, non-selective MAO inhibitor.

Lipid-regulating Drugs see Cholestyramine and Colestipol; Clofibrate Group; Nicotinic Acid; Statins.

Lisinopril see ACE Inhibitors.

Lithium

* *ACE Inhibitors:* lithium excretion reduced (increased plasma-lithium concentration).
* *Analgesics:* excretion of lithium reduced by Azapropazone, Diclofenac, Ibuprofen Indomethacin, Ketorolac (avoid concomitant use), Mefenamic acid, Naproxen, Piroxicam and probably other NSAIDs (risk of toxicity).
* *Antacids:* Sodium bicarbonate increases excretion of Lithium (reduced plasma-lithium concentrations).
* *Anti-arrhythmics:* increased risk of hypothyroidism with Amiodarone.
* *Antibacterials:* lithium toxicity reported with Metronidazole and Spectinomycin.
* *Antidepressants:* SSRIs increase risk of CNS effects (lithium toxicity reported).
  Antidiabetics: Lithium may occasionally impair glucose tolerance.
  Antiepileptics: neurotoxicity may occur with Carbamazepine and Phenytoin without increased plasma-lithium concentration.
* *Antihypertensives:* neurotoxicity may occur with Methyldopa without increased plasma-lithium concentration.
  Antipsychotics: increased risk of extrapyramidal effects and possibility of neurotoxicity (notably with Haloperidol).
  Calcium-channel Blockers: neurotoxicity may occur with Diltiazem and Verapamil without increased plasma-lithium concentration.
* *Diuretics:* Lithium excretion reduced by loop diuretics, potassium-sparing diuretics, and Thiazides (increased plasma-lithium concentration and risk of toxicity- loop diuretics safer than Thiazides); lithium excretion increased by Acetazolamide.
* *$5HT_1$ -Agonists:* Sumatriptan increases risk of CNS toxicity.
  Metoclopramide and Domperidone: increased risk of extrapyramidal effects and possibility of neurotoxicity with Metoclopramide.
  Muscle Relaxants: muscle relaxant effect enhanced, Baclofen possibly aggravates hyperkinesis.
  Parasympathomimetics: Lithium antagonizes effect of Neostigmine and Pyridostigmine.
  Theophylline: lithium excretion increased (reduced plasma-lithium concentration).

Loratadine see Antihistamines.
Lorazepam see Anxiolytics and Hypnotics.
Losartan as for ACE Inhibitors.
Lumefantrine see Artemether with Lumefantrine.
Macrolides see Erythromycin and other Macrolides.
Magnesium Salt (see also Antacids and Adsorbents)
Muscle Relaxants: effect of non-depolarizing muscle relaxants enhanced by parenteral magnesium salts.

Magnesium Trisilicate see Antacids.

MAOIs
Note : For interactions of reversible MAO-A inhibitors (RIMAS), see Moclobemide, and for interactions of MAO-B inhibitors see Selegiline.

* *Alcohol:* some alcoholic and dealcoholised beverages contain Tyramine which interacts which interacts with MAOIs (hypertensive crisis)-but if no Tyramine, enhanced hypotensive effect; foods, see section.
* *Alpha$_2$–adrenoceptor Stimulants:* manufacturers of Apraclonidine and Brimonidine advise avoid concomitant use.
* *Altretamine:* risk of severe postural hypotension.
* *Analgesics:* CNS excitation or depression(hypertension or hypotension) with Pethidine and possibly other opioid analgesics- avoid concomitant use and for two weeks after MAOI discontinued; manufacturer advises avoid Nefopam
* *Anorectics:* see Sympathomimetics, below.
* *Other Antidepressants:* enhancement of CNS effects and toxicity with other MAOIs (avoid for at least a week after stopping previous MAOIs then start with reduced dose); increased risk of toxicity with Nefazodone (important: if MAOIs discontinued shortly before, initiate Nefazodone cautiously with gradual dose increase); CNS effects of SSRIs increased by MAOI should not be started until at least I week after Citalopram or Fluvoxamine have been stopped, at least 5 weeks for Fluoxetine, at least 2 weeks for Paroxetine and Sertraline; CNS excitation and hypertension with most Tricyclics and related antidepressants (avoid for at least 2 weeks after stopping MAOI, and avoid MAOI for at least I week 1 week after stopping Tricyclic); CNS excitation and confusion with Tryptophan (reduce Tryptophan dose); enhancement of CNS effects and toxicity possible with Reboxetine and Venlafaxine (avoid for at least 2 weeks after stopping MAOI, and avoid MAOI for at least 1 week after stopping Reboxetne or Venlafaxine).
  Antidiabetics: effect of Insulin, Metformin, and Sulphonylureas enhanced
* *Antiepileptics:* antagonism of anticonvulsant effect (convulsive threshold lowered); manufacturer advises avoid Carbamazepine with or within 2 weeks of MAOIs.
* *Antihypertensives:* hypotensive effect enhanced; manufacturer advises avoidance of Indoramin; manufacturer advises avoid concomitant use with Methyldopa.
  Antihistamines: increased antimuscarinic and sedative effects.
  Antimuscarinics: increased side-effects.
* *Antipsychotics:* CNS excitation and hypertension with Oxypertine; Clozapine possibly enhances central effects.
  Anxiolytics and Hypnotics: manufacturer advises avoidance of Buspirone
* *Barbiturates:* see under Antiepileptics, above.
* *Dopaminergics:* hypertensive crisis with Levodopa (avoid for at least 2 weeks after stopping MAOI); hypotension with Selegiline; manufacturer advises avoid concomitant use with Entacapone.
* *5HT$_1$Angonists:* risk of CNS toxicity (avoid Rizatriptan or Sumatriptan for 2 weeks after MAOI).
* *Sympathomimetics:* hypertensive crisis with sympathomimetics such as Dopamine, Dopexamine, Ephedrine, Isometheptene, Methylphenidate, Phentermine, Phenylephrine, Phenylpropanolamine, and Pseudoephedrine
* *Tetrabenazine:* CNS excitation and hypertension.

Maprotiline see Antidepressants, Tricyclic.

Maraviroc

Maraviroc is a substrate for the cytochrome P450 isoenzyme CYP3A4 and for P-glycoprotein, and may therefore have several clinically significant interactions. Inhibitors of CYP3A4, such as HIV-protease inhibitors (other than tipranavir), increase the serum concentration of maraviroc. Inducers of CYP3A4 such as efavirenz may decrease serum maraviroc concentrations. No clinically significant interaction is

expected between maraviroc and NRTIs, nevirapine, or boosted fosamprenavir or tipranavir.
Non-antiretroviral medications that significantly alter maravirocmetabolism include the CYP3A4 inhibitors ketoconazole, itraconazole, clarithromycin, and nefazodone and the CYP3A4 inducers rifampicin and St John's wort. Maraviroc does not appear to cause clinically significant changes in concentrations of other medications.

Mebendazole
Ulcer-healing Drugs: metabolism possibly inhibited by Cimetidine (increased plasma-mebendazole concentration).

Medroxyprogesterone see Progestogens.
Mefenamic Acid see NSAIDs.

Mefloquine
* *Anti-arrhythmics:* increased risk of ventricular arrhythmias with Amiodarone (avoid concomitant use) and Quinidine.
* *Antiepileptics:* antagonism of anticonvulsant effect.
* *Other Antimalarials:* increased risk of convulsions with Chloroquine and Quinine, but should not prevent use of intravenous quinine in severe cases; increased risk of ventricular arrhythmias with Halofantrine (important: see also advice under Halofantrine).
* *Antipsychotics:* increased risk of ventricular arrhythmias-avoid concomitant use with Pimozide.
  Beta-blockers: possible increased risk of bradycardia with some calcium-channel blockers.
  Cardiac Glycosides: possible increased risk of bradycardia with Digoxin.

Meloxicam see NSAIDs

Melphalan
Antibacterials: increased toxicity with Nalidixic acid.
* *Ciclosporin:* increased risk of nephrotoxicity.

Mercaptopurine
* Allop*urinol:* enhancement of effect (increased toxicity-reduce dose of Mercaptopurine).

Meropenem
Antiepileptics: plasma concentration of Valproate reduced.
Uricosurics: excretion reduced by Probenecid (concomitant use not recommended by manufacturer)

Mestranol see Contraceptives, Oral.
Metformin see Antidiabetics.
Methotrexate
* *Analgesics:* excretion reduced by aspirin, Azapropazone (avoid concomitant use), Diclofenac, Ibuprofen, Indomethacin, Ketoprofen, Meloxicam, Naproxen and probably other NSAIDs (increased risk of toxicity).
  Antibacterials: antifolate effect increased by Co-trimoxazole and Trimethoprim; risk of Methotrexate toxicity in creased by Sulphonamides; excretion reduced by Penicillins (increased risk of toxicity).
  Antiepileptics: Phenytoin increases antifolate effect.
  Antimalarials: antifolate effect increased by Pyrimethamine (ingredient of Fansidar ®).
* *Ciclosporin:* increased toxicity.

* *Retinoids:* plasma concentration of Methotrexate increased by Acitretin (also increased risk of hepatotoxicity).

Methyldopa

Alcohol: enhanced hypotensive effect.
* *Anaesthetics:* enhanced hypotensive effect.
Analgesics: NSAIDs antagonize hypotensive effect.
Antidepressants: enhanced hypotensive effect.
Other Antihypertensives: enhanced hypotensive effect.
Antipsychotics: increased risk of extrapyramidal effects; enhanced hypotensive effect.
Anxiolytics and Hypnotics: enhanced hypotensive effect.
Beta-Blockers: enhanced hypotensive effect.
Calcium-channel Blockers: enhanced hypotensive effect.
Corticosteroids: antagonism of hypotensive effect.
Diuretics: enhanced hypotensive effect.
Dopaminergics: antagonism of antiparkinsonian effect; Levodopa enhances hypotensive effect; effect of Methyldopa possible enhanced by Entacapone
Lithium: neurotoxicity may occur without increased plasma-lithium concentration
Muscle Relaxants: enhanced hypotensive effect with Baclofen and Tizanidine
Nitrates: enhance hypotensive effect.
Oestrogens and Progestogens: Oestrogens and combined oral contraceptives antagonize hypotensive effect.
Sympathomimetics: see Sympathomimetics (main list).
Ulcer-healing Drugs: Carbenoxolone antagonizes hypotensive effect.

Methylprednisolone see Corticosteroids.
Metolazone see Diuretics
Metoclopramide

Analgesics: increased absorption of aspirin and Paracetamol (enhanced effect); opioid analgesics antagonize effect on gastro-intestinal activity.
Antipsychotics: increased risk of extrapyramidal effects.
Atovaquone: plasma concentration reduced by Metoclopramide.
Dopaminergics: antagonism of hypoprolactinaemic effect of Bromocriptine; increased plasma concentration of Levodopa; antagonism of antiparkinsonian effects of Pergolide.
Lithium: increased risk of extrapyramidal effects and possibility of neurotoxicity.
Tetrabenazine: increased risk of extrapyramidal effects.

Metolazone see Diuretics
Metoprolol see Beta-Blockers.
Metronidazole

Alcohol: Disulfiram-like reaction.
* *Anticoagulants:* effect of Nicoumalone and Warfarin enhanced.
* *Antiepileptics:* Metronidazole inhibits metabolism of Phenytoin (increased plasma-Phenytoin concentration); Phenobarbital accelerates metabolism of Metronidazole (reduced plasma-metronidazole concentration).
* *Barbiturates:* see under Antiepileptics, above.
Cytotoxics: Metronidazole inhibits metabolism of Fluorouracil (increased toxicity)
Disulfiram: psychotic reactions reported.
Lithium: increased toxicity reported.
Ulcer-healing Drugs: Cimetidine inhibits metabolism (increased plasma-metronidazole concentration).

Mianserin

Alcohol: enhanced effect.
Alpha$_2$-Adrenoceptor Stimulants: manufactures of Apraclonidine and Brimonidine advise avoid concomitant use.
other Antidepressants: as for Antidepressants, Tricyclic.

* *Antiepileptics:* antagonism (convulsive threshold lowered); metabolism accelerated by Carbamazepine, Phenobarbital, and Phenytoin (reduced plasma-mianserin concentration).
Anxiolytics and Hypnotics: enhanced effect.
* *Barbiturates:* see under Antiepileptics, above.

Miconazole see Antifungals, Imidazole and Triazole.
Midazolam see Anxiolytics and Hypnotics.
Mirtazapine
Alcohol: enhanced sedative effect.
Anticoagulants: Mirtazapine enhances anticoagulant effect of Warfarin.

- *Other Antidepressants*: as for Antidepressants, tricyclic.
Antiepileptics: Carbamazepine and Phenytoin reduce plasma concentration of Mirtazapine.
Antifungals: Ketoconazole increases plasma concentration of Mirtazapine.
- *Antimalarials*: manufacturer of Artemether with Lumefentrine advises avoid concomitant use.
Anxiolytics and Hypnotics: enhanced sedative effect.
Ulcer-healing Drugs: Cimetidine increases plasma concentration of Mirtazapine.

Misoprostol
Analgesics: increased risk of CNS toxicity with Phenylbutazone.

Monoamine-oxidase Inhibitors see MAOIs, Moclobemide, and Selegiline.
Montelukast see Leukotriene Antagonists.
Morphine see Opioid Analgesics.
Moxifloxacin see Quinolones
Moxonidine
The hypotensive effect of moxonidine may be enhanced by other antihypertensives and drugs that cause hypotension. The effect of sedatives and hypnotics, including benzodiazepines, may be enhanced bymoxonidine.
Muscle Relaxants
ACE Inhibitors and Angiotensin-II Antagonists: enhanced hypotensive effect with Baclofen and Tizanidine.
Alcohol: enhanced sedative effect with Baclofen and Tizanidine.
Analgesics: ibuprofen and possible other NSAIDs reduce excretion of Baclofen (increased risk of toxicity).

* *Anti-arrhythmics:* Procainamide and Quinidine enhance muscle relaxant effect; Lignocaine prolongs action of Suxamethonium.
* *Antibacterials:* effect of non-depolarizing muscle relaxants enhanced by Aminoglycosides, Azlocillin, Clindamycin, Colistin and Piperacillin.
Antidepressants: Tricyclics enhance muscle relaxant effect of Baclofen.
Antiepileptics: effect of non-depolarizing muscle relaxants antagonized by Carbamazepine and Phenytoin (recovery form neuromuscular blockade accelerated).
Antihypertensives: enhanced hypotensive effect with Baclofen and Tizanidine.
Anxiolytics and Hypnotics: enhanced sedative effect with Baclofen and Tizanidine.
Beta-blockers: Propranolol enhances muscle relaxant effect; possible enhanced hypotensive effect and bradycardia with Tizanidine.

* *Botulinum Toxin:* neuromuscular block enhance by non-depolarizing muscle relaxants (risk of toxicity).
Calcium-channel Blockers: Nifedipine and Verapamil enhance effect of non-depolarizing muscle relaxants; hypotension, myocardial depression, and hyperkalaemia reported with intravenous Dantrolene and Verapamil; risk of arrhythmias with Diltiazem and intravenous Dantrolene.
Cardiac Glycosides: arrhythmias if Suxamethonium given with Digoxin; possible bradycardia if Tizanidine given with Digoxin.
Cytotoxics: Cyclophosphamide and Thiotepa enhance effect of Suxamethonium
Diuretics: enhanced hypotensive effect with Baclofen and Tizanidine.
Lithium: lithium enhances muscle relaxant effect; Baclofen possibly aggravates hyperkinesis.
Magnesium Salts: parenteral magnesium enhances effect of non-depolarizing muscle relaxants.
Parasympathomimetics: Ecothiophate eye-drops, Edrophonium, Neostigmine, Pyridostigmine, Rivastigmine and possibly Donepezil enhance effect of Suxamethonium but antagonize effect of non-depolarizing muscle relaxants.
Sympathomimetics: Bambuterol enhances effect of Suxamethonium.

Mycophenolate Mofetil

Anion-exchange Resins: Cholestyramine reduces absorption.
Antacids: reduced absorption of Mycophenolate Mofetil.
Antivirals: higher plasma concentrations of Mycophenolate Mofetil and of Aciclovir on concomitant administration.

Nalidixic Acid see Quinolones.
Nandrolone see Anabolic Steroids.
Naproxen see NSAIDs.
Nateglinide see Antidiabetics.
Nebivolol see Beta-blockers
Nelfinavir
Nelfinavir is reported to be metabolised in part by cytochrome P450 isoenzymes CYP3A4 and CYP2C19. Drugs that induce these isoenzymes may reduce the plasma concentration of nelfinavir. Conversely, whennelfinavir is given with drugs that inhibit CYP3A4 plasma concentrations,nelfinavir concentrations may be increased. It may also alter the pharmacokinetics of drugs metabolised by this isoenzyme system and possibly cause serious adverse effects.
Although specific guidance varies between licensing authorities, licensed product information generally contra-indicates the use ofnelfinavir with drugs that are highly dependent on CYP3A4 for clearance and for which elevated plasma concentrations are associated with serious or life-threatening events. These drugs include

- the alpha1-adrenoceptor antagonist alfuzosin
- antiarrhythmics (amiodarone and quinidine)
- antihistamines (astemizole and terfenadine)
- antipsychotics (pimozide)
- ergot derivatives (dihydroergotamine, ergometrine, ergotamine, and methylergometrine)
- gastrointestinal motility agents (cisapride)
- sedatives and hypnotics (triazolam and oral midazolam)
- statins (simvastatin and lovastatin)

Owing to the potential for increased serum concentrations of sildenafil,nelfinavir should be avoided with sildenafil when given at the doses needed for the treatment of pulmonary hypertension. Similarly, nelfinavir may increase serum concentrations of inhaled salmeterol and the combination is not recommended. Omeprazole, rifampicin,

and St John's wort decrease the concentration ofnelfinavir; use with the antiretroviral is not recommended due to the possible loss of its activity and development of resistance.

Neomycin see Aminoglycosides.

Neostigmine see Parasympathomimetics.

Nevirapine

Nevirapine is metabolised mainly by the cytochrome P450 isoenzymes CYP3A4 and CYP2B6. Consequently it may compete with other drugs metabolised by this system, possibly resulting in mutually increased plasma concentrations and toxicity.

Alternatively, enzyme inducers may decrease plasma concentrations ofnevirapine; nevirapine itself acts as a mild to moderate enzyme inducer and may thus reduce plasma concentrations of other drugs.

Rifampicin and St John's wort decrease the concentration ofnevirapine; use with the antiretroviral is not recommended due to the possible loss of its activity and development of resistance.

Netilmicin see Aminoglycosides.

Nicorandil

Nicorandil should not be used with phosphodiesterase type-5 inhibitors such as sildenafil as the hypotensive effect of nicorandil may be significantly enhanced.

Nicotinic Acid

Note : Interactions apply to lipid-regulating doses of nicotinic acid.

Other Lipid-regulating Drugs: increased risk of myopathy with Statins.

Nifedipine see Calcium-channel Blockers.

Nimodipine see Calcium-channel Blockers.

Nitazoxanide see antiprotozoal

Nitrofurantoin

Antacids and Adsorbents: Magnesium Trisilicate reduces excretion of Nitrofurantoin (risk of toxicity).

Nitrous Oxide see Anaesthetics, General.

Nizatidine see Histamine H_2 – antagonists.

Noradrenaline see Sympathomimetics.

Norethisterone see Progestogens.

Norgestrel see Progestogens.

Nortriptyline see Antidepressants, Tricyclic.

NSAIDs (see also Aspirin).

Note : Interaction do not generally apply to topical NSAIDs.

* *ACE Inhibitors:* antagonism of hypotensive effect; increased risk of renal impairment and increased risk of hyperkalaemia on administration with Ketorolac and possibly other NSAIDs.
* *Other Analgesics:* avoid concomitant administration of two or more NSAIDs, including Aspirin (increased side effects).
  Antacids: absorption of Diflunisal reduced.
* *Antibacterials:* NSAIDs possibly increase risk of convulsions with Quinolones; Indomethacin possibly increases plasma concentration of Gentamicin and Amikacin in neonates.
* *Anticoagulants:* anticoagulant effect of Nicoumalone, Warfarin (and possibly Phenindione) seriously enhanced by Azapropazone (avoid concomitant use) and possibly enhanced by Diclofenac, Diflunisal, Flurbiprofen, Ibuprofen, Mefenamic acid, Meloxicam, Piroxicam, Sulindac, and other NSAIDs; increased risk of hemorrhage with parenteral Diclofenac and Ketorolac and all anticoagulants, including low-dose heparin (avoid concomitant use).

Antidepressants: Moclobemide enhances effect of Ibuprofen and possibly other NSAIDs.

* *Antidiabetics:* effect of Sulphonylureas enhances effect of ibuprofen and possibly other NSAIDs.
* *Antiepileptics:* effect of Phenytoin enhanced by Azapropazone (avoid concomitant use) and possibly other NSAIDs.

Antihypertensives: antagonism of hypotensive effect.

Antiplatelet Drugs: possibly increased risk of gastrointestinal bleeding with Clopidogrel.

Antipsychotics: severe drowsiness possible if Indomethacin given with Haloperidol.

* *Antivirals:* plasma concentration of Piroxicam increased by Ritonavir (risk of toxicity-avoid concomitant use); plasma concentration of other NSAIDs possibly increased by Ritonavir.

Beta-blockers: antagonism of hypotensive effect.

Bisphosphonates: bioavailability of Tiludronic acid increased by Indomethacin; Alendronic acid possibly increases gastro-intestinal side-effects of NSAIDs.

Cardiac Glycosides: NSAIDs may exacerbate heart failure, reduce GFR, and increase plasma-cardiac glycoside concentration.

Corticosteroids: increased risk of gastro-intestinal bleeding and ulceration.

* *Ciclosporin:* increased risk of nephrotoxicity; Ciclosporin increases plasma concentration of Diclofenac (halve Diclofenac dose).

Cytotoxics: excretion of Methotrexate reduced by Aspirin, Azaproazone (avoid concomitant use), Diclofenac, Ibuprofen, Indomethacin, Ketoprofen, Meloxicam, Naproxen and probably other NSAIDs (increased risk of toxicity).

Desmopressin: effect potentiated by Indomethacin.

Diuretics: risk of nephrotoxicity of NSAID increased; NSAIDs notably Indomethacin and Ketorolac antagonize diuretic effect; Indomethacin and possibly other NSAIDs increase risk of hyperkalaemia with potassium-sparing diuretics; occasional reports of decreased renal function when Indomethacin given with Triamterene.

* *Lithium:* excretion of Lithium reduced by Azapropazone, Diclofenac, Ibuprofen, Indomethacin, Ketorolac (avoid concomitant use), Mefenamic acid, Naproxen, Piroxicam, and probably other NSAIDs (risk of toxicity).

Muscle Relaxants: Ibuprofen and possibly other NSAIDs reduce excretion of Baclofen (increased risk of toxicity).

* *Tacrolimus:* Ibuprofen increases risk of nephrotoxicity.

Ulcer-healing drugs: plasma concentration of Azapropazone possibly increased by Cimetidine.

* *Uricosurics:* Probenecid delays excretion of Indomethacin, Ketoprofen, Ketorolac (avoid concomitant use), and Naproxen and increases plasma – NSAID concentration.
* *Vasodilators:* risk of Ketorolac-associated bleeding increased by Oxpentifylline (avoid concomitant use).

Oestrogens see Contraceptives, Oral.
Ofloxacin see Quinolones.
Olanzapine see Antipsychotics.
Olmesartan see Angiotensin-II Receptor Antagonists
Omeprazole see Proton Pump Inhibitors.
Opioid Analgesics

Alcohol: enhanced sedative and hypotensive effect.

Antiarrhythmics: delayed absorption of Mexiletine.

Antibacterials: Rifampicin accelerates metabolism of methadone (reduced effect); Erythromycin increases plasma concentration of Alfentanil; manufacturer of Ciprofloxacin advises avoid premedication with opioid analgesics (reduced plasma-Ciprofloxacin concentration).

* *Anticoagulants:* Dextropropoxyphene may enhance effect of Nicomumalone and Warfarin.
* *Antidepressants:* CNS excitation or depression (hypertension or hypotension) if Pethidine and possibly other opioid analgesics given to patients receiving MAOIs (including Moclobemide)-avoid concomitant use and for 2 weeks after MAOI discontinued; Tramadol possibly increases risk of convulsions with SSRIs and Tricyclics.
* *Antiepileptics:* Dextropropoxyphene enhances effect of Carbamazepine; effect of Methadone and Tramadol decreased by Carbamazepine; Phenytoin accelerates Methadone metabolism (reduced effect and risk of withdrawal effects)

Antifungals: metabolism of Alfentanil inhibited by Ketoconazole (risk of prolonged or delayed respiratory depression).

Antipsychotics: enhanced sedative and hypotensive effect.

* *Antivirals:* Methadone possibly increases plasma concentration of Zidovudine; plasma concentration of Dextroproposyphene and Pethidine increased by Ritonavir (risk of toxicity — avoid concomitant use); plasma concentration of other opioid analgesics possibly in increased by Ritonavir.

Anxiolytics and Hypnotics: enhanced sedative effect.

* *Dopaminergics:* hyperpyrexia and CNS toxicity reported if Pethidine given to patients receiving Selegiline (avoid concomitant use).

Metoclopramide and Domperidone: antagonism of gastro-intestinal effects.

Ulcer-healing Drug: Cimetidine inhibits metabolism of opioid analgesics notably Pethidine (increased plasma concentration).

Orciprenaline see Sympathomimetics.

Ornidazole

* Alcohol: A disulfiram-like reaction has been reported in a patient taking ornidazole after drinking alcohol.

*Rifampicin: Rifampicin slightly decreases ornidazole exposure.

Orlistat

Antidiabetics: manufacturer advises avoid concomitant use with Acarbose or Metformin.

Lipid-regulating Drugs: manufacturer advises avoid concomitant use with Clofibrate group; Orlistat increases plasma concentration of Pravastatin (increased risk of toxicity-reduce dose of Pravastatin).

Sympathomimetics: manufacturer advises avoid concomitant use with Phentermine.

Oseltamivir

Pharmacokinetic properties of oseltamivir, such as low protein binding and metabolism independent of the CYP450 and glucuronidase systems, suggest that clinically significant drug interactions via these mechanisms are unlikely.

Oxazepam see Anxiolytics and Hypnotics.

Oxcarbazepine

- *Antibacterials*: see Linezolide
- *Antidepressants*: antagonism of anticonvulsant effect (convulsive threshold lowered); manufacturer advises avoid concomitant use with MAOIs.
- *Other Antiepileptics*: interactions include enhanced effects, increased sedation, and reductions in plasma concentrations.
- *Antimalarials*:Mefloquine antagonises anticonvulsant effect; Chloroquine and hydroxychloroquine occasionally reduce seizure threshold.

- *Oestrogens and Progestogens*: Oxcarbazepine accelerates metabolism of oral Contraceptives (reduced contraceptive effect)

Oxprenolol see Beta-blockers.
Oxybutynin see Antimuscarinics
Oxymetazoline see Sympathomimetics.
Oxytetracycline see Tetracyclines.

Oxytocin

Anaesthetics: inhalational anaesthetics possibly reduce oxytocic effect (also enhanced hypotensive effect and risk of arrhythmias).
Prostaglandins: uterotonic effect potentiated.
Sympathomimetics: enhancement of vasopressor effect of vasoconstrictor sympathomimetics.

Paclitaxel

Antifungals : Ketoconazole possibly inhibits metabolism of Paclitaxel.

Pancreatin

Antidiabetics : hypoglycemic effect of Acarbose reduced.

Pancuronium see Music Relaxants (non-depolarizing).
Pantoprazole see Proton Pump Inhibitors.
PARA-Aminosalicylic acid same as Aminosalicylic acid

The adverse effects of aminosalicylates and salicylates may be additive. Probenecid may also increase toxicity by delaying renal excretion and enhancing plasma concentrations of aminosalicylate. The activity of aminosalicylic acid may be antagonised by ester-type local anaesthetics such as procaine.

Paracetamol

Anion-exchange Resins: Cholestyramine reduces absorption of Paracetamol.
Anticoagulants: prolonged regular use of Paracetamol possibly enhances Warfarin.
Metoclopramide and Domperidone: Metoclopramide and Domperidone accelerate absorption of Paracetamol (enhanced effect).

Parasympathomimetics

Anti-arrhythmics: Procainamide, Quinidine and possibly Propafenone antagonize effect of Neostigmine and Pyridostigmine.
Antibacterials: Aminoglycoside, Clindamycin and Colistin antagonize effect of Neostigmine and Pyridostigmine.
Antimalarials: Chloroquine and Hydroxychloroquine have potential to increase symptoms of myasthenia gravis and thus diminish effect of Neostigmine and Pyridostigmine.
Antimuscarinics: antagonism of effect.
Beta-blockers: Propranolol antagonizes effect of Neostigmine and Pyridostigmine.
Lithium: antagonism of effect of Neostigmine and Pyridostigmine.
Muscle Relaxants: Ecothiophate eye-drops, Edrophonium, Neostigmine, Pyridostigmine, Rivastigmine and possibly Donepezil enhance effect of Suxamethonium, but antagonize effect of non-depolarizing muscle relaxants.

Paroxetine see Antidepressants, SSRI
Pefloxacin see fluoroquinolone
Penicillamine

Antacids: reduced absorption of Penicillamine.

Iron: reduced absorption of Penicillamine.
Zinc: reduced absorption of Penicillamine.

Penicillins
Antacids: reduced absorption of Pivampicillin.
Anticoagulants: see Phenindione and Warfarin.
Cytotoxics: reduced excretion of Methotrexate (increased risk of toxicity).
Muscle relaxants: enhanced by Azlocillin and Piperacillin.
Oestrogens and Progestogens: see Contraceptives, Oral.
Uricosurics: excretion of Penicillins reduced by Probenecid.

Pentazocine see Opioid Analgesics.
Perindopril see ACE Inhibitors and Angiotensin-II Antagonists.
Perphenazine see Antipsychotics.
Pethidine see Opioid Analgesics.
Pheniramine see Antihistamines.
Phenobarbital see Barbiturates.
Phenothiazines see Antipsychotics.
Phenoxymethyl Penicillin see Penicillins.
Phenylephrine see Sympathomimetics.

Phenytoin
* *Analgesics:* plasma-phenytoin concentration increased by Aspirin, Azapropazone (avoid concomitant use) and possibly other NSAIDs; metabolism of Methadone accelerated (reduced effect and risk of withdrawal effects).
  Antacids: reduced Phenytoin absorption.
* *Anti-arrhythmics:* Amiodarone increases plasma-phenytoin concentration; phenytoin reduces plasma concentrations of Disopyramide, Mexiletine, and Quinidine.
* *Antibacterials:* plasma-phenytoin concentration increased by Chloramphenicol, Cycloserine, Isoniazid, and Metronidazole; plasma-phenytoin concentration and antifolate effect increased by Co-trimoxazole and Trimethoprim and possibly by other Sulphonamides; plasma-phenytoin concentration reduced by Rifampicin; plasma concentration of Doxycycline reduced by Phenytoin; plasma-phenytoin concentration possibly altered by Ciprofloxacin.
* *Anticoagulants:* metabolism of Nicoumalone and Warfarin accelerated (possibility of reduced anticoagulant effect, but enhancement also reported).
* *Antidepressants:* antagonism of anticonvulsant effect (convulsive threshold lowered); Fluoxetine, Fluvoxamine, and Viloxazine increase plasma-phenytoin concentration; Phenytoin reduces plasma-concentrations of Mianserin, Paroxetine, and Tricyclics.
  Antidiabetics: plasma-phenytoin concentration transiently increased by Tolbutamide possibility of toxicity); Phenytoin possibly reduces plasma concentration of Repaglinide (manufacturer advises avoid concomitant use).
* *Other Antiepileptics:* concomitant administration of tow or more antiepileptics may enhance toxicity without a corresponding increase in Antiepileptic effect; moreover interactions between individual Antiepileptics can complicate monitoring of treatment; interactions include enhanced effects, increased sedation, and reductions in plasma concentrations.
* *Antifungals:* plasma-phenytoin concentration increased by Fluconazole and Miconazole; plasma concentration of Itraconazole and Ketoconazole reduced
* *Antimalarials:* antagonism of anticonvulsant effect; increased risk of antifolate effect with Pyrimethamine (includes Fansidar ® and Maloprim ®).
* *Antiplatelet Drugs:* plasma-phenytoin concentration increased by aspirin.

* *Antipsychotics:* antagonism of anticonvulsant effect (convulsive threshold lowered); Phenytoin accelerates metabolism of Clozapine and Quetiapine (reduced plasma concentrations).
* *Antivirals:* plasma concentration of Indinavir, Nelfinavir and Saquinavir possibly reduced; plasma-phenytoin concentrations increased or decreased by Zidovudine.
* *Anxiolytics and Hypnotics:* Diazepam and possibly other Benzodiazepines increase plasma-phenytoin concentration.
* *Calcium-channel Blockers:* Diltiazem and Nifedipine increase plasma concentration of Phenytoin; effect of Felodipine, Isradipine and probably Nicardipine, Nifedipine and other Dihydropyridines, Diltiazem, and Verapamil reduced.
  Cardiac Glycosides: metabolism of digitoxin only accelerated (reduced effect).
* *Corticosteroids:* metabolism of Corticosteroids accelerated (reduced effect).
* *Ciclosporin:* metabolism of Ciclosporin accelerated (reduced plasma concentration).
  Cytotoxics: reduced absorption of Phenytoin; increased antifolate effect with Methotrexate.
* *Disulfiram:* Plasma-phenytoin concentration increased.
* *Diuretics:* increased risk of osteomalacia with Carbonic Anhydrase inhibitors.
* *Folic Acid and Folinic Acid:* plasma-phenytoin concentration possibly reduced by Folic acid and Folinic acid.
* *Hormone Antagonists:* metabolism of Toremifene possibly accelerated.
* *Lithium:* neurotoxicity may occur without increased plasma-lithium concentration.
* *Muscle Relaxants:* effect of non-depolarizing muscle relaxants antagonized (recovery from neuromuscular blockade accelerated).
* *Oestrogens and Progestogens:* metabolism of Gestrinone, Tibolone, and oral contraceptives accelerated (reduced contraceptive effect).
* *Sympathomimetics:* plasma-phenytoin concentration increased by Metheylphenidate.
* *Theophylline:* metabolism of Theophylline accelerated (reduced plasma-theophylline concentration).
* *Thyroxine:* metabolism of Thyroxine accelerated (may increase Thyroxine requirements in hypothyroidism).
* *Ulcer-healing Drugs:* Cimetidine inhibits metabolism (increased plasma-phenytoin concentration); Sucralfate reduces absorption; Omeprazole enhances effect of Phenytoin (interaction with Lansoprazole possibly differs).
* *Uricosurics:* Plasma-phenytoin concentration increased by Sulphinpyrazone.
* *Vaccines:* effect enhanced by influenza vaccine vitamins D requirements possibly increased.

Phytomenadione see Vitamins (Vitamins K).
Pilocarpine see Parasympathomimetics.

Pimecrolimus
Alcohol intolerance, described as flushing, rash, burning, itching, or swelling, has occurred rarely after the consumption of alcohol by patients using topical pimecrolimus.
Pindolol see Beta-blockers.
Pioglitazone see Antidiabetics
Piroxicam see NSAIDs.

Pitavastatin

The interactions of statins with other drugs are described under simvastatin. Pitavastatin is only marginally metabolised by the cytochrome P450 isoenzyme CYP2C9 and may not have the same interactions with CYP3A4 inhibitors as simvastatin. However, ciclosporin significantly increases pitavastatin exposure and the combination should be avoided. On theoretical grounds, use with ritonavir-boosted lopinavir is also contra-indicated. Rifampicin and erythromycin also increase pitavastatin exposure; if such combinations must be used, lower doses of pitavastatin should be used.

Pizotifen

Antihypertensives: hypotensive effect of adrenergic neurone blockers antagonized.

Polymyxins see Colisten.

Potassiam Salts (including salt substitutes)

* *ACE Inhibitors:* increased risk of hyperkalaemia.
* *Ciclosporin:* increased risk of hyperkalaemia.
* *Diuretics:* hyperkalaemia with potassium-sparing diuretics.

Prasugrel

- Analgesics: possible increased risk of bleeding when prasugrel given with NSAIDs
- Anticoagulants: possible increased risk of bleeding when prasugrel given with coumarins or phenindione
- Clopidogrel: possible increased risk of bleeding when prasugrel given with clopidogrel

Prazosin see Alpha-blockers (post synaptic).

Prednisolone see Corticosteroids.

Primaquine

Mepacrine: increased plasma concentration of Primaquine (risk of toxicity).

Primidone see Barbiturates and Primidone.

Probenecid

* *ACE Inhibitors:* reduced excretion of Captopril.
* *Analgesics:* Aspirin antagonizes effect; excretion of Indomethacin, Ketoprofen, Ketorolac (avoid concomitant use), and Naproxen delayed and increased plasma-NSAID concentrations.
* *Antibacterials:* reduced exertion of Cephalosporins, Cinoxacin, Ciprofloxacin, and Penicillins (increased plasma-concentrations); antagonism by Pyrazinamide.
* *Antivirals:* reduced excretion of Aciclovir, Vanciclovir, Zidovudine, and possibly Famciclovir and Zalcitabine (increased plasma concentrations).
* *Cytotoxics:* reduced excretion of Methotrexate (increased risk of toxicity).

Procainamide

ACE Inhibitors: increased risk of toxicity with captopril, especially in renal impairment.

* *Other Anti-arrhythmics:* Amiodarone increases Procainamide-plasma concentrations (increased risk of ventricular arrhythmias-avoid concomitant use); increased myocardial depression with any anti-arrhythmic.

* *Antibacterials:* increased risk of arrhythmias with Grepafloxacin (avoid concomitant use); Trimethoprim increases plasma concentration of Procainamide.
* *Antidepressants:* increased risk of ventricular arrhythmias with Tricyclics.
* *Antihistamines:* increased risk of ventricular arrhythmias with Mizolastine (avoid concomitant use).
* *Antimalarials:* increased risk of ventricular arrhythmias with Halofantrine.
* *Antipsychotics:* increased risk of ventricular arrhythmias –.avoid concomitant use with Pimozide, Sertindole or Thioridazine.
* *Beta-blockers:* increased risk of ventricular arrhythmias associated with Sotalol (avoid concomitant use).
* *Muscle Relaxants:* muscle relaxant effect enhanced.
  Parasympathomimetics: antagonism of effect of Neostigmine and Pyridostigmine.
* *Ulcer-healing Drugs:* Cimetidine inhibits excretion increased plasma-procainamide concentration).

Procarbazine
Alcohol: Disulfiram-like reaction.

Prochlorperazine see Antipsychotics.
Procyclidine see Antimuscarinics.

Progestogens (see also Contraceptives, Oral).
Antibacterials: metabolism accelerate by Rifampicin (reduced effect).
* *Antivirals:* Nevirapine accelerates metabolism of hormonal contraceptives (reduced contraceptive effect).
* *Ciclosporin:* increased plasma-ciclosporin concentration (inhibition of metabolism).
  Hormone Antagonists: Aminoglutethimide reduces plasma concentration of Medroxyprogesterone.

Promethazine see Antihistamines.

Propafenone
Propafenone is extensively metabolised by the cytochrome P450 enzyme system, mainly by the isoenzyme CYP2D6, although CYP1A2 and CYP3A4 are also involved. Interactions may therefore occur with other drugs that are metabolised by these enzymes. Plasma-propafenone concentrations may be reduced by enzyme inducers such as rifampicin; enzyme inhibitors, such as cimetidine, fluoxetine, quinidine, and HIV-protease inhibitors, may increase plasma-propafenoneconcentrations.Propafenone itself may alter the plasma concentrations of other drugs, including beta blockers, ciclosporin, desipramine, digoxin, theophylline, venlafaxine, and warfarin. The absorption of propafenone may be reduced by orlistat. There may be an increased risk of arrhythmias if propafenone is given with other antiarrhythmics or arrhythmogenic drugs.

Propantheline see Antimuscarinics.
Propofol see Anaesthetics, General.
Propranolol see Beta-blockers.

Prostaglandins
Oxytocin: uterotonic effect enhanced.

Proton Pump Inhibitors

Analgesics: plasma concentration of Omeprazole increased by Valdecoxib.
Antacids: possibly reduced absorption of Lansoprazole.
* *Anticoagulants:* effect of Warfarin enhanced by Omeprazole; interaction with Lansoprazole possibly differs.
* *Antiepileptics:* effects of Phenytoin enhanced by Esomeprazole and Omeprazole; interaction with Lansoprazole possibly differs.
Antifungals: absorption of Ketoconazole and possibly Itraconazole reduced.
Anxiolytics and Hypnotics: metabolism of diazepam possibly inhibited by Omeprazole and Esomeprazole (increased effect possible).
Cardiac Glycosides: plasma concentration of Digoxin possibly increased.
Oestrogens and Progestogens: manufacturer advises that Lansoprazole possibly accelerates metabolism of oral contraceptives.
Tacrolimus: Omeprazole possibly increases plasma-tacrolimus concentration.
Ulcer-healing Drugs: Sucralfate reduces absorption of Lansoprazole.

Protriptyline see Antidepressants, Tricyclic.
Pseudoephedrine see Sympathomimetics.
Pyrantel
* Piperazine: Piperazine opposes the anthelmintic actions of pyrantel.
*Aminophylline: A single case report describes rapidly increased theophylline levels in a child given pyrantel.
Pyrazinamide
Uricosurics: antagonism of effect of Probenecid and Sulphinpyrazone.

Pyridoxine see Vitamins.

Pyrimethamine
* *Antibacterials:* increased antifolate effect with Co-trimoxazole and Trimethoprim.
Antiepileptics: increased antifolate effect with Phenytoin.
Cytotoxics: increased antifolate effect with Methotrexate.

Quinidine
Antacids and Adsorbents: reduced excretion in alkaline urine(plasma-quinidine concentration occasionally increased);absorption possibly reduced by Kaolin (possibly reduced plasma concentration).
* *Other Anti-arrhythmics:* Amiodarone increases plasma-quinidine. concentrations(and increases risk of concentration of Propafenone increased ; increased myocardial depression with any anti-arrhythmic.
* *Antibacterials:* Rifampicin accelerate metabolism (reduced plasma-quinidine concentration).
Antidepressants: increased risk of ventricular arrhythmias with Tricyclics.
Antiepileptics: Phenobarbitone, Phenytoin, and Primidone accelerate metabolism (reduced plasma-quinidine concentration).
* *Antihistamines:* increased risk of ventricular arrhythmias with Mizolastine (avoid concomitant use).
* *Antimalarials:* increased risk of ventricular arrhythmias with Halofantrine and Mefloquine.
* *Antipsychotics:* increased risk of ventricular arrhythmias- avoid concomitant use with Pimozide, Sertindole or Thioridazine.
* *Antivirals:* increased risk of ventricular arrhythmias with Nelfinavir and Ritonavir (avoid concomitant use).
Barbiturates: see under Antiepileptics.
* *Beta-blockers:* increased risk of ventricular arrhythmias associated with Sotalol (avoid concomitant use).

* *Calcium-channel Blockers:* Nifedipine reduces plasma-quinidine concentration; Verapamil increases plasma-quinidine concentration (possibility of extreme hypotension).
* *Cardiac Glycosides:* plasma concentration of Digoxin increased (halve Digoxin maintenance dose).
* *Diuretics:* Acetazolamide reduces excretion (plasma-quinidine concentration occasionally increased); Quinidine toxicity increased if hypokalaemia occurs with Acetazolamide, loop diuretics, and Thiazides.
* *Muscle Relaxants:* muscle relaxant effect enhanced. *Parasympathomimetics:* antagonism of effect of Neostigmine and Pyridostigmine.
* *Ulcer-healing Drugs:* Cimetidine inhibits metabolism (increased plasma-quinidine concentration).

Quinine

* *Anti-arrhythmics:* plasma concentration of Flecainide increased ; increased risk of ventricular arrhythmias with Amiodarone (avoid concomitant use).
* *Antipsychotics:* increased risk of ventricular arrhythmias-avoid concomitant use with Pimozide.
* *Other Antimalarials:* see Halofantrine, Mefloquine.
* *Cardiac Glycosides:* plasma concentration of Digoxin increased (halve Digoxin maintenance of Digoxin increased use of quinine for cramps.
* *Ulcer-healing Drugs:* Cimetidine inhibits metabolism (increased plasma-quinine concentration).

Quinolones

* *Analgesics:* possible increased risk of convulsions with NSAIDs; manufacturer of Ciprofloxacin advises to avoid premedication with opioid analgesics (reduced plasma-Ciprofloxacin concentration).
  Antacids and adsorbents: Antacids reduce absorption of Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin and Ofloxacin.
* *Anti-arrhythmics:* increased risk of arrhythmias with drugs that prolong QT interval(avoid concomitant use with Moxifloxacin, Amiodarone, Disopyramide, Procainamide and Quinidine).
  Other Antibacterials: increased risk of ventricular arrhythmias with Moxifloxacin and parenteral Erythromycin (avoid concomitant use)
  Anticoagulants: anticoagulant effect of Warfarin enhanced by Ciprofloxacin, Nalidixic acid, Norfloxacin and Ofloxacin.
  Antidepressants: increased risk of ventricular arrhythmias with Moxifloxacin and tricyclic antidepressants (avoid concomitant use)

  Antidiabetics: effect of Glibenclamide possibly enhanced by Ciprofloxacin.
  Antiepileptics: Ciprofloxacin possibly alters plasma concentration of Phenytoin.
  Antimalarials: manufacturer of Artemether with Lumefantrine advises avoid concomitant use; increased ventricular arrhythmias with Moxifloxacin and Chloroquine, Mefloquine or Quinine (avoid concomitant use)
  Antipsychotics: increased risk of ventricular arrhythmias with Moxifloxacin and Haloperidol, Phenothiazines (avoid concomitant use).
* *Beta-blockers:* increased risk of ventricular arrhythmias with Moxifloxacin and Sotalol.(avoid concomitant use).
  Calcium Salts: reduced absorption of Ciprofloxacin.
* *Ciclosporin:* increased risk of nephrotoxicity.
  Cytotoxics: toxicity of Melphalan increased by Nalidixic acid.
* *$5HT_1$-Agonists:* Quinolones possibly inhibit metabolism of Zolmitriptan (reduce dose of Zolmitriptan).

Iron: absorption of Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin, and Ofloxacin reduced by oral iron.

* *Theophylline:* possible increased risk of convulsions; Ciprofloxacin and Norfloxacin increase plasma-theophylline concentration.
Ulcer-healing Drugs: Sucralfate reduces absorption of Ciprofloxacin, Levofloxacin, Moxifloxacin, Norfloxacin, and Ofloxacin.
Uricosurics: Probenecid reduces excretion of Ciprofloxacin, Nalidixic acid and Norfloxacin.
Zinc Salts: Zinc reduces absorption of Ciprofloxacin, Moxifloxacin and Norfloxacin.

Rabeprazole see Proton Pump Inhibitors

Raloxifen

Anticoagulants: antagonism of anticoagulant effect of Warfarin.

Raltegravir

Raltegravir is not a substrate for cytochrome P450 isoenzymes, and does not appear to interact with drugs metabolised by this mechanism. However, rifampicin induces the glucuronidase responsible for raltegravirmetabolism (UGT1A1) and reduces plasma concentrations ofraltegravir; if use with rifampicin cannot be avoided, increasing the dose of raltegravir may be considered.

- Antivirals: Plasma concentrations of raltegravir were modestly increased by atazanavir and ritonavir-boosted atazanavir in healthy subjects; this increase is not considered to be clinically significant.
  In a pharmacokinetic study, use of raltegravir andmaraviroc together resulted in decreased plasma concentrations of both drugs, although these changes were also not thought to be clinically significant.
- Gastrointestinal drugs: The solubility of raltegravir is pH-dependent, and use ofomeprazole has been noted to increase plasma concentrations of raltegravir in healthy subjects. However, some HIV-infected patients (and particularly those with AIDS) have increased gastric pH relating to their illness, and data from HIV-infected patients suggests acceptable safety and only modest pharmacokinetic interaction when gastric-acid reducing drugs are used withraltegravir. US licensed product information forraltegravir therefore suggests that no dose adjustment is needed whenraltegravir is used with gastric-acid reducing drugs, although UK licensed information has advised that such combinations should be avoided unless considered essential.

Ramipril see ACE Inhibitors.

Ranitidine see Histamine H_2-antagonists.

Ranolazine

- Anti-arrhythmics: manufacturer of ranolazine advises avoid concomitant use with disopyramide
- Antibacterials: plasma concentration of ranolazine possibly increased by clarithromycin and telithromycin; plasma concentration of ranolazine reduced by rifampicin
- Antidepressants: plasma concentration of ranolazine increased by paroxetine
- Antifungals: plasma concentration of ranolazine possibly increased by .itraconazole, posaconazole and voriconazole
- Antivirals: plasma concentration of ranolazine possibly increased by atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, ritonavir, saquinavir and tipranavir

- Beta-blockers: manufacturer of ranolazine advises avoid concomitant use with sotalol
- Calcium-channel Blockers: plasma concentration of ranolazine increased by diltiazem and verapamil (consider reducing dose of ranolazine)
- Cardiac Glycosides: ranolazine increases plasma concentration of digoxin
- Ciclosporin: plasma concentration of both drugs may increase when ranolazine given with ciclosporin
- Grapefruit Juice: plasma concentration of ranolazine possibly increased by grapefruit juice - manufacturer of ranolazine advises avoid concomitant use
- Lipid-regulating Drugs: ranolazine increases plasma concentration of simvastatin
- Tacrolimus: ranolazine increases plasma concentration of tacrolimus

Remifentanil see Opioid Analgesics.
Repaglinide see Antidiabetics.

Retinoids

Alcohol: Etretinate formed from Acitretin in presence of alcohol.
Antibacterials: possible increased risk of benign intracranial hypertension with Tetracyclines and Acitretin, Isotretinoin and Tretinoin.

* *Anticoagulants :* Acitretin possibly reduces anticoagulant effect of Warfarin.
* *Antiepileptics:* plasma concentration of Carbamazepine possibly reduced by Isotretinoin.
* *Cytotoxics:* Acitretin increases plasma concentration of Methotrexate (also increased risk of hepatotoxicity).
* *Oestrogens and Progestogens:* Tretinoin reduces efficacy of Progestogen only and possibly combined oral contraceptives.

Vitamins: risk of hypervitaminosis A with vitamin A and Acitretin, Isotretinoin and Tretinoin.

Rifabutin as for Rifampicin

Rifampicin

Analgesics: metabolism of methadone accelerated (reduced effect).
Antacids: reduced absorption of Rifampicin.

* *Anti-arrhythmics:* metabolism accelerated-reduced plasma concentrations of Disopyramide, Mexiletine, Propafenone, and Quinidine.
* *Other Antibacterials:* metabolism of Chloramphenicol accelerated by Rifampicin (reduced plasma concentration); plasma concentration of Dapsone reduced; plasma concentration of Rifabutin increased by Clarithromycin and possibly other Macrolides (risk of uveitis-reduce Rifabutin dose).
* *Anticoagulants:* metabolism of Nicoumalone and Warfarin accelerated (reduced anticoagulant effect).
* *Antidepressants:* metabolism of some Tricyclics accelerated by Rifampicin (reduced plasma concentration).
* *Antidiabetics:* metabolism of Chlorpropamide, Tolbutamide and possibly other Sulphonylureas accelerated (reduced effect); Rifampicin possibly reduces plasma concentration of Repaglinide (manufacturer advises avoid concomitant use).
* *Antiepileptics:* metabolism of Carbamazepine and Phenytoin accelerated (reduced plasma concentration).
* *Antifungals:* metabolism of Fluconazole, Itraconazole and Ketoconazole accelerated by Rifampicin (reduced plasma concentrations); plasma concentration of Rifampicin may be reduced by Ketoconazole; plasma concentration of Terbinafine reduced plasma concentration of Terbinafine

reduced by Rifampicin; plasma concentration of Rifabutin increased by Fluconazole and possibly other Triazoles (risk of uveitis - reduce Rifabutin dose).

* *Antipsychotics:* metabolism of Haloperidol accelerated by Rifampicin (reduced plasma concentration).
* *Antivirals:* concomitant administration of Indinavir and Rifabutin increases plasma-Rifabutin concentration and decreases plasma-indinavir concentration (reduce dose of Rifabutin and increase dose of Indinavir); metabolism of Indinavir enhanced by Rifampicin (plasma-indinavir concentration significantly reduced - avoid concomitant use); plasma concentration of Nelfinavir significantly reduced by Rifampicin (avoid concomitant use); plasma concentration of Rifabutin increased by Nelfinavir (halve Rifabutin dose); plasma concentration of Rifabutin increased by Ritonavir (risk of uveitis-avoid concomitant use); plasma concentration of Saquinavir reduced (avoid concomitant use).
* A*nxiolytics and Hypnotics:* metabolism of Diazepam and possibly other Benzodiazepines accelerated (reduced plasma concentration).
* *Atovaquone:* plasma concentration reduced by Rifampicin (possible therapeutic failure of Atovaquone).
* *Beta-blockers:* metabolism of Bisoprolol and Propranolol accelerated by Rifampicin (plasma concentrations significantly reduced).
* *Calcium-channel Blockers:* metabolism of Diltiazem, Nifedipine, and Verapamil and possibly Isradipine, Nicardipine (plasma concentrations significantly reduced).
* *Cardiac Glycosides:* metabolism of Digitoxin only accelerated (reduced effect).
* *Corticosteroids:* metabolism of Corticosteroids accelerated (reduced effect).
* *Ciclosporin:* metabolism accelerated (reduced plasma-ciclosporin concentration).
* *Cytotoxics:* manufacturer reports interaction with Azathioprine (transplants possibly rejected).
* *Lipid-regulating Drugs:* metabolism of Fluvastatin accelerated (reduced effect).
* *Oestrogens and Progestogens:* metabolism accelerated (contraceptive effect of both combined and Progestogen-only oral contraceptives reduced).
* *Tacrolimus:* Rifampicin decreases plasma-tacrolimus concentration.

Theophylline: metabolism accelerated by Rifampicin (reduced plasma-theophylline concentration).

Thyroxine: metabolism of Thyroxine accelerated by Rifampicin (may increase requirements in hypothyroidism).

Ulcer-healing Drugs: metabolism of Cimetidine accelerated by Rifampicin (reduced plasma concentration).

Rifaximin

There is no experience regarding administration of rifaximin to subjects who are taking another rifamycin antibacterial agent to treat a systemic bacterial infection. In vitro data show that rifaximin did not inhibit the major cytochrome P-450 (CYP) drug metabolizing enzymes (CYPs1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, and 3A4). In in vitro induction studies, rifaximin did not induce CYP1A2 and CYP 2B6 but was a weak inducer of CYP3A4.

In healthy subjects, clinical drug interaction studies demonstrated that rifaximin did not significantly affect the pharmacokinetics of CYP3A4 substrates, however, in hepatic impaired patients it cannot be excluded that rifaximin may decrease the exposure of concomitant CYP3A4 substrates administered (e.g. warfarin, antiepileptics, antiarrhythmics), due to the higher systemic exposure with respect to healthy subjects.

An in vitro study suggested that rifaximin is a moderate substrate of P-glycoprotein(P-gp) and metabolized by CYP3A4. It is unknown whether

concomitant drugs which inhibit P-gp and/or CYP3A4 can increase the systemic exposure of rifaximin.
The potential for drug-drug interactions to occur at the level of transporter systems has been evaluated in vitro and these studies suggest that a clinical interaction between rifaximin and other compounds that undergo efflux via P-gp and other transport proteins is unlikely (MDR1, MRP2, MRP4, BCRP and BSEP).

Risedronate sodium see Bisphosphonates
Risperidone see Antipsychotics
Ritodrine see Sympathomimetics, $Beta_2$ Sympathomimetics.

Ritonavir

* *Analgesics:* plasma concentration of Dextropropoxyphene, Pethidine and Piroxicam increased (risk of toxicity - avoid concomitant use); plasma concentrations of other opioid analgesics and other NSAIDs possibly increased.
* *Anti-arrhythmics:* increased plasma concentration of Amiodarone, Flecainide, Propafenone and Quinidine 9 increased risk of ventricular arrhythmia-avoid concomitant use).
* *Antibacterials:* plasma concentration of Rifabutin increased by Ritonavir (risk of uveitis - avoid concomitant use); plasma concentration of Macrolides possibly increased.
* *Anticoagulants:* plasma concentration of Warfarin and other anticoagulants possibly increased.
* *Antidepressants:* plasma concentration of SSRIs and Tricyclics possibly increased.
  Antidiabetics: plasma concentration of Tolbutamide possibly increased.
* Antiepileptics: plasma concentration of Carbamazepine possibly increased.
* *Antifungals:* plasma concentration of Imidazoles and Triazoles possibly increased.
* *Antihistamines:* plasma concentration of non-sedating antihistamines possibly increased.
* *Antipsychotics:* increased plasma concentration of Pimozide (risk of ventricular arrhythmias - avoid concomitant use); increased plasma concentration of Clozapine (risk of toxicity - avoid concomitant use); possibly increased plasma concentration of other antipsychotics.
* *Other Antivirals:* combination with Nelfinavir may lead to increased plasma concentration of either drug; Ritonavir increases plasma concentration of Saquinavir.
* *Anxiolytics and Hypnotics:* plasma concentration of Alprazolam, Clorazepate, Diazepam, Flurazepam, Midazolam and Zolpidem increased (risk of extreme sedation and respiratory depression – avoid concomitant use); plasma concentration of other anxiolytics and hypnotics possibly increased.
* *Calcium-channel Blockers:* plasma concentration of calcium-channel blocker possibly increased.
  Corticosteroids: plasma concentration of Dexamethasone and Prednisolone (and possibly other Corticosteroids) possibly increased.
* *Ciclosporin:* plasma-ciclosporin concentration possibly increased.
* *Ergotamine:* risk of ergotism - avoid concomitant use.
* *Oestrogens and Progestogens:* metabolism accelerated by Ritonavir (contraceptive effect of combined oral contraceptives reduced).
* *Tacrolimus:* plasma-tacrolimus concentration possibly increased.
* *Theophylline:* metabolism accelerated by Ritonavir (reduced plasma-theophylline concentration).

Rivaroxaban
Rivaroxaban is metabolised by the cytochrome P450 isoenzyme CYP3A4 and is also a substrate for P-glycoprotein. It should not be given with potent inhibitors of both CYP3A4 and P-glycoprotein, such as ketoconazole, itraconazole, posaconazole, voriconazole, or HIV-protease inhibitors, although it may be used cautiously with fluconazole. Drugs that inhibit only one of these pathways or are less potent inhibitors, such as clarithromycin and erythromycin, do not appear to have clinically relevant effects. Potent inducers of CYP3A4, such as rifampicin, may reduce the effect of rivaroxaban.
Caution is needed if rivaroxaban is given with other anticoagulants or with drugs that affect bleeding, including NSAIDs and antiplatelet drugs.
Rivstigmine see Parasympathomimetics.
Rizatriptan see $5HT_1$ Agonists.
Rocuronium see Muscle Relaxants(non-depolarizing).
Rofecoxib see NSAIDs.
Rosiglitazone see Antidiabetics
Roxithromycin see drug interactions of macrolide antibacterials, or see Erythromycin
Salbutamol see $Beta_2$ Sympathomimetics.
Salicylic acid There are no interaction messages
Salmeterol see $Beta_2$ Sympathomimetics.

Saquinavir
Note : Limited clinical data available, but possibly of interactions with number of drugs consult product literature for details.
* *Antibacterials:* metabolism accelerated by Rifampicin (reduced plasma concentration - avoid concomitant use).
* *Antiepileptics:* plasma concentration possibly reduced by Carbamazepine, Phenobarbitone and Phenytoin.
* *other Antivirals:* Nevirapine reduces plasma concentration of Saquinavir (avoid concomitant use); combination with Nelfinavir may lead to increased plasma concentration of Saquinavir.
  Barbiturates: see under Antiepileptics above.
* *Corticosteroids:* plasma concentration possibly reduced by Dexamethasone.

Selegiline
Note : Selegiline is an MAO-B inhibitor.
* *Analgesics:* hyperpyrexia and CNS toxicity with Pethidine (avoid concomitant use).
* *Antidepressants:* hypertension and CNS excitation with Fluoxetine, Paroxetine and Sertraline (Selegiline should not be started until 5 weeks after discontinuation of Fluoxetine, avoid Fluoxetine for 2 weeks after stopping Selegiline); hypotension with MAOIs; CNS toxicity reported with Tricyclic antidepressants.

Sertraline see Antidepressants, SSRI.
Sildenafil
- Alpha-blockers: enhanced hypotensive effect when sildenafil given with alpha-blockers (avoid alphablockers for 4 hours after sildenafil)
- Anti-arrhythmics: avoidance of sildenafil advised by manufacturer of disopyramide (risk of Ventricular arrhythmias)
- Antibacterials: plasma concentration of sildenafil increased by clarithromycin, erythromycin and telithromycin—reduce initial dose of sildenafil
- Antifungals: plasma concentration of sildenafil increased by itraconazole

- Antivirals: side-effects of sildenafil possibly increased by atazanavir; plasma concentration of sildenafil reduced by etravirine; plasma concentration of sildenafil possibly increased by fosamprenavir; plasma concentration of sildenafil increased by indinavir—reduce initial dose of sildenafil; plasma concentration of sildenafil significantly increased by ritonavir— avoid concomitant use; increased risk of ventricular arrhythmias when sildenafil given with saquinavir— avoid concomitant use; avoidance of sildenafil advised by manufacturer of telaprevir Bosentan: plasma concentration of sildenafil reduced by bosentan
- Calcium-channel Blockers: enhanced hypotensive effect when sildenafil given with amlodipine
- Cobicistat: plasma concentration of sildenafil possibly increased by cobicistat manufacturer of cobicistat advises avoid concomitant use of sildenafil for pulmonary arterial hypertension or reduce dose of sildenafil for erectile dysfunction
- Dapoxetine: avoidance of sildenafil advised by manufacturer of dapoxetine
- Grapefruit Juice: plasma concentration of sildenafil possibly increased by grapefruit juice
- Nicorandil: sildenafil significantly enhances hypotensive effect of nicorandil (avoid concomitant use)
- Nitrates: sildenafil significantly enhances hypotensive effect of nitrates (avoid concomitant use)
- Ulcer-healing Drugs: plasma concentration of sildenafil increased by cimetidine (consider reducing dose of sildenafil)

Simvastatin see Statins.
Sodium Aurothiomalate
Note : Increased risk of toxicity with other nephrotoxic and meylosuppressive drugs.

Sodium Bicarbonate see Antacids.
Sodium Fusidate
Although the exact metabolic pathways of fusidic acid are not known, an interaction has been suspected with drugs metabolised by the hepatic cytochrome P450 isoenzyme CYP3A4, and UK licensed product information suggests avoiding their use with fusidic acid.
Sodium Valproate see Valproate.

Somatropin
Corticosteroids: may inhibit growth promoting effect of Somatropin.
Sotalol see Beta-blockers.
Sparfloxacin *see Ciprofloxacin*
Spectinomycin
* *Botulinum Toxin:* neuromuscular block enhanced (risk of toxicity).
* *Lithium:* increased toxicity reported.

Spiramycin see drug interactions of macrolide antibacterials, or see Erythromycin
Spironolactone see Diuretics(potassium-sparing).

Statins
Note: Grapefruit juice increases plasma concentration of Simvastatin.
* *Antibacterials:* metabolism of Fluvastatin accelerated by Rifampicin(reduced effect); Clarithromycin and Erythromycin increase risk of myopathy with Simvastatin (avoid concomitant use); Erythromycin possibly increases risk of

myopathy with Atorvastatin; Clarithromycin increases plasma concentration of Atorvastatin.

* *Anticoagulants:* effect of Nicoumalone and Warfarin enhanced by Simvastatin.
* *Antifungals*: Itraconazole, Ketoconazole and possibly other Imidazoles and Triazoles increase risk of myopathy with Simvastatin – avoid concomitant use of Itraconazole, Ketoconazole or Miconazole with Simvastatin; Itraconazole and possibly other Imidazoles and Triazoles increase risk of myopathy with Atorvastatin – avoid concomitant use of Itraconazole with Atorvastatin.
  Cardiac Glycosides: plasma-digoxin concentration possibly increased by Atorvastatin.
* *Ciclosporin:* increased risk of myopathy.
  Cytotoxics: plasma concentration of Simvastatin increased by Imatinib.
* *Other Lipid-regulating Drugs:* increased risk of myopathy with Fibrates and Nicotinic acid.

Streptomycin see Aminoglycosides.

Sucralfate

Antibacterials: reduced absorption of Ciprofloxacin, Grepafloxacin, Levofloxacin, Norfloxacin, Ofloxacin, and Tetracycline.

* *Anticoagulants:* absorption of Warfarin possibly.
* *Antiepileptics:* reduced absorption of Phenytoin.
  Antifungals: reduced absorption of Ketoconazole.
  Cardiac Glycosides: absorption of Cardiac Glycosides possibly reduced
  Thyroxine: reduced absorption of Thyroxine.
  Other Ulcer-healing Drugs: reduced absorption of Lansoprazole.

Sulfadoxine see Co-trimoxazole and Sulphonamides.
Sulindac see NSAIDs.
Sulphadiazine see Co-trimoxazole and Sulphonamides.
Sulphadimidine see Co-trimoxazole and Sulphonamides.

Sulphasalazine

Cardiac Glycosides: absorption of Digoxin possibly reduced.

Sulphonamides see Co-trimoxazole and Sulphonamides.
Sulphonylureas see Antidiabetics.
Sulpiride see Antipsychotic.
Sumatriptan see $5HT_1$ Agonists.
Suxamethonium see Muscle Relaxants.

Sympathomimetics (see below for $Beta_2$- Sympathomimetics).

$Alpha_2$-adrenoceptor Stimulants: possible risk of hypertension with Adrenaline and Noradrenaline.

* *Anaesthetics:* risk of arrhythmias if adrenaline and Isoprenaline given with volatile liquid anaesthetics such as halothane.
* *Antidepressants:* with Tricyclics administration of adrenaline and Noradrenaline may cause hypertension and arrhythmias (but local anaesthetics with adrenaline appear to be safe); methylphenidate may inhibit metabolism of Tricyclics; with MAOIs administration of inotropics such as Dopamine and Dopexamine may cause hypertensive crisis; also with MAOIs administration of dexamphetamine and other Amphetamines, Ephedrine, Isometheptene, Methylphenidate, Phentermine, Phenylephrine, Phenylpropanolamine, and Pseudoephedrine may

cause hypertensive crisis(these drugs are contained in anorectics or cold and cough remedies).

Antiepileptics: methylphenidate increases plasma concentration of Phenytoin and possibly of Phenobarbitone and Primidone.

* *Antihypertensives:* Sympathomimetics in anorectics and cold and cough remedies (see above) and methylphenidate antagonize hypotensive effect of adrenergic neurone blockers.

Barbiturates: see under Antiepileptics, above.

* *Beta-blockers:* severe hypertension with Adrenaline and Noradrenaline and possibly with Dobutamine (especially with non-selective beta-blockers).

Corticosteroids: ephedrine accelerates metabolism of Dexamethasone.

* *Dopaminergics:* increased risk of toxicity when Isometheptene or Phenylpropanolamine given with Bromocriptine; effect of Adrenaline, Dobutamine, Dopamine, Isoprenaline and Noradrenaline possibly enhanced by Entacapone.

Orlistat: manufacturer advises avoid concomitant use with Phentermine.

Doxapram: risk of hypertension.

Oxytocin: hypertension with vasoconstrictor Sympathomimetics.

* *Other Sympathomimetics:* Dopexamine possibly potentiates effect of Adrenaline and Noradrenaline.

Sympathomimetics, Beta$_2$

Corticosteroids: increased risk of hypokalaemia if high doses of Corticosteroids given with high doses of Bambuterol, Eformoterol, Fenoterol, Reprotrol, Ritodrine, Salbutamol, Salmeterol, Terbutaline and Tulobuterol.

Diuretics: increased risk of hypokalaemia if with high doses of Bambuterol, Eformoterol, Fenoterol, Reproterol, Ritodrine, Salbutamol, Salmeterol, Terbutaline, and Tulobuterol.

Muscle Relaxants: effect of Suxamethonium enhanced by Bambuterol.

Theophylline: increased risk of hypokalaemia if given with high doses of Bambuterol, Eformoterol, Fenoterol, Reproterol, Ritodrine, Salbutamol, Salmeterol, Terbutaline, and Tulobuterol.

Tamoxifen

* *Anticoagulants:* anticoagulant effect of Nicoumalone and Warfarin enhanced.

Other Hormone Antagonists: Aminoglutethimide reduces plasma-tamoxifen concentration.

Terazosin see Alpha-blockers (post-synaptic).

Terbinafine

Antibacterials: plasma concentration reduced by Rifampicin.

Ulcer-healing Drugs: plasma concentration increased by Cimetidine.

Terbutaline see Sympathomimetics, Beta$_2$.

Testosterone

* *Anticoagulants:* anticoagulant effect of Warfarin, Nicoumalone and Phenindione enhanced.

Antidiabetics: hypoglycemic effect possibly enhanced.

Tetracyclines

ACE Inhibitors: Quinapril reduces absorption (tablets contain Magnesium Carbonate excipient).

Antacids and Adsorbents: reduced absorption with antacids and possibly with Kaolin.
Anticoagulant: see Phenindione and Warfarin.
Antiepileptics: Carbamazepine, Phenobarbitone and Phenytoin increase metabolism of Doxycycline (reduced plasma concentration).
Atovaquone: plasma-atovaquone concentration reduced by tetracycline.
Barbiturates: see under Antiepileptics.
Calcium Salts: reduced absorption of Tetracyclines.
* *Ciclosporin:* Doxycycline possibly increases plasma-ciclosporin concentration.
Dairy products: reduced absorption (except Doxycycline and Minocycline).
Iron: absorption of oral iron reduced by Tetracyclines and vice versa.
Oestrogens and Progestogens: see Contraceptives, Oral (main list).
Retinoids: possible increased risk of benign intracranial hypertension with Tetracyclines and Acitretin, Isotretinoin and Tretinoin.
Ulcer-healing Drugs: Tripotassium Dicitrato-bismuthate and Sucralfate reduce absorption.
Zinc Salts: reduced absorption (and vice versa).

Theophylline

Anaesthetics: increased risk of arrhythmias with halothane.
Anthelmintics: Thiabendazole may increase plasma-theophylline concentration.
Anti-arrhythmics: antagonism of anti-arrhythmic effect of adenosine; plasma-theophylline concentration increased by Mexiletine and Propafenone; plasma-theophylline concentration reduced by Moracizine.
* *Antibacterials:* possible increased risk of convulsions with Quinolones; plasma-theophylline concentration increased by Ciprofloxacin, Clarithromycin, Erythromycin (if erythromycin given by mouth, also decreased plasma-erythromycin concentration), and Norfloxacin and possibly increased by Isoniazid; plasma-theophylline concentration reduced by Rifampicin.
* *Antidepressants:* plasma-theophylline concentration increased by Fluvoxamine (concomitant use should usually be avoided, but where not possible halve theophylline dose and monitor plasma-theophylline concentration) and Viloxazine.
Antiepileptics: plasma-theophylline concentration reduced by Carbamazepine, Phenobarbital and Phenytoin.
* *Antifungals:* plasma-theophylline concentration possibly increased by Fluconazole and Ketoconazole.
* *Antivirals:* plasma-theophylline concentration reduced by Ritonavir.
Barbiturates: see under Antiepileptics.
Beta-blockers: should be avoided on pharmacological grounds (bronchospasm).
* *Calcium-channel Blockers:* plasma-theophylline concentration increased by Diltiazem, Verapamil, and possibly other calcium-channel blockers.
Disulfiram: increased plasma-theophylline concentration.
Doxapram: increases CNS stimulation.
Hormone Antagonists: plasma-theophylline concentration reduced by Aminoglutethimide.
Interferons: plasma-theophylline concentration increased by interferon alfa.
Leukotriene Antagonists: Zafirlukast possibly increases plasma-theophylline concentration; plasma-zafirlukast concentration reduced.
Lithium: Lithium excretion accelerated (reduced plasma-lithium concentration).
Nicotine and Tobacco: plasma-theophylline concentration reduced by tobacco smoking.
Oestrogens and Progestogens: plasma-theophylline concentration increased by combined oral contraceptives.

Sympathomimetics: increased risk of hypokalaemia if theophylline given with high doses of Bambuterol, Eformoterol, Fenoterol, Reproterol, Ritodrine, Salbutamol, Salmeterol, Terbutaline and Tulobuterol.

* *Ulcer-healing Drugs:* plasma-theophylline concentration increased by cimetidine.
Uricosurics: plasma-theophylline concentration increased by Cimetidine.
Vaccines: plasma-theophylline concentration occasionally increased by influenza vaccine.

Thiabendazole

Theophylline: plasma concentration may be increased.

Thioacetazone may enhance the ototoxicity of streptomycin

Tioconazole there are no interaction messages

Thiopentone see Anaesthetics, General.

Thioridazine see Antipsychotics.

Thyroxine

Anion-exchange Resins: Cholestyramine reduces absorption of Thyroxine.
Antibacterials: Rifampicin accelerates metabolism of Thyroxine (may increase requirements in hypothyroidism).

* *Anticoagulants:* effect of Nicoumalone, Phenindione and Warfarin enhanced.
Antidepressants: manufacturer of Lofepramine advises avoid Thyroxine.
Antiepileptics: Carbamazepine, Phenobarbital and Phenytoin accelerate. metabolism of Thyroxine (may increase requirements in hypothyroidism).
Barbiturates: see under Antiepileptics.
Beta-blockers: metabolism of Propranolol accelerated (reduced effect).
Ulcer-healing Drugs: Sucralfate reduces absorption of Thyroxine.

Timolol see Beta-blockers.

Tinidazole

Alcohol: possibly Disulfiram-like reaction.

Tizanidine see Muscle Relaxants.

Tobramycin see Aminoglycosides.

Tolbutamide see Antidiabetics (sulphonylurea).

Torasemide see Diuretics (loop)

Tramadol see Opioid Analgesics.

Tranexamic

Drugs with actions on haemostasis should be given with caution to patients on antifibrinolytic therapy. The risk of thrombosis may be increased if tranexamic acid is given with factor IX complex concentrates or factor VIII inhibitor bypassing fraction, and such combinations are not recommended. Antifibrinolytics and thrombolytics have antagonistic effects, and concomitant use may reduce the efficacy of both. The potential for thrombus formation may be increased by oestrogens.
*Retinoids: Antifibrinolytics should be used with caution in patients receiving oral tretinoin as thrombotic events have been reported in patients being treated with tranexamic acid and tretinoin.

Tretinoin see Retinoids.

Triamcinolone see Corticosteroids.

Trifluoperazine see Antipsychotics

Trimetaphan

Trimetaphan should be used with caution in patients being treated with other antihypertensives, drugs that depress cardiac function, or muscle relaxants, and in those taking NSAIDs or corticosteroids. The hypotensive effect is enhanced by general and spinal anaesthetics. Adrenaline should not be infiltrated locally at the site of incision when trimetaphan is being given since this may antagonise the effect of trimetaphan.

Trimetazidine no clinically significant drug interaction is reported.

Trimethoprim

Anti-arrhythmics: plasma concentration of Procainamide increased.
Anticoagulants: effect of Nicoumlone and antifolate effect of Phenytoin increased.
* *Antimalarials:* increased risk of antifolate effect with Pyrimethamine (in Fansidar® and Maloprim).
Antivirals: plasma concentration of Lamivudine and possibly Zalcitabine increased - avoid high-dose Co-trimoxazole with Lamivudine.
* *Ciclosporin:* increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous Trimethoprim.
Cytotoxics: antifolate effect of Methotrexate increased.

Trimipramine see Antidepressants, Tricyclic.
Tropicamide see Antimuscarinics.
Tulobuterol see Sympathomimetics, $Beta_2$.
Ulcer-healing Drugs see individual drugs.
Uricosurics see individual drugs.
Vaccines
For a general warning on live vaccines and Immunoglobulins, see under Normal Immunoglobulin.

Valdecoxib see NSAIDs
Valproate

Analgesics: aspirin enhances effect.
Anion- exchange Resins: Cholestyramine possibly reduces absorption.
Antibacterials: erythromycin possibly inhibits metabolism (increased plasma-valproate concentration).
Anticoagulants: anticoagulant effect of Nicoumalone and Warfarin possibly increased.
* *Antidepressants:* antagonism of anticonvulsant effect (convulsive threshold lowered).
* *Other Antiepileptics:* concomitant administration of two or more antiepileptics may enhance toxicity without a corresponding increase in antiepileptics effect; Moreover, interactions between individual antiepileptics can complicate monitoring of treatment; interactions include enhanced effects, increased sedation, and reductions in plasma concentrations.
* *Antimalarials:* Chloroquine and Mefloquine antagonize anticonvulsant effect.
* *Antipsychotics:* antagonism of anticonvulsant effect (convulsive threshold lowered).
Antivirals: plasma concentration of Zidovudine possibly increased (risk of toxicity).
Ulcer-healing Drugs: Cimetidine inhibits metabolism (increased plasma-valproate concentration).

Valsartan see ACE Inhibitors and Angiotensin-II Antagonists.

Vancomycin

Anaesthetics: hypersensitivity-like reactions can occur with concomitant Vancomycin infusion.
Anion-exchange Resins: Aminoglycosides and Capreomycin.
Diuretics: increased risk of ototoxicity with Loop diuretics.

Vecuronium see Muscle Relaxants (non-depolarizing).
Verapamil see Calcium-channel Blockers.

Vincristine

Antifungals: Itraconazole may inhibit metabolism (increased risk of neurotoxicity).

Vitamins

* *Anticoagulants:* anticoagulant effect of Nicoumalone, Phenindione, and Warfarin antagonized by vitamin K (present in some enteral feeds).
Antiepileptics: Vitamin D requirements possibly increased by Carbamazepine, Phenobarbital and Phenytoin.
Barbiturates: see Antiepileptics.
Diuretics: increased risk of hypercalcaemia if Thiazides given with vitamin D.
Dopaminergics: effect of Levodopa antagonized by pyridoxine (unless a dopa decarboxylase inhibitor also given).
Retinoids: risk of hypervitaminosis A with Vitamin A and Acitretin, Isotretinoin and Tretinoin.

Warfarin and Other Coumarins

Note : Change in patient's clinical condition particularly associated with liver disease, intercurrent illness, or drug administration, necessitates more frequent testing. Major changes in diet (especially involving salads and vegetables) and in alcohol consumption may also affect Warfarin control.

* *Alcohol:* enhanced anticoagulant effect with large amounts (see also above).
* *Allopurinol:* anticoagulant effect possibly enhanced.
* *Anabolic Steroids:* Oxymetholone, Stanozolol and others enhance anticoagulant effect.
* *Analgesics:* Aspirin increases risk of bleeding due to antiplatelet effect ; anticoagulant effect seriously enhanced by Azapropazone (avoid concomitant use) and possibly enhanced by Diclofenac, Diflunisal, Flurbiprofen, Ibuprofen, Mefenamic acid, Meloxicam, Piroxicam, Sulindac, and other NSAIDs; anticoagulant effect possibly also enhanced by Dextropropoxyphene and by prolonged regular use of Paracetamol; increased risk of hemorrhage with parenteral Diclofenac and Ketorolac(avoid concomitant use).
* *Anion-exchange Resins:* Cholestyramine may enhance or reduce anticoagulant effect.
* *Anti-arrhythmics:* Amiodarone and Propafenone enhance anticoagulant effect; Quinidine may enhance anticoagulant effect.
* *Antibacterials:* anticoagulant effect reduced by Rifampicin; anticoagulant effect enhanced by Cephamandole, Chloramphenicol, Ciprofloxacin, Co-trimoxazole, Erythromycin, Metronidazole, Ofloxacin, and Sulphonamides; anticoagulant effect possibly also enhanced by Aztreonam, Clarithromycin and some other Macrolides, Nalidixic acid, Neomycin, Norfloxacin. Tetracyclines, and Trimethoprim; although studies have failed to demonstrate interaction, common experience in anticoagulant clinics is that INR can be altered following course of oral broad-spectrum antibiotic, such as Ampicilli (may also apply to antibiotics given for local action on gut such as Neomycin).

* *Antidepressants:* SSRIs and Viloxazine possibly enhance anticoagulant effect
  Antidiabetics: possibly enhanced hypoglycemic effects of Sulphonylureas and changes to anticoagulant effect.
* *Antiepileptics:* reduced anticoagulant effect with Carbamazepine and Phenobarbital; anticoagulant effect possibly increased by Valproate; both reduced and enhanced effects reported with Phenytoin.
* *Antifungals:* anticoagulant effect reduced by Griseofulvin; anticoagulant effect enhanced by Fluconazole, Itraconazole, Ketoconazole, and Miconazole (note: oral gel absorbed).
* *Antimalarials:* anticoagulant effect possibly enhanced by Proguanil.
* *Antiplatelet Drugs:* Aspirin, Clopidogrel and Dipyridamole increase risk of bleeding due to antiplatelet effect.
* *Antivirals:* Ritonavir possibly increases plasma concentration.
  Anxiolytics and Hypnotics: Chloral may transiently enhance anticoagulant effect
  Barbiturates: Anticoagulant effect reduced.
* *Corticosteroids:* anticoagulant effect possibly altered.
* *Cytotoxics:* anticoagulant effect possibly enhanced by Ifosfamide.
* *Disulfiram:* enhanced anticoagulant effect.
* *Hormone Antagonists:* Aminoglutethimide reduces anticoagulant effect; Danazol, Flutamide, Tamoxifen and possibly Bicalutamide and Toremifene enhance anticoagulant effect.
  Leukotriene Antagonists: Zafirlukast enhances anticoagulant effect of Warfarin.
* *Lipid-regulating Drugs:* Fibrate group and Simvastatin enhance anticoagulant effect.
  Raloxifene: antagonism of anticoagulant effect.
* *Retinoids:* Acitretin possibly reduces anticoagulant effect.
  Rowachol: possibly reduced anticoagulant effect.
* *Testosterone:* anticoagulant effect of Warfarin and Nicoumalone enhanced.
* *Thyroxine:* enhanced anticoagulant effect.
* *Ulcer-healing Drugs:* Sucralfate possibly reduces anticoagulant effect (reduced absorption); Cimetidine and Omeprazole enhance anticoagulant effect.
* *Uricosurics:* Sulphinpyrazone enhances anticoagulant effect.
  Vaccines: Influenza vaccine occasionally enhances anticoagulant effect.
  Vitamins: Vitamin K reduces anticoagulant effect; major changes in diet. (especially involving vegetables) may affect control; vitamin K also present in some enteral feeds.

Xamoterol

Beta-blockers: antagonism of effect of Xamoterol and reduction in beta-blockade.

Xylometatzoline see Sympathomimetics.
Zafirlukast see Leukotriene Antagonists.

Zalcitabine

Note : Clinical data limited. Avoid use with other drugs that have potential to cause peripheral neuropathy or pancreatitis-for further details consult product literature.

Antacids: possibly reduce absorption.
Antibacterials: Trimethoprim possibly increases plasma concentration of Zalcitabine.
Uricosurics: Probenecid possibly increases plasma concentration of Zalcitabine.

Zidovudine

Note : Increased risk of toxicity with nephrotoxic and myelosuppressive drugs; for further details, consult product literature.

Analgesics: increased risk of haematological toxicity with NSAIDs; methadone possibly increases plasma-zidovudine concentration.
Antibacterials: Clarithromycin tablets reduce absorption of Zidovudine.
Antiepileptics: plasma-phenytoin concentrations increased or decreased; plasma-Zidovudine concentration possibly increased by Valproate (risk of toxicity).
Antifungals: plasma concentration of Zidovudine increased by Fluconazole (increased risk of toxicity).
* *Other Antivirals:* profound myelosuppression with Ganciclovir (if possible avoid concomitant administration, particularly during initial Ganciclovir therapy).
Uricosurics: Probenecid increases plasma-zidovudine concentration and risk of toxicity.

Zinc

Antibacterials: reduced absorption of Ciprofloxacin, Moxifloxacin and Norfloxacin, Tetracyclines reduce absorption of zinc (and vice versa).
Iron: reduced absorption of oral Iron (and vice versa).
Penicillamine: reduced absorption of Penicillamine.

Zoledronic Acid see Bisphosphonates
Zopiclone see Anxiolytics and hypnotics.
Zuclopenthixol see Antipsychotics.

Appendix- 3

LIVER DISEASES

Drug induced hepatotoxicity has been associated with over 600 drugs. Drugs can cause direct cellular injury to the liver or otherwise interfere with its function. Acute liver injury can be cytitoxic or cholestatic. Cytotoxic injury involves direct injury to the hepatocytes with necrosis that can be localized or diffuse throughout the liver. Prominent signs and symptoms include fatigue, anorexia, nausea and jaundice.Cholestatic injury results in a characteristic decrease in bile flow. Hepatic injury of this type leads to jaundice and pruritus. Chronic liver damage consists of a group of disorders including chronic hepatitis, steatosis. Pseudo-alcoholic liver diseases, granulomatous disease and cirrosis. Chronic lesions can result from continued or repeated exposure to hepatotoxic agents.

Liver injury occurs as the dose of some drugs is increased causing *centrizonal necrosis* with paracetamol in overdose and also carbon tetrachloride., Isoniazid, Methyl dopa and Phenytoin have been associated with direct cytotoxic reactions that led to mortality rates over 10% or hogher. *Hepatocellular necrosis* with salicylates, particularly in patients with collagen diseases, when more than 2gm/day are taken. *Fatty change* in liver cells and *Hepatic failure* occur with tetracyclines with high doses. *Acute Hepatocellular necrosis* can be induced by several drugs including general anaesthetics (halothane), antiepileptics (carbamazepine, phenytoin, sodium valporate, phenobarbitone), antidepressants (MAO inhibitors), anti-inflammatory drugs (indomethacin, ibuprofen), antimicrobials (isoniazid, sulphonamides, nitrofurantoin) and cardiovascular drugs (methyldopa, hydralazine). *Chronic active hepatitis* may develop with prolonged use of methyldopa, isoniazid, dantrolene. *Hepatic fibrosis or cirrhosis* may be caused by prolonged intake of excess of alcohol and therapeutic use of methotrexate (for psoriasis). *Benign liver tumours* may develop when synthetic androgen, e.g. anabolic steroids usually in high doses and oral contraceptives are used for more than five years; there is also increased risk of hepatocellular carcinoma, although the absolute risk of either complication is very low.

It is especially important that drugs should be prescribed for patients with liver disease only if there is a real need. Patients at greatest risk are those with ascites, jaundice or evidence of encephalopathy. Pharmacokinetic and pharmacodynamic changes are caused by liver diseases which may affect adversely to other cells and organs.

Central Nervous System. The brain receives concentrations of toxic substances (ammonia, amines) to which it is normally not exposed, as a result of failure of liver cells to metabolise naturally occuring substances and also of shunting of blood from the portal to the systemic circulation.
Opioids should be avoided as comma may occur, but if an opioid is essential, pethidine is probably less dangerous than morphine. Lorazepam and oxazepam are preferred as anxiolytics and temazepam as a hypnotic. Antiepileptic drugs should be monitored with particular care. Phenobarbitone may induce comma. A tricyclic antidepressant may be used when anti-depressant therapy is deemed necessary but MAO inhibitors are hazardous.

Cardiovascular System. Beta-adrenoceptor blockers (e.g. propranolol, labetalol etc) that are metabolized by liver should be given in reduced initial oral dose, as should calcium channel antagonists, e.g. nicardipine, nifedipine, or verapamil.

Gastrointestinal System. Antacids that contain much sodium may cause fluid retention and those containing aluminium and calcium may constipate, which predisposes to encephalopathy as there is greater opportunity for absoption of toxic substances from the gut.

Infections. Avoid or use in reduced doses of drugs that have known risk of hepatotoxicity, e.g. isoniazid, erythromycin, rifampicin, tetracyclines.

Endocrine System. Avoid C-17α-substituted androgens and anabolic steroids which are hepatoxic. It is better to avoid combined oral contraceptives especially in cholestatic liver disease. Metformin is normally inactivated by the liver and should be avoided as it may cause lactic acidosis.

Ascites. Abrupt diuresis, e.g. with large doses of a loop diuretic, may precipitate electrolyte imbalance, renal dysfunction and hepatic encephalopathy. In patients who fail to respond or who develop adverse effects of diuretic therapy, up to 4-6 litres of ascitic fluid may be removed per day by paracentesis, with simultaneous IV infusion of albumin (6-8 gm per litre of ascitic fluid) to prevent hypovolaemia.

Portal hypertension and variceal bleeding. Bleeding from rupture of varices is serious, the mortality from an initial event being up to 50%, and 30% for subsequent bleeds. If endoscopic expertise is available, bleeding from oesophageal varices can be stopped by injection of a sclerosing substance or by band ligation.

Viral hepatitis. Chronic hepatitis caused by hepatitis B, C or D may lead to cirrhosis, hepatocellular failure or hepatocellular carcinoma. Collectively, hepatitis is probably the commonest of serious viral diseases in general, and constitutes a major health problem.

The list of drugs to be avoided or used with caution in liver disease is given below based on current information concerning the use of these drugs in therapeutic dosage:

Drugs	**Comment**
Acamprosate	Avoid.
Acarbose	Avoid.
ACE inhibitors	Most of the ACE inhibitors are associated with liver injury on chronic use. Use cilazapril, enalapril, fosinopril, imidapril, moexipril, perindopril, quinapril, ramipril, trandolapril and monitoring is required for the patients with impaired liver functions.
Acitretin	Avoid, further impairment of liver function may occur.
Alprazolam	See Anxiolytics and Hypnotics.
Altretamine	Rare reports of hepatotoxicity.
Aminophylline	See Theophylline.
Amitriptyline	See Antidepressants, Tricyclics.
Amlodipine	Half-life prolonged, may need dose reduction.
Anabolic Steroids	Preferably avoid, dose related toxicity.
Androgens	Avoid, dose related toxicity with some, and produce fluid retention.
Antacids	In patients with fluid retention, avoid those containing large amounts of sodium e.g. magnesium trisilicate mixture.
Anticoagulants, Oral	Avoid in severe liver disease, especially if prothrombin time already prolonged.

Antidepressants, SSRI	Reduce dose or avoid in severe liver disease.
Antidepressants, tricyclic (and related)	Tricyclics preferable to MAOIs but sedative effects are increased (avoid in severe liver disease.)
Antipsycotics	All can precipitate coma; phenothiazines are hepatotoxic.
Anxiolytics and hypnotics	All can precipitate coma; small dose of oxazepam or temazepam is probably the safest; reduce oral dose of clomethiazole or zopiclone or avoid in liver injury).
Aspirin	Avoid, increased risk of gastro-intestinal bleeding.
Atorvastatin	See Statins.
Azathioprine	May need dose reduction.
Azithromycin	Avoid; jaundice is reported.
Bendrofluazid	See Thiazides.
Bromazipam	See Anxiolytic and Hypnotics.
Budesonide	Plasma concentration of Budesonide may increase on oral administration.
Bupivacaine	See Lidocaine.
Buprenorphine	See Opioid Analgesics.
Carbamazepine	Metabolism is impaired in advanced liver disease.
Carvedilol	Avoid.
Ceftriaxone	Reduce dose and monitor plasma concentration in both hepatic and severe renal impairment.
Celecoxib	See NSAIDs.
Chloramphenicol	Avoid. Increased risk of bone-marrow depression.
Chlorpheniramine	Sedation inappropriate in severe liver disease, avoid.
Chlorpromazine	See Antipsychotics.
Chlorpropamide	See Sulphonylureas.
Cilazapril	See ACE Inhibitors.
Cimetidine	Increased risk of confusion; reduce dose.
Cinnarizine	Sedation inappropriate in severe liver disease;-avoid.
Ciprofloxacin	See Quinolones.
Clarithromycin	Hepatic dysfunctions including jaundice are reported.
Clobazam	See Anxiolytics and Hypnotics.
Clomipramine	See Antidepressants, Tricyclic.
Clozapine	Initial dose of 12.5mg daily can be increased slowly with regular monitoring of liver function; avoid in symptomatic or progressive liver disease or liver failure.
Cyclophosphamide	Reduce dose.
Cyclosporin	May need dose adjustment.
Cytarabine	Reduce dose.
Dalteparin	See Heparin.
Daunorubicin	Reduce dose.
Dextromethorphan	See Opioid Analgesics.
Diazepam	See Anoxiolytics and Hypnotics.
Diclofenac	See NSAIDs.
Diltiazem	Reduce dose.
Diphenhydramine	Caution in mild to moderate liver disease; avoid in severe liver disease if sedation is inappropriate.
Disopyramide	Half-life is prolonged; may need dose reduction.
Docetaxel	Monitor liver function; reduce dose according to liver enzymes; avoid in severe hepatic impairment.
Doxazosin	No information, manufacturer advises caution.
Doxycycline	See Tetracycline.
Droperidol	See Antipsychotics.

Enalapril	See ACE Inhibitors.
Enoxaparin	See Heparin.
Entacapone	Avoid.
Epoetin	Manufacturers advise caution in chronic liver failure.
Ergometrine	Avoid in severe liver disease.
Ergotamine	Avoid in severe liver disease; risk of toxicity is increased.
Erythromycin	May cause idiosyncratic hepatotoxicity.
Estradiol	See Oestrogens.
Estriol	See Oestrogens.
Felodipine	Reduce dose.
Fentanyl	See Opioid Analgesics.
Flucloxacillin	May cause cholesttic jaundice.
Fluconazole	Toxicity with related drugs.
Fluoxetine	See Antidepressants, SSRI.
Flupentixol	See Antipsychotics.
Fluphenazine	See Antipsychotics.
Flurazepam	See Anxiolytics and Hypnotics.
Flutamide	Use with caution (hepatotoxic).
Fluvastatin	See Statins.
Fosfestrol	See Oestrogens.
Frusemide	See Loop Diuretics.
Fusidic Acid	Impaired biliary excretion; may increase risk of hepatotoxicity; avoid or reduce dose.
Gemfibrozil	Avoid in liver disease.
Glibenclamide	See Sulphonylureas.
Glimepiride	Manufacturer advises avoid in severe liver impairment.
Glipizide	See Sulphonylureas.
Gold (auranofin, aurothiomalate)	Avoid in severe liver diseases.
Griseofulvin	Avoid in severe liver diseases.
Haloperidol	See Antipsychotics.
Halothane	Avoid in the history of unexplained pyrexia or jaundice .
Heparin	Reduce dose in severe **liver** disease.
Hydralazine	Reduce dose.
Hydrochlorothiazide	See Thiazides.
Hydroxyprogesterone caproate	See Progesteron.
Hydroxyzine	Sedation inappropriate in severe liver disease; avoid.
Ibuprofen	See NSAIDs.
Ifosfamid	Avoid.
Imidapril	See ACE Inhibitors.
Imipramine	See Antidepressants, Tricyclic.
Indapamide	See Thiazides.
Indometacin	See NSAIDs.
Interferon alfa	Close monitoring in mild to moderate liver impairment; avoid in severe liver disease.
Interferon beta	Avoid in decompensated liver disease.
Irinotecan	Monitor closely for neutropenia if plasma-bilirubin concentration increases up to 1.5 times upper limit of normal range; avoid if plasma-bilirubin concentration is greater than 1.5 times upper limit of normal range.
Isoniazid	Avoid if possible; idiosyncratic hepatotoxicity is common.
Isotretinoin	Avoid; further impairment of liver function may occur.
Isradipine	Reduce dose.

Itraconazole	Half-life is prolonged; dose reduction may be necessary.
Ketoconazole	Avoid.
Ketoprofen	See NSAIDs.
Ketorolac	See NSAIDs.
Ketotifen	Sedation inappropriate in severe liver disease; avoid.
Lacidipine	Antihypertensive effect is possibly increased.
Lamotrigine	Try to avoid.
Lansoprazole	In severe liver disease dose should not exceed 30mg daily.
Levonorgestrel	See Progesterones.
Lidocaine	Avoid (or reduce dose) in severe liver disease.
Lignocaine	See Lidocaine.
Loop Diuretics	Hypokalaemia may precipitate coma (use potassium-spring diuretic to prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis.
Maprotiline	See Antidepressants, Tricyclic (and related).
Mefenamic Acid	See NSAIDs.
Mefloquine	Avoid for prophylaxis in severe liver disease.
Meloxicam	See NSAIDs.
Meropenem	Monitor transaminase and bilirubin concentrations.
Mesterolone	See Androgens.
Metformin	Avoid; increased risk of lactic acidosis.
Methyldopa	Manufacturer advises caution in history of liver disease; avoid in active liver disease.
Metoclopramide	Reduce dose.
Metronidazole	In severe liver disease reduce total daily dose to one-third, and give once daily.
Mainserin	See Antidepressants, Tricyclic (and related).
Miconazole	Avoid.
Morphine	See Opioid Analgesics.
Nalidixic Acid	See Quinolones.
Nandrolone	See Anabolic Steroids.
Naproxen	See NSAIDs.
Neomycin	Increased risk of ototoxicity.
Nefedipine	Reduce dose.
Nimodipine	Elimination is reduced in cirrhoss; monitor blood pressure
Nitrazepam	See Anxiolytics and Hypnotics.
Nitrofurantoin	Cholestatic jaundice and chronic active hepatitis are reported
Nitroprusside	Avoid in severe liver disease.
Norethisterone	See Progesterone.
Norfloxacin	See Quinolones.
Norgestrel	See Progesterone.
Nortriptyline	See Antidepressants, Tricyclic.
NSAIDs	Increased risk of gastro-intestinal bleeding and can cause fluid retention; avoid in severe liver disease; aceclofenac:, use initially 100 mg daily; rofecoxib max 12.5 mg daily in mild impairment.
Oestrogens	Avoid; See also Contraceptives (Oral).
Ofloxacin	See Quinolones.
Olanzapine	Consider initial dose of 5mg daily.
Omeprazole	Not more than 20 mg daily should be used.
Ondasetron	Reduce dose; use not more than 8 mg daily in severe liver disease.
Opioid Analgesics	Avoid or reduce dose, may precipitate coma.

Oxazepam	See Anxiolytics and Hypnotics.
Oxcarbazepine	No dosage adjustment required in mild to moderate impairment; no information in severe impairment
Oxprenolol	Reduce dose.
Oxytetraycline	See Tetracyclines.
Paclitaxel	Avoid in severe liver disease.
Pancuronium	Possibly slower onset, higher dose requirement and prolonged recovery time.
Paracetamol	Dose-related toxicity; avoid large doses.
Pentazocine	See Opioid Analgesics.
Pethidine	See Opioids Anlagesics.
Pheniramine	Sedation inappropriate in severe liver disease, avoid.
Phenobarbital	May precipitate coma.
Phenytoin	Reduce dose to avoid toxicity.
Pholcodine	See Opioids Analgesics.
Pilocarpine	Reduce initial oral dose in moderate or severe cirrhosis.
Piracetam	Avoid.
Piroxicam	See NSAIDs.
Prazosin	Initial 500 microgram daily dose can be increased with caution.
Prednisolone	Side-effects are more common.
Prochlorperazine	See Antipsychotics.
Progesterone	Avoid.
Promethazine	Avoid; may precipitate coma in severe liver disease; hepatotoxic.
Propranolol	Reduce dose.
Propylthiouracil	May cause chronic active hepatitis
Pyrazinamide	Avoid; idiosyncreatic hepatotoxicity is more common.
Quinolones	Hepatitis with necrosis is reported with ciprofloxacin; hepatitis is also reported for norfloxacin; nalidixic acid is partially conjugated in liver; reduce dose of ofloxacin in severe liver disease.
Ranitidine	Increased risk of confusion; reduce dose.
Rifampicin	Impaired elimination; may increase risk of hepatotoxicity; avoid or do not exceed 8 mg/kg daily.
Risperidone	Manufacturer advices initial dose of 500 micrograms twice daily; stepwise increase of dose to 1-2 mg twice daily is possible.
Rivastigmine	No information available;-manufacturer advises avoid in sever liver disease.
Rofecoxib	See NSAIDs.
Saquinavir	Plasma concentration is possibly increased; manufacturer advises caution with fortovase (Saquinavir) in moderate impairment; avoid fortovase in severe impairment.
Sertraline	See Antidepressants, SSRI.
Simbastatin	See Statins.
Sodium aurothiomalate	See Gold.
Sodium Fusidate	See Fusidic Acid.
Sodium Nitroprusside	See Nitroprusside.
Sodium Valproate	See Valproate.
Statins	Avoid in active liver disease or unexplained persistent elavations in serum transaminases.

Sulindac	See NSAIDs.
Sulpiride	See Antipsychotics.
Sulfonamides	Increased risk of chronic hepatitis; AIDS patients are more sensitive
Sulphonylureas	Increased risk of hypoglycemia in severe liver disease; avoid or use small dose; can produce jaundice.
Suxamethonium	Prolongd apnoea may occur in severe liver disease due to reduced hepatic synthesis of pseudocholinesterase.
Tenoxicam	See NSAIDs.
Terbinafine	Reduce dose.
Testosterone	See Androgens.
Tetracyclines	Avoid (or use with caution).
Theophylline	Reduce dose.
Thiazides	Avoid in severe liver disease; hypokalaemia may precipitate coma (potassium sparing diuretic can prevent); increased risk of hypomagnesaemia in alcoholic cirrhosis.
Thiopental	Reduce dose for induction in severe liver disease.
Thioridazine	See Antipsychotics.
Ticlopidine	Manufacturer advises caution; discontinue if hepatitis or jaundice develop.
Tramadol	See Opioid Analgesics.
Tretinoin (Oral)	Reduce dose.
Trifluoperazine	See Antipsychotics.
Trimipramine	See Antidepressants, Tricyclic.
Valproate	Avoid if possible, hepatotoxicity and liver failure may occasionally occur.
Valsartan	Halve dose in mild to moderate hepatic impairment; avoid if severe.
Verapamil	Reduce oral dose.
Vinblastine	Dose reduction may be necessary.
Vincristine	Dose reduction may be necessary.
Warfarin	See Anticoagulants, oral.
Zafirlukast	Manufacturer advises avoid in liver diseases.
Zalcitabine	Further impairment of liver function may occur.
Zaleplon	See Anxiolytics and Hypnotics.
Zidovudine	Accumulation may occur.
Zopiclone	See Anxiolytics and Hypnotics.
Zuclopenthixol	See Antipsychotis.

Appendix- 4

RENAL IMPAIRMENT

Kidney is an important organ in regulating body fluid levels, electrolyte balance and removal of metabolic waste products and drugs (intact and/or metabolites) from the body.

Renal impairment or renal failure (chronic and acute) is a reduced functional activity of kidney. Some common causes or renal impairment are pyelonephritis, hypertension, diabetes mellitus, nephrotoxic drugs/metals, hypovolemia or hypoperfusion and nephroallergens.

Problems faced by renal impaired patient on drugs :
As most of the drugs and their metabolites have to encounter kidney prior to excretion from the body, the rate and extent of their excretion from the body largely depend on the functional activity of the kidney. Therefore a patient with reduced renal function (renal insufficiency) develops primarily accumulation of drugs and or metabolites (inactive or active) or both in his/her body and eventually gets exposed to the following problems:

- Accumulation of drugs and / or its metabolites may produce toxicity.
- Sensitivity to some drugs may be increased.
- Poor tolerance to many common and new side-effects.
- Reduction in efficacy of some drugs.

However many of the before mentioned problems can be avoided by simply adjusting (reducing) the dose or using an alternative drug which is therapeutic equivalent.

Diagnosis and assessment of renal failure:
Renal function is indicated by Glomerular Filtration Rate (GFR), which is in turn clinically measured by the creatinine clearance or blood urea nitrogen (BUN) levels. The serum creatinine concentration provides only a rough guide for the assessment of renal impairment unless corrected for age, weight and sex. For prescribing purpose, renal impairment is divided into five stages of chronic kindey disease and GRF including :

Stages	Grade	GFR	Serum Creatinine level
Normal	No protein in the urine	90-130 mL/min/ 1.73m^2	Men: 0.6–1.2 (mg/100mL) Women: 0.5–1.1 mg/100mL Child: 0.3–0.7 mg/100mL
Stage 1	Protein in the urine	> 90 mL/min/ 1.73m^2	1.2-1.5 (mg/100mL), men
Stage 2	Mild CKD	60-89 mL/min/ 1.73m^2	1.6-2.8 (mg/100mL), men
Stage 3A	Moderate CKD	45-59 mL/min/ 1.73m^2	2.9 -3.9 (mg/100mL), men
Stage 3B	Moderate CKD	30-44 mL/min/ 1.73m^2	4.0-5. 0 (mg/100mL), men
Stage 4	Severe CKD	15-29 mL/min/ 1.73m^2	5.1-7.5 (mg/100mL), men
Stage 5	End Stage Renal Disease (ESRD)	<15 mL/min/ 1.73m^2	7.6 (mg/100mL) and above, men

APPENDIX 4 : RENAL IMPAIRMENT

Principles of dose adjustment in renal impairment :

Alteration in renal clearance of drugs in renal impairment is by far the most important parameter to consider while making dosage calculation. In clinical practice the estimation of the appropriate drug dosage regimen in renally impaired patient is primarily focused on the remaining renal function of the patient and a prediction of the total body clearance (Cl_T). The loading dose of a drug is based on apparent volume of distribution (V_D) of the patient. Generally, drugs in patients with uremia or kidney impairment have prolonged elimination half-lives and a change in the apparent volume of distribution. But practically the apparent volume of distribution of drug in renally impaired patient is assumed to be same as that of normal patients. Consequently, the methods for dose adjustment in renally impaired patients are based on an accurate estimation of the drug clearance in these patients.

The maintenance dose is based on the clearance of the drug in the patient and hence it has to be individualized for such patients. Generally two pharmacokinetic approaches for dosage adjustment in clinical situation have been used monitoring kidney function which includes:-

a) dosage adjustment method based on drug clearance-

To maintain the same desired C^{α}_{av}, the dose must change to D^{u}_{o} or the dosage interval must change to τ^{u}, as shown in the following equation.

$$C^{\alpha}_{av} = D^{N}_{0} / Cl^{N}_{T.}\,\tau^{N} = D^{R}_{0} / Cl^{R}_{T.}\,\tau^{R} \ldots.(i)$$

(normal) (renally impaired)

$$D^{R}_{0} = D^{N}_{0} \times \frac{Cl^{R}_{T}\,.\,\tau^{R}}{Cl^{N}_{T}\,.\,\tau^{N}}$$

Where,

C^{α}_{av} = average plasma concentration
D^{R}_{0} = dose for renally impaired patient
D^{N}_{0} = dose for normal patient
Cl^{R}_{T} = Clearance for renally impaired paitent
Cl^{N}_{T} = Clearance for normal patient
τ^{R} = Dosing interval for renal impaired patient
τ^{N} = Dosing interval for normal patient

If dosing interval (τ) is kept unchanged ($\tau^{R} = \tau^{N}$), the adjusted dose of renally impaired patients (D^{R}_{0}) will be equal to a fraction (Cl^{R}_{T} / Cl^{N}_{T}) of the normal dose, as shown in the equation-

$$D^{R}_{0} = D^{N}_{0} \times \frac{Cl^{R}_{T}}{Cl^{N}_{T}} \quad \ldots\ldots \quad (ii)$$

b) dosage adjustment method based on changes in drug elimination rate constant-

The overall elimination rate constant for many drugs is reduced in the renally impaired patients. A dosage regimen may be designed for such renally impaired patients either

1. by reducing the normal dose of the drug and keeping the frequency of dosing or dosage interval (τ) constant or
2. by decreasing the frequency of dosing (prolong the dosage interval) and keeping the dose constant.

According to above equations, keeping dosing interval (τ) unchanged ($\tau^R = \tau^N$), the usual approach to estimate a multiple-dosage regimen in the renally impaired patients the maintenance dose will be-

$$D^R_0 = D^N_0 \times \frac{Cl^R_T}{Cl^N_T} \quad \ldots\ldots \quad (ii)$$

Putting the $Cl_T = K.V_D$ in both normal and renally impaired patients the equation is -

$$D^R_0 = D^N_0 \times \frac{K_R.V_D{}^R}{K_N.V_D{}^N}$$

Where,

K_N = elimination rate constant of normal patient
K_R = elimination rate constant of renally impaired patient
$V_D{}^N$ = volume of distribution of normal patient
$V_D{}^N$ = volume of distribution of renally impaired patient

Assuming V_D is same in both normal and uremic patients, the uremic dose D^u_0 is a fraction (k^R/k^N) of the normal dose-

$$D^R_0 = D^N_0 \times \frac{K_R}{K_N} \quad \ldots\ldots \quad (iv)$$

N.B.: Drugs with known nephrotoxicity should be, if possible, avoided in patients with renal failure or disease.

Drugs	Degree of Impairment	Comment
Acarbose	Moderate to severe	Avoid; no information available.
Acebutolol	Mild to moderate	See Beta-blockers.
Acetazolamide	Mild	Avoid; metabolic acidosis.
Aciclovir	Moderate to severe	Reduce intravenous dose.
Acrivastine Moderate	Moderate	Avoid; excreted by kidney.
ACE inhibitor	Mild to moderate	Use with caution and monitor response. Hyperkalamia and other side-effects more common. Captopril :12.5 mg b.i.d. Cilazapril: 500 microgm once daily. Enalapril: 2.5 mg once daily. Imidapril: 2.5 mg once daily. Moexipril: 3.75 mg once daily. Perindopril: 2 mg once daily. Quinapril: 2.5 mg once daily. Ramipril: 1.25 mg once daily. Trandorapril: 500 micrograms daily.
Alprazolam	Severe	See Anxiolytics and Hypnotics.
Amikacin	Mild	See Aminoglycosides.
Aminoglycosides	Mild	Reduce dose and monitor plasma concentrations.
Amoxicillin	Severe	Reduce dose; rashes more common.
Ampicillin	Severe	Reduce dose; rashes more common.

Anxiolytics and hypnotics	Severe	Start with small dose; increased cerebral sensitivity.
Anti psychotics	Severe	Start with small doses; increased cerebral sensitivity.
Aspirin	Severe	Avoid; sodium and water retention; deterioration in renal function; increased risk of gastro-intestinal bleeding.
Atenolol	Mild, Moderate	See Beta Blockers.
Azithromycin	Moderate	No information available
Balsalazide	Moderate	Avoid.
Beta-Blockers	Mild,	Start with 2.5 mg of nebivolol.
	moderate	Start with small dose; acebutolol reduce dose of atenolol, nadolol, pindolol, sotalol.
		All excreted unchanged.
	Severe	Start with small dose; higher plasma concentrations after oral administration; may reduce renal blood flow and adversely affect renal function in severe impairment.
Bendrofluazide		See Thiazide.
Betaxolol		See Beta Blockers.
Bleomycin	Moderate	Reduce dose.
Bromazepam		See Anxiolytics and Hypnotics.
Captopril		See ACE Inhibitors.
Carbamazepine		Take caution.
Cefalexin	Severe	Max. 500 mg daily.
Cefazolin	Mild	Reduce dose.
Cefotaxime	Severe	Use half dose.
Ceftazidime	Mild	Reduce dose.
Ceftriaxone	Severe	Reduce dose; also monitor plasma concentration if both severe renal renal and hepatic impairment.
Cefuroxime	Moderate to Severe	Reduce parenteral dose.
Celecoxib		See NSAIDs.
Cetirizine	Moderate	Use half dose.
Chloramphenicol	Severe	Avoid unless no alternative; dose-related depression of haematopoiesis.
Chloroquine	Mild to Moderate	Reduce dose.
	Severe	Avoid (but for malaria prophylaxis adjust dose).
Chlorpromazine		See Antipsychotics.
Chlorpropamide		Avoid.
Chlortetracycline		See Tetracyclines.
Cilazapril		See ACE Inhibitors.
Climetidine	Mild to Moderate	600-800 mg daily; occasional risk of confusion
	Severe	400 mg daily.
Ciprofloxacin	Moderate	Use half dose.
Cisplatin	Mild	Avoid if possible; nephrotoxic and neurotoxic.
Clarithromycin	Moderate	Use half dose.

	to Severe	neurotoxic.
Clavulanic Acid		See Coamoxiclav.
Clobazam		See Anxiolytics and Hypnotics.
Clozapine	Mild to Moderate	Initial dose 12.5 mg daily.
Cotrimoxazole	Moderate	Reduce dose; rashes and blood disorder may cause further deterioration in renal function.
Cycophosphamide		Reduce dose.
Cyclosporin		See Ciclosporin.
Dalteparin		See Heparin.
Dextromethorphan		See Opioid Analgesics.
Diazepam		See Anxiolytics and Hypnotics.
Diclofenac		See NSAIDs.
Digoxin	Mild	Reduce dose; toxicity increased by electrolyte disturbances.
Disopyramide	Mild	100 mg every 8 hours or 150 mg every 12 hours.
	Moderate	100 mg every 12 hours.
	Severe	150 mg every 24 hours.
Doxycycline		See Tetracyclines.
Droperidol		See Antipsychotics.
Enalapril		See ACE Inhibitors.
Ergometrine	Severe	Avoid.
Ergotamine	Moderate	Avoid; nausea and vomiting; risk of renal vasoconstriction.
Erythromycin	Severe	Max. 1.5 gm daily (ototoxicity).
Ethambutol	Mild	Reduce dose; if creatinine clearance less than 30 ml/minute; monitor plasma ethambutol concentration; optic nerve damage.
Famotidine	Severe	Reduce dose.
Fenoprofen		See NSAIDs.
Flucloxacillin	Severe	Reduce dose.
Fluconazole	Mild to Moderate	Usual initial dose then halve the subsequent doses.
Fluoxetine	Mild to Moderate	Reduce dose (give on alternate days).
	Severe	Avoid.
Flupenthixol		See Antipsychotics.
Fluphenazine		See Antipsychotics.
Flurazepam		See Anxiolytics and Hypnotics.
Fluvastatin	Severe	Avoid.
Fosinopril		See ACE Inhibitors.
Floxacin	Mild	Usual initial dose, then use half dose.
	Moderate	Usual initial dose, then 100 mg every 24 hours.
Frusemide		See Furosemide.
Gallamide	Moderate	Avoid; prolonged paralysis.
Gemfibrozil	Severe	Start with 900 mg daily.
Gentamicin		See Aminoglycosides.
Glimepiride	Severe	Avoid.
Glipizide	Mild to moderate	Increased risk of hypoglycaemia; avoid if hepatic impairment also present.

	Severe	Avoid.
Haloperidol		See Antipsychortics.
Heparin	Severe	Risk of bleeding increased.
Hydrochlorothiazide		See Thiazides.
Ibuprofen		See NSAIDs.
Ifosfamide	Mild	Avoid if serum creatinine concentration greater than 120 µmol/litre.
Imidapril		See ACE Inhibitors.
Indapamide		See Thiazides.
Indometacin		See NSAIDs.
Insulin	Severe	May need dose reduction; insulin requirements fall; compensatory response to hypoglycaemia is impaired.
Interferon alfa	Mild to Moderate	Close monitoring. required.
	Severe	Avoid.
Interferon beta		No information available-monitoring advised.
Irinotecan		No information available.
Isoniazid	Severe	Max. 200 mg daily; peripheral neuropathy.
Isotretinoin	Mild	Avoid; Increased risk of toxicity
Itraconazole		Bioavailability possibly reduced.
Kanamycin		See Aminoglycosides.
Ketoprofen		See NSAIDs.
Ketorolac		See NSAIDs.
Lamotrigine	Moderate to Severe	Metabolite may. accumulate.
Lamivudine	Mild	Reduce dose; consult product literature.
Lisinopril		See ACE Inhibitors.
Lithium	Mild	Avoid if possible or reduce dose and monitor plasma concentration carefully.
Lorazepam		See Anxiolytics and Hypnotics.
Losartan	Moderate to Severe	Start with 25 mg once . daily.
Mefenamic Acid		See NSAIDs.
Meloxicam		See NSAIDs.
Melphalan		Reduce dose initially; avoid high doses in moderate to severe impairment.
Mercaptopurine	Moderate	Reduce dose.
Meropenem	Mild	Increase dose interval to every 12 hours.
Metformin	Mild	Avoid; increased risk if lactic acidosis.
Methyldopa	Moderate	Start with small dose; increased sensitivity to hypotensive and sedative effect.
Metoclopramide	Severe	Avoid or use small dose; increased risk of extrapyramidal reactions.
Metoprolol		See Beta Blockers.

Midazolam		See Anxiolytics and Hypnotics.
Morphine		See Opioid Analgesics.
Naproxen		See NSAIDs.
Neomycin	Mild	Avoid; ototoxic; nephrotoxic.
Neostigmine	Moderate	May need dose reduction.
Netilmicin		See Aminoglycosides.
Nicotine	Severe	May affect clearence of nicotine or its metabolities.
Nitrazepam		See Anxiolytics and Hypnotics.
Nitrofurantoin	Mild	Avoid; peripheral neuropathy; ineffective because of inadequate urine concentrations
Norfloxacin	Mild to Moderate	Halve dose if creatinine clearance less than 30 ml/minute.
NSAIDs	Mild	Use lowest effective dose and monitor renal function; sodium and water retention ; deterioration in renal function possibly leading to renal failure; deterioration also reported after topical use.
	Moderate to Severe	Avoid if possible.
Olanzapine		Consider initial dose of 5 mg daily.
Oxazepam		See Anxiolytics and Hypnotics.
Oxytetracycline		See Tetracyclines.
Pancuronium	Severe	Prolonged duration of block.
Penicillamine	Mild	Avoid if possible or reduce dose; naphrotoxic.
Pentazocine		See Opioid Analgesics.
Pentoxifylline (oxpentifylline)	Mild	Reduce dose by 30-50% if creatinine clearance less than 30 ml/minute.
Pethidine		See Opioid Analgesics.
Pholcodine		See Opioid Analgesics.
Pilocarpine		Caution with tablets.
Pindolol		See Beta blockers.
Pipotiazine		See Antipsychotics.
Piroxicam		See NSAIDs.
Povidone Iodine	Severe	Avoid regular application to inflamed or broken mucosa.
Prazosin	Moderate to Severe	Initially 500 microgram daily; increase with caution.
Procarbazine	Moderate	Reduce dose.
Prochlorperazine		See Antipsychotics.
Promazine		See Antipsychotics.
Propranolol		See Beta Blockers.
Pseudoephedrine	Severe	Avoid; increased CNS toxicity.
Quinine		Reduce parenteral maintenance dose for malaria treatment.
Ramipril		See ACE Inhibitors.
Ranitidine	Severe	Use half normal dose; occasional risk of confusion.
Risperidone		Initial dose of 500 micrograms twice daily increased in steps of 500 micrograms twice daily to 1-2

		mg twice daily.
Rofecoxib		See NSAIDs.
Simvastatin	Moderate to Severe	Doses above 10 mg daily should be used with caution.
Sodium Bicarbonate	Severe	Avoid; specialised role in some forms of renal disease.
Sodium Clodronate		See Clodronate Sodium.
Sodium Nitroprusside		See Nitroprusside.
Sodium Salts	Severe	Avoid.
Sodium valproate		See Valproate.
Spironolactone		See Diuretics, potassium-sparing.
Sucralfate	Severe	Avoid; aluminium is absorbed and may accumulate.
Sulfadiazine	Severe	Avoid; high risk of crystalluria.
Sulfasalazine	Moderate	Risk of toxicity including . crystalluria-ensure high fluid intake
	Severe	Avoid.
Sulpiride	Moderate	Avoid if possible, or reduce dose.
Tenoxicam		See NSAIDs.
Terbinafine	Mild	Use half normal dose.
Tetracycline (except doxycycline and minocycline mild)		Avoid, use doxycycline or minocycline if necessary; anti-anabolic effect, increased plasma urea, further deterioration in renal function.
Thiazides and related diureties	Moderate	Avoid; ineffective (metolazone remains effective but risk of excessive diuresis).
Timolol		See Beta blockers.
Tobramycin		See Aminoglycosides.
Tramadol		See Opioid Analgesics.
Triamterene		See Diuretics, potassium-sparing.
Trimethoprim	Moderate	Reduce dose.
Valsartan	Moderate to Severe	Start with 40 mg once daily.
Warfarin		See Anticoagulants, Oral.
Zafirlukast	Moderate to Severe	Caution to be taken.
Zalcitabine	Mild to Moderate	750 micrograms every. 12 hours.
	Severe	750 micrograms daily.
Zidovudine	Severe	Reduce dose; manufacturer advises oral dose of 300-400 mg daily.
Zopiclone		See Anxiolytics and Hypnotics.
Zuclopenthixol		See Antipsychotics.

Fluids/Solutions used in Haemodialysis

Acetic Acid 0.469 % + Calcium Chloride 1.008 % + Magnesium Chloride 0.754 % + Potassium Chloride 0.554 % + Sodium Chloride 21.968 %

Proprietary Preparations
Not Available in the market

Dextrose Anhydrous 7 % + Sodium Chloride 0.561 %

Proprietary Preparations
Not available in the market

Calcium Chloride 9 mg + Dextrose Anhydrous 70 mg + Magnesium Chloride 1.189 mg + Potassium Chloride 594.57 mg + Sodium Acetate 0.03 mg + Sodium Chloride 5.94 mg in 100 mL

Proprietary Preparations
Not available in the market

Calcium Chloride 22 mg + Dextrose Anhydrous 1.5 gm + Magnesium Chloride 15 mg + Potassium Chloride 22 mg + Sodium Acetate 476 mg + Sodium Chloride 556 mg in 100 mL

Proprietary Preparations
Not available in the market

Calcium Chloride 257 mg + Dextrose Anhydrous 3.86 gm + Magnesium Chloride 15.2 mg + Sodium Acetate 369 mg + Sodium Chloride 561 mg in 100 mL

Proprietary Preparations
Not available in the market.

Calcium Chloride 9.74 gm + Glacial Acetic Acid 8.84 gm + Magnesium Chloride 3.74 gm + Potassium Chloride 5.50 gm + Sodium Chloride161.43 gm in 1000 mL

Proprietary Preparations
Dialyte-A 10L; Maximum retail price: Tk. 450.87/=; Popular Pharmaceuticals Ltd
Renal Care –A 10L, MRP: Tk. 409.93/=; Greenland Pharmaceuticals Ltd

Calcium Chloride Dihydrate 5.14 gm + Magnesium Chloride 3.56 gm + Potassium Chloride 5.2 gm + Sodium Acetate 181.01+ Sodium Chloride 198.4gm in 1000 mL

Proprietary Preparations
Dialyte-AC 10L; Maximum retail price: Tk. 490.29/=; Popular Pharmaceuticals Ltd
Renal Care-AC 10L; MRP: Tk. 462.26/=; Greenland Pharmaceuticals Ltd

Sodium Bicarbonate 66 gm + Sodium Chloride 30.5 gm in 1000 mL

Proprietary Preparations
Renal Care-B; Retail price: Tk. 358.93/= for 10L solution, Popular Pharmaceuticals Ltd
Renal Care-B 10L; MRP: Tk. 327.07/=;Greenland Pharmaceuticals Ltd

Appendix- 5

PREGNANCY

When prescribing it should be kept in mind that drugs can have harmful effects on the embryo or fetus at any time during pregnancy, so the expected benefit to the mother must be greater than the risk to the fetus. Drugs that have been extensively used in pregnancy and appear to be usually safe should be prescribed in preference to new or untried drugs. Lists of drugs are mentioned below that should be avoided or used with caution in pregnancy. Absence of a drug from the list does not imply safety.
The US FDA has divided all the drugs in 6 categories depending upon the studies undertaken on human and animal, which are much good implication of safety and easier to understand, so FDA pregnancy drug category is included here for quick access. Whereas category 'A' stands for the safest drug category 'X' stands for potentially harmful drugs which must be avoided. Category 'B' and 'C' drugs have shown toxicity in animals but category 'B' has failed to prove toxicity in humans. Category 'D' drugs are dangerous.

Drugs	FDA pregnancy drug category	Comments (Trimester risks 1,2,3)
Abacavir	C	All treatment options need careful assessment.
Acamprosate calcium	C	Avoid
Acarbose	B	Avoid; insulin is substituted **1, 2, 3**
Aceclofenac	D	Avoid the use of NSAIDs during pregnancy or avoid them unless the potential benefit outweighs the risk. It should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.**3**
Acemetacin	D	Avoid the use of NSAIDs during pregnancy or avoid them unless the potential benefit outweighs the risk. It should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.
Acetazolamide	C	Toxicity in animal studies; avoid, especially in first trimester.
Acetylcysteine	B	Acetylcysteine is only recommended for use during pregnancy when benefit outweighs risk.

Acetylsalicylic acid or Aspirin	D	Delayed onset and increased duration of labour with increased blood loss; avoid in last few weeks at analgesic doses; low doses probably not harmful; high doses cause closure of fetal ductus arteriosus in utero and persistent newborn.**3**
Acitretin	X	Avoid—teratogenic; effective contraception must be used
Acrivastine	B	No evidence of teratogenicity except for hydroxyzine where toxicity has been reported with high doses in animal studies. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability, paradoxical excitability and tremor.
Acyclovir	B	Use only when potential benefit outweighs the risks; limited absorption from topical preparations.
Adefovir dipivoxil	C	Toxicity in animal studies , use only if potential benefit outweighs risk; effective contraception needed during treatment
Adenosine	C	Large doses may produce fetal toxicity; use only if potential benefit outweighs risk.
Adrenaline	C	May reduce placental perfusion and can delay 2nd stage of labour; use only if benefit outweighs risk
Agomelatine		Avoid
Albendazole	C	Should not be used in pregnant women except in clinical circumstances where no alternative management is appropriate.
Alcohol		Regular intake is teratogenic (fetal alcohol syndrome) and may cause growth retardation. Withdrawal syndrome may occur in babies of alcoholic mother. **1, 2, 3**
Alendronate sodium	C	Avoid.
Alendronic acid	C	Avoid.
Alfuzosin	B	Alfuzosin should only be given during pregnancy when need has been clearly established.
Aliskiren	D	Avoid, no information available; other drugs acting on the renin-angiotensin system have been associated with fetal malformations and neonatal death.
Allopurinol	C	Avoid; use only when there is no alternative and disease carries risk for mother or child. **3**

Allystrenol	C	Use only when potential benefit outweighs the risks;
Almotriptan	C	Limited experience of using $5HT_1$-receptor agonists during pregnancy; they should be avoided unless the potential benefit outweighs the risk.
Alprazolam	D	Avoid (during late pregnancy or labour, high doses may cause neonatal hypothermia, hypotonia and respiratory depression). **1,2,3**
Alverine citrate		Use with caution.
Amantadine	C	Avoid; toxicity in animal studies.
Ambrisentan	X	Avoid (teratogenic in animal studies); exclude pregnancy before treatment and ensure effective contraception during treatment; monthly pregnancy tests advised.
Amikacin	D	Chance of damage of 8th cranial nerve; if prescribed then monitor plasma concentration. **2,3**
Amiloride	B	Avoid. **1,2,3**
Aminocaproic acid	C	Aminocaproic acid is only recommended for use during pregnancy when benefit outweighs risk.
Aminophylline	C	Asthma should be well controlled during pregnancy.
Amiodarone	D	Possible risk of neonatal goitre; use only if no alternative is available.
Amitriptyline	C	Use only if potential benefit outweighs risk
Amlexanox	B	Should be used during pregnancy only if clearly needed.
Amlodipine	C	Avoid, but risk to fetus should be balanced against risk of uncontrolled maternal hypertension.
Amoxicillin	B	Not known to be harmful
Amphotericin	B	Avoid unless potential benefit outweighs risk.
Anastrozol	D	Avoid.
Aprepitant	B	Avoid unless potential benefit outweighs risk.
Aripiprazole	C	Use only if potential benefit outweighs risk.
Artemether with lumefantrine	C	Toxicity in animal studies with artemether; use only if potential benefit outweighs risk.

Artesunate		Use only if potential benefit outweighs risk.
Asenapine	C	Use only if potential benefit outweighs risk, toxicity in animal studies.
Atenolol & acebutolol	D	Cause intrauterine growth retardation, neonatal hypoglycemia and bradycardia.**3**
Atomoxetine	C	Avoid unless potential benefit outweighs risk.
Atorvastatin	X	Should be avoided in pregnancy as congenital anomalies have been reported and the decreased synthesis of cholesterol possibly affects fetal development. Adequate contraception is required during treatment and for 1 month afterwards.
Atracurium	C	Avoid unless benefit outweighs risk. There may be fetal distress (slower to start breathing)**1,2**
Atropine	C	Prescribe with caution.
Azathioprine	C	Treatment should not generally be initiated during pregnancy. Transplant patients immuno-suppressed with this drug should not be discontinued if not becoming pregnant; intra-uterine growth retardation; there is on evidence that this drug is teratogenic. (see cytotoxic drugs)**1,2,3**
Azelaic Acid	B	Should only be used during pregnancy when need has been clearly established.
Azilsartan medoxomil	C	Should be avoided in pregnancy unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Azithromycin	B	No adverse fetal outcomes were reported.
Aztreonam	B	Avoid unless essential.
Bacitracin	C	Potential benefits may warrant use of the drug in pregnant women despite potential risks.
Baclofen	C	Potential benefits may warrant use of the drug in pregnant women despite potential risks.
Bambuterol	C	Asthma should be well controlled during pregnancy.
Beclometasone dipropionate	C	Asthma should be well controlled during pregnancy.

Benzalkonium Chloride	N	Prescribe with caution.
Benzocaine	C	Benzocaine topical is only recommended for use during pregnancy when benefit outweighs risk.
Betahistine hydrochloride	B	Manufacturers advise to avoid.
Betaine	C	Avoid; manufacturer advises effective contraception during and for at least 1 month after treatment in men or women.
Betamethasone	C	Transient effect on fetal movements and heart rate.
Betaxolol	C	Use when benefit outweighs risk.
Bevacizumab	C	Avoid, toxicity in animal studies; effective contraception required during and for at least 6months after treatment in women.
Bimatoprost	C	Use only if potential benefit outweighs risk.
Bisacodyl	B	Animal studies have failed to reveal evidence of teratogenicity or fetotoxicity.
Bismuth subcitrate/subsalicylate	X	Avoid.
Bisoprolol fumarate	C	Beta-blockers may cause intra-uterine growth restriction, neonatal hypoglycaemia, and bradycardia; the risk is greater in severe hypertension. If beta-blockers are used close to delivery, infants should be monitored for signs of beta-blockade.(and alpha-blockade with labetalol or carvedilol).
Bosentan	X	Avoid (teratogenic in animal studies); effective contraception required during administration (hormonal contraception not considered effective); monthly pregnancy tests are advised.
Bromazepam	D	Prescribe with caution; discourage regular use; high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression.
Brimonidine tartrate	B	Use only if benefit outweighs risk.
Brinzolamide	C	Avoid; toxicity in animal studies.
Bromfenac	C	Should be avoided during late pregnancy.
Bromocriptine	B	Exclude pregnancy before starting and discontinue 1 month before intended

		conception (ovulatory cycles persist for 6 months), discontinue if pregnancy occurs during treatment (specialist advice needed).
Budesonide	B,C	Transient effect on fetal movements and heart rate.
Bumetanide	C	Avoid, should not be used to treat gestational hypertension because of the maternal hypovolemia associated with this condition.
Bupivacaine	C	Large doses during delivery can cause neonatal respiratory depression, hypotonia, and bradycardia after epidural block; use lower doses for intrathecal use during late pregnancy.
Buprenorphine	C	Acute withdrawal of opioids should be avoided in pregnancy because it can cause fetal death. Opioid substitution therapy is recommended during pregnancy because it carries a lower risk to the fetus than continued use of illicit drugs.
Bupropion hydrochloride	C	Manufacturer advises avoid.
Buspirone hydrochloride	B	Manufacturer advises avoid.
Busulphan	D	Avoid; toxicity in animal studies; effective contraceptive measure must be taken during administration in women.
Butenafine	B	Use only if benefit outweighs risk.
Cabergoline	D	Exclude pregnancy before starting and discontinue 1 month before intended conception (ovulatory cycles persist for 6 months), discontinue if pregnancy occurs during treatment (specialist advice needed).
Calcipotriol	C	Avoid if possible.
Calcitonin	C	Avoid unless benefit outweighs risk; toxicity in animal studies.
Candesartan cilexetil	D	Should be avoided in pregnancy unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Capecitabine	D	Women of childbearing potential be advised to avoid becoming pregnant while receiving treatment with it.
Capsaicin	B	Should be used during pregnancy only when benefit outweighs risk.
Captopril	D	Avoid; may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios;

		toxicity in animal studies. **1, 2, 3**
Carbamazepine	D	Teratogenic; increased risk of neural tube defects if used in first trimester; neonatal bleeding if used in third trimester. **1, 3**
Carbimazole		Neonatal goitre and hypothyroidism if used in second or third trimester **2,3**
Carbocysteine		Avoid. **1**
Carboplatin	D	Avoid.
Carvedilol	C	Beta-blockers may cause intra-uterine growth restriction, neonatal hypoglycaemia, and bradycardia; the risk is greater in severe hypertension. Information on the safety of carvedilol during pregnancy is lacking. If beta-blockers are used close to delivery, infants should be monitored for signs of beta-blockade (and alpha-blockade with labetalol or carvedilol).
Cefaclor	B	Not known to be harmful.
Cefadroxil	B	Not known to be harmful.
Cefdinir	B	Should be given during pregnancy only if need is clearly established.
Cefditoren	B	Recommended for use during pregnancy when benefit outweighs risk.
Cefepime	B	Should only be given in pregnancy when the need has been clearly established.
Cefotaxime	B	Should be given during pregnancy only if need is clearly established.
Cefoxitin	B	Should be given during pregnancy only if need is clearly established.
Cefpodoxime	B	Should only be given in pregnancy when the need has been clearly established.
Cefprozil	B	Recommended for use during pregnancy when benefit outweighs risk.
Ceftazidime	B	Should only be given in pregnancy when the need has been clearly established.
Ceftriaxone	B	Should only be given in pregnancy when the need has been clearly established.
Cefuroxime	B	Manufacturers advise to avoid.
Celecoxib	D	Avoid (teratogenic in animal studies).

Celiprolol hydrochloride	C	Should not be used to treat gestational hypertension. They may cause neonatal thrombocytopenia, bone marrow suppression, jaundice, electrolyte disturbances, and hypoglycaemia; placental perfusion may also be reduced. Stimulation of labour, uterine inertia, and meconium staining have also been reported.
Cephalexin	B	Should only be given in pregnancy when the need has been clearly established.
Cephradine	B	Should only be given in pregnancy when the need has been clearly established.
Cetirizine hydrochloride	B	No evidence of teratogenicity except for hydroxyzine where toxicity has been reported with high doses in animal studies. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability, paradoxical excitability and tremor.
Cetrimide	B	Not known to do any harm.
Chloramphenicol	C	Avoid; Grey baby syndrome may occur. **3**
Chlorhexidine gluconate	B	Should only be given in pregnancy when the need has been clearly established.
Chloroquine phosphate	N	Prescribe with caution; potential teratogenic effect; for malaria if benefit outweighs risk.**1,3**
Chloroxylenol	C	Use during pregnancy when benefit outweighs risk.
Chlorpheniramine maleate	B	No evidence of teratogenicity except for hydroxyzine where toxicity has been reported with high doses in animal studies. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability, paradoxical excitability and tremor.
Chlorpromazine	C	Prescribe with caution; possibility of lethargy an extrapyramidal effect due to slow elimination. **3**
Chlorpromazine hydrochloride	C	Extrapyramidal effects and withdrawal syndrome have been reported occasionally in the neonate when antipsychotic drugs are taken during the third trimester of pregnancy. Following maternal use of antipsychotic drugs in the third trimester, neonates should be monitored for symptoms including agitation, hypertonia, hypotonia, tremor, drowsiness, feeding

		problems, and respiratory distress.
Chlorambucil	D	Avoid; effective contraceptive measure must be taken during administration.
Chlortetracycline	B	Should be used only if benefit outweighs risk.
Chlorthalidone	B	Should not be used, may cause neonatal thrombocytopenia, bone marrow suppression, jaundice, electrolyte disturbances and hypoglycaemia.
Ciclesonide	C	Only recommended for use during pregnancy when there are no alternatives.
Cilastatin	C	Should be used only if benefit outweighs risk.
Cilostazol	C	An increase in the incidence of stillbirth and of cardiovascular, renal, and skeletal defects has been reported in animal. Should be used only if benefit outweighs risk.
Cimetidine	B	Avoid unless benefit outweighs risk.
Cinacalcet	C	Patient taking the drug should be under observation.
Cinnarizine	C	Most manufacturers of antihistamines advise avoiding their use during pregnancy; however there is no evidence of teratogenicity. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability , paradoxical excitability , and tremor.
Ciprofloxacin	C	Prescribe with caution; **1, 2, 3**
Cisatracurium	B	Non-depolarising neuromuscular blocking drugs are highly ionised at physiological pH and are therefore unlikely to cross the placenta in significant amounts. Contact with physician before use.
Cisplatin	D	Avoid; toxicity in animal studies.
Citalopram	C	SSRIs should not be used during pregnancy unless the potential benefit outweighs the risk. There is small increased risk of congenital heart defects when SSRIs are taken during early pregnancy. If SSRIs are of neonatal withdrawal symptoms , and persistent pulmonary hypertension in the newborn has been reported.

Citicoline	D	Avoid.
Clarithromycin	C	Avoid unless potential benefit outweighs risk.
Clindamycin	B	Use when benefit outweighs risk.
Clioquinol	C	Potential benefits may warrant use of the drug in pregnant women despite potential risks.
Clobazam	C	Use during pregnancy when benefit outweighs risk. Avoid in late pregnancy.
Clobetasol propionate	C	Use when there are no alternatives.
Clomifene citrate	X	Exclude pregnancy before treatment; possible effects on fetal development.
Clomipramine	C	Neonatal withdrawal symptoms reported if used during third trimester.
Clonazepam	D	Risk of neonatal withdrawal symptoms when benzodiazepines are used during pregnancy. Avoid regular use and use only if a clear indication such as seizure control. High doses administered during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression.
Clonidine hydrochloride	C	Use when benefit outweighs risk.
Clopidogrel	B	Use when the need is clearly established.
Cloprostenol		Use with caution.
Clotrimazole	B	Use when established need is clearly. No proven risk in human.
Cloxacillin	B	Use when established need is clearly. No proven risk in human.
Clozapine	B	Potential benefit should outweigh the potential risk.
Colestipol hydrochloride	N	Should be used with caution as although the drugs are not absorbed, they may cause fat-soluble vitamin deficiency on prolonged use.
Colistin sulphate	C	Use only if benefit outweighs risk.
Crotamiton	C	Avoid especially during the first trimester. **1**
Cyanocobalamin	C	Administer as recommended dose.

Cyclizine	B	Use only if benefit outweighs risk.However there is no evidence of teratogenicity.
Cyclobenzaprine	B	Use of drug is not recommended unless clearly needed.
Cyclopentolate	C	Discuss with physician before use.
Cyclophosphamide	D	Avoid; evidence of embryotoxicity and fetotoxicity.
Cyclosporine	C	Evidence of toxicity in animals. Use with caution.
Cypermethrin	C	Evidence of toxicity in animals. Use with caution.
Cytarabine	D	Most of the manufacturers advises to avoid.
Danazol	X	Avoid; has weak androgenic effects and virilisation of female fetus reported.
Dactinomycin	X	Avoid; teratogenic in animal studies.
Dapsone	C	Neonatal haemolysis and methaemoglobinaemia; adequate Folate supplements should be given to mother.
Darifenacin	C	Only recommended for use during pregnancy when benefit outweighs risk.
Daunorubicin	D	Avoid; teratogenic and carcinogenic in animal studies.
Deferasirox	B	Use only when the need is established.
Deferiprone	D	Women of reproductive potential should be advised to avoid pregnancy when taking deferiprone.
Demeclocycline	D	Only recommended for use during pregnancy when there are no alternatives and benefit outweighs risk.
Desferrioxamine	C	Toxicity in animal studies.
Desloratadine	C	No evidence of teratogenicity except for hydroxyzine where toxicity has been reported with high doses in animal studies. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability, paradoxical excitability and tremor.
Desmopressin	C	Small oxytocic effect if used in third trimester.

Desogestrel	X	Avoid.
Desonide	C	Should only be used during pregnancy when benefit outweighs risk.
Dexamethasone	C	The benefit of treatment with corticosteroids during pregnancy and breast-feeding outweighs the risk; pregnant women with fluid retention should be monitored closely.
Dexibuprofen	C	Should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.
Dexketoprofen	C	Should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.
Dexlansoprazole	B	No evidence of human toxicity, use with caution.
Dexpanthanol	C	Discuss with physician before use.
Dextran 70	C	Avoid , reports of anaphylaxis in mother.
Dextromethorphan	C	Prescribe with caution.
Dextromethorphan	C	Use when benefit outweighs risk.
Diacerein	N	Contraindicated in pregnancy.
Diazepam	N	Prescribe with caution; neonatal withdrawal symptoms or floppy instant syndrome may develop if used in third trimester.
Dibromopropamidine isethionate	N	Avoid; no information available.
Diclofenac	D	Avoid unless benefit outweighs risk.
Dicloxacillin	B	Use when the need is clearly established.
Dicycloverine hydrochloride	C	Use when no alternative is available.
Diethylstilbestrol	C	In first trimester, high doses associated with vaginal carcinoma, urogenital abnormalities and reduced fertility in female offspring; increased risk of hypospadias in male offspring.
Diflorasone diacetate	C	Consult with physician before use.

Digoxin	C	Dosage adjustment is required.
Dihydroergotamine		Oxytocic effects on pregnant uterus. **1, 2, 3**
Diloxanide fuorate	C	Avoid.
Diltiazem hydrochloride	C	Avoid; teratogenic in animal studies.
Dimethothiazine mesylate	C	Avoid.
Dinoprostone	C	Use during pregnancy when benefit outweighs risk.
Diosmin	B	No evidence of toxicity. Use with caution.
Diphenhydramine	B	Use only if potential benefit outweighs risk.
Dipyridamole	B	Use only if potential benefit outweighs risk.
Disopyramide	C	Avoid; may induce labor due to uterine contraction if used in third trimester.
Dobutamine	B	Use only if potential benefit outweighs risk.
Docetaxel	D	Avoid; toxicity in animal studies.
Docosanol	N	Consult with physician before use.
Domperidone	N	Avoid.
Donepezil hydrochloride	C	Use only if potential benefit outweighs risk.
Dopamine hydrochloride	C	Use only if potential benefit outweighs risk.
Dorzolamide	C	Use only if potential benefit outweighs risk.
Doxepin	C	Use with caution.
Doxorubicin hydrochloride	D	Avoid; teratogenic in animal studies.
Doxycycline	D	When travel to malarious areas is unavoidable during pregnancy, doxycycline can be used for malaria prophylaxis if other regimens are unsuitable and if the entire

		course of doxycycline can be completed before 15 weeks gestation.
Dronedarone	X	Avoid, toxicity in animal studies.
Drospirenone	X	Avoid.
Drotaverine hydrochloride	C	Use only if potential benefit outweighs risk.
Duloxetine	C	Toxicity in animal studies, use only if potential benefit outweighs risk; risk of neonatal withdrawal symptoms.
Dutasteride	X	Avoid.
Dydrogesterone	B	Use with caution.
Ebastine	B	Use with caution.
Econazole nitrate	C	Use only if potential benefit outweighs risk.
Efavirenz	D	Avoid (effective contraception required during treatment and for 12 weeks after treatment); use efavirenz only if no alternative available.
Enalapril maleate	D	Should be avoided in pregnancy unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Enoxaparin	B	Manufacturer advises avoid.
Enrofloxacin	C	Use only if benefit outweighs risk.
Entacapone	C	Avoid.
Entecavir	C	Toxicity in animal studies, use only if potential benefit outweighs risk effective contraception required during treatment.
Ephedrine hydrochloride	C	Use only if benefit outweighs risk.
Epinastine hydrochloride	C	Use only if benefit outweighs risk.
Epirubicin hydrochloride	D	Use of epirubicin is not recommended unless there are no alternatives and benefit outweighs risk.
Eplerenone	B	Use only if needed clearly.

Epoetin	X	Avoid.
Eprosartan	D	Should be avoided in pregnancy unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Eptifibatide	B	Use only if potential benefit outweighs risk.
Ergometrine maleate	X	Avoid.
Ergotamine		Oxytocic effects on pregnant uterus. **1, 2, 3**
Erlotinib	D	Avoid; harmful for fetus.
Ertapenem	B	Avoid; unless potential benefit outweighs risk.
Erythromycin	B	Avoid; unless potential benefit outweighs risk.
Escitalopram	C	Should not be used during pregnancy unless the potential benefit outweighs the risk. A small increased risk of congenital heart defects when SSRIs are taken during early pregnancy. If SSRIs are used during the third trimester a risk of neonatal withdrawal symptoms and persistent pulmonary hypertension in the newborn has been reported.
Eslicarbazepine acetate	C	Women of child-bearing potential should discuss with a specialist the impact of both epilepsy and its treatment, on the outcome of pregnancy. An increased risk of teratogenicity associated with the use of antiepileptic drugs (especially if used during the first trimester and particularly if the patient takes two or more antiepileptic drugs).
Esomeprazole	C	Use with caution.
Eszopiclone	C	Use only if potential benefit outweighs risk.
Ethambutol	C	Use only if potential benefit outweighs risk.
Ethosuximide	N	Women of child-bearing potential should discuss with a specialist the impact of both epilepsy and its treatment on the outcome of pregnancy.
Etodolac	C	Avoid during pregnancy or avoid unless the potential benefit outweighs the risk, should be avoided during the third trimester

		because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.
Etomidate	C	May depress neonatal respiration if used during delivery.
Etoposide	D	Avoid, teratogenic in animal studies.
Etoricoxib	X	Avoid.
Etravirine	B	Treatment of HIV infection in pregnancy aims to reduce the risk of toxicity to the fetus (although the teratogenic potential of most antiretroviral drugs is unknown) to minimize the viral load and disease progression in the mother and to prevent transmission of infection to the neonate.
Everolimus	D	Avoid.
Ezetimibe	C	Use only if potential benefit outweighs risk.
Famotidine	B	Avoid unless benefit outweighs risk.
Febuxostat	C	Avoid unless benefit outweighs risk.
Felodipine	C	Avoid.
Fenofibrate	C	Avoid , embryo toxicity in animal studies.
Fentanyl	C	Depress neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour**. 3**
Fenticonazole nitrate	C	Use only if potential benefit outweighs risk.
Filgrastim	C	There have been reports of toxicity in animal studies and not to use granulocyte-colony stimulating factors during pregnancy unless the potential benefit outweighs the risk.
Finasteride	X	Unprotected intercourse may cause feminisation of male fetus **1, 2, 3**
Flavoxate hydrochloride	B	Use during pregnancy when there are no alternatives and benefit outweighs risk.
Flucloxacillin	B	Use during pregnancy when there are no alternatives and benefit outweighs risk.

Fluconazole	C,D	Avoid; teratogenic, craniofacial and limb abnormality with long term high doses.
Fludrocortisone acetate	C	The benefit of treatment with corticosteroids during pregnancy and breast-feeding outweighs the risk; Pregnant women with fluid retention should be monitored closely.
Fluocinolone acetonide	C	Avoid.
Fluorescein sodium	C	Use during pregnancy when there are no alternatives and benefit outweighs risk.
Fluorometholone	C	Only recommended for use during pregnancy when benefit outweighs risk.
Fluorouracil	X	Avoid.
Fluoxetine	C	Should not be used during pregnancy unless the potential benefit outweighs the risk. a small increased risk of congenital heart defects when SSRIs are taken during early pregnancy. If SSRIs are used during the third trimester a risk of neonatal withdrawal symptoms, and persistent pulmonary hypertension in the newborn has been reported.
Flupenthixol	C	Only recommended for use during pregnancy when benefit outweighs risk.
Fluphenazine hydrochloride	C	Prescribe with caution. **3**
Flurazepam	N	Prescribe with caution; discourage regular use.
Flurbiprofen	C	Avoid during pregnancy or avoid unless the potential benefit outweighs the risk, should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.
Flutamide	D	Should only be given during pregnancy when there are no alternatives and benefit outweighs risk.
Fluticasone furoate	C	Prescribe with caution.
Fluvastatin	X	Avoid, teratogenic

Fluvoxamine maleate	C	Should not be used during pregnancy unless the potential benefit outweighs the risk, a small increased risk of congenital heart defects when SSRIs are taken during early pregnancy. If SSRIs are used during the third trimester a risk of neonatal withdrawal symptoms and persistent pulmonary hypertension in the newborn has been reported.
Folinic acid	C	Should only be given during pregnancy when there are no alternatives and benefit outweighs risk.
Follitropin alfa & beta	X	Avoid.
Formoterol fumarate	C	It is particularly important that asthma should be well controlled during pregnancy.
Frusemide	C	Should not be used to treat gestational hypertension because of the maternal hypovolemia associated with this condition.
Fusidic Acid	C	Use with caution.
Gabapentin	C	Women of child-bearing potential should discuss with a specialist the impact of both epilepsy and its treatment on the outcome of pregnancy, an increased risk of teratogenicity associated with the use of antiepileptic drugs (especially if used during the first trimester and particularly if the patient takes two or more antiepileptic drugs).
Gadodiamide	C	Use with caution.
Gadoversetamide	C	Should only be given during pregnancy when there are no alternatives and benefit outweighs risk.
Galantamine	C	Use with caution.
Ganciclovir	C	Avoid; women of childbearing potential should use effective contraception during ganciclovir therapy.
Gatifloxacin	C	Should only be given during pregnancy when there are no alternatives and benefit outweighs risk.
Gemcitabine	D	Avoid.

Gemefloxacin	C	Use with caution.
Gemfibrozil	C	Avoid; theoretical possibility of interference with embryonic growth and development due to anti-cholesterol effect.
Gentamicin	C, D	Avoid unless benefit outweighs risk; probably very small auditory or vestibular nerve damage. **1, 2, 3**
Glibenclamide		Insulin is substituted. **3**
Gliclazide	C	Insulin is substituted. **3**
Glimepiride	C	Avoid; toxicity in animal studies. **3**
Glipizide	C	Insulin is substituted.
Glycerin	C	Use with caution.
Glycopyrrolate	B	Use only when benefit outweighs risk.
Gonadorelin	B	Consult with physician.
Granisetron	B	Use during pregnancy when there are no alternatives and benefit outweighs risk.
Griseofulvin	C	Avoid; teratogenic. **1, 2, 3**
Guaiphenesin	C	Potential benefits may warrant use of the drug in pregnant women despite potential risks.
Halcinonide	C	Potential benefits may warrant use of the drug in pregnant women despite potential risks.
Halobetasol propionate	C	Potential benefits may warrant use of the drug in pregnant women despite potential risks.
Haloperidol	C	Prescribe with caution; extra pyramid effects reported in neonates if administered in third trimester. **3**
Halothane		Depress neonatal respiration if administered in third trimester.
Heparin sodium	C	Safer than warfarin for fetus; mother may develop haemorrhage, thrombocytopenia; osteoporosis may develop after prolonged use. does not cross the placenta; maternal osteoporosis reported after prolonged use;

		multi dose vials may contain benzyl alcohol , some avoid.**1, 2, 3**
Hexachlorophene	C	Use when benefit outweighs risk.
Homatropine hydrobromide	C	Use when benefit outweighs risk.
Hydrochlorothiazide	B	Not recommended to treat hypertension; causes neonatal thrombocytopenia if used in third trimester. **3**
Hydrocortisone	C	The benefit of treatment with corticosteroids during pregnancy and breast-feeding outweighs the risk; pregnant women with fluid retention should be monitored closely.
Hydroquinone	C	Consult with physician before use.
Hydroxocobalamin	C	Use when benefit outweighs risk.
Hydroxyurea	D	Avoid.
Hydroxychloroquine	N	It is not necessary to withdraw an antimalarial drug during pregnancy if the rheumatic disease is well controlled; however, the manufacturer of hydroxychloroquine advises avoiding use.
Hydroxyzine hydrochloride	C	Avoid; may associate with fetal abnormality.
Hyoscine butyl bromide	C	Avoid unless benefit outweighs.
Hyoscine hydrobromide	C	Use only if potential benefit outweighs risk, injection may depress neonatal respiration.
Hypromellose	X	Avoid.
Ibandronic Acid	C	Avoid unless benefit outweighs risk.
Ibuprofen	C,D	Avoid unless benefit outweighs risk. **3**
Idoxuridine	C	Toxicity in animal studies.
Ifosfamide	D	Avoid.
Imatinib	D	Avoid, potential benefits may warrant use of the drug in pregnant women despite potential risks.
Imipramine hydrochloride	N	Tachycardia, irritability and muscle spasm in neonate. **1, 2, 3**

Indapamide	B	Prescribe with caution.**1, 3**
Indomethacin	C	Most avoiding the use of NSAIDs during pregnancy or avoiding them unless the potential benefit outweighs the risk. NSAIDs should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn.
Inositol	C	Avoid unless potential benefit outweighs risk.
Insulin	B	Dose should be adjusted frequently **1, 2, 3**
Interferons	C	Avoid unless compelling reasons.
Iodixanol	B	Use with caution.
Iohexol	B	Use with caution.
Iopamidol	B	Use with caution.
Ipratropium bromide	B	It is particularly important that asthma should be well controlled during pregnancy.
Irbesartan	D	Should be avoided in pregnancy unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Isoflurane	C	May depress neonatal respiration if used during delivery.
Isoniazid	C	There are no controlled data in human pregnancies. Embryocidal effects were noted in both rats and rabbits after administration of isoniazid orally during pregnancy. While cases of suspected isoniazid induced anomalies have been reported, causality is unknown and retrospective analyses have failed to document significant teratogenic risk. It should only be given during pregnancy when need has been clearly established.
Isosorbide dinitrate	C	May cross placenta, avoid unless potential benefit outweighs risk.
Isosorbide mononitrate	C	Avoid unless potential benefit outweighs risk.
Isotretinoin	X	Topical retinoids are contra-indicated in pregnancy; women of child-bearing age must use effective contraception (oral

		progestogen-only contraceptives not considered effective).
Itraconazole	C	Use only in life threatening situations (toxicity at high doses in animal studies); ensure effective contraception during treatment and until the next menstrual period following end of treatment.
Ivabradine	D	Avoid, toxicity in animal studies.
Ivermectin	C	Consult physician before use.
Ketamine	C	Depress neonatal respiration if used during delivery.
Ketoconazole	C	Teratogenicity in animal studies; packs carry a warning to avoid in pregnancy.
Ketoprofen	C	Toxicity in animal studies.
Ketorolac trometha	C	Avoid; manufacturer advises use only if potential benefit outweighs risk.
Ketotifen	C	Prescribe with caution.
Levothyroxine sodi	A	Monitor maternal serum-thyrotropin concentration, levothyroxine may cross the placenta and excessive maternal concentration can be detrimental to fetus.
Labetalol hydrochloride	C	Use only if potential benefit outweighs risk.
Lacidipine		Avoid; may inhibit labour.
Lacosamide	C	Increased risk of teratogenicity,associated with the highest risk of major and minor congenital malformations.
Lactulose	B	Use only when need has been clearly established.
Lamivudine	C	Avoid during first trimester.
Lamotrigine	C	Prescribe with caution; increased risk when used more than one antiepileptic drug.
Lansoprazole	B	Avoid.
Latanoprost	C	Use only if potential benefit outweighs risk.
Leflunomide	X	Avoid.
Letrozole	D	Avoid (isolated cases of birth defects reported).

Levamisole	C	Use only if potential benefit outweighs risk.
Levetiracetam	C	Use when the potential benefits justify the potential risk to the fetus.
Levobunolol hydrochloride	C	Use only if potential benefit outweighs risk.
Levobupivacaine hydrochloride		Large doses during delivery can cause neonatal respiratory depression, hypotonia and bradycardia after epidural block; avoid if possible in the first trimester, toxicity in animal studies.
Levocarnitine	B	Use only if potential benefit outweighs risk.
Levocetirizine hydrochloride	B	Use only if potential benefit outweighs risk.
Levofloxacin	C	Avoid-shown to cause arthropathy in animal studies.
Lidocaine	B	Use only if potential benefit outweighs risk.
Linagliptin	B	Linagliptin is only recommended for use during pregnancy when there are no alternatives and benefit outweighs risk.
Linezolid	C	Use only if potential benefit outweighs risk.
Lisinopril	D	Animal studies show still birth, renal failure and oligohydramnios.**1,2,3**
Lithium carbonate	D	Avoid in possible if first trimester, risk of teratogenicity including cardiac abnormalities; dose requirement is increased if necessary as because of the risk of toxicity in neonate. **1,2, 3**
Lomefloxacin	C	Use only if potential benefit outweighs risk.
Lomustine	D	Use only when there are no alternatives and benefit outweighs risk.
Loperamide	C	Avoid.
Loratidine	C	Avoid.
Lorazepam	D	Risk of neonatal withdrawal symptoms high doses administered during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression.
Losartan potassium	D	Use only if potential benefit outweighs risk.
Loteprednol etabon	C	Use only if potential benefit outweighs risk.

Lovastatin	X	Use only if potential benefit outweighs risk.
Lubiprostone	C	Use only if clearly needed and benefit outweighs potential risk.
Magaldrate		Use only if potential benefit outweighs risk.
Magnesium hydroxi		Use only if potential benefit outweighs risk.
Magnesium sulphat		Not known to be harmful for short-term intrave administration in eclampsia but excessive dos third trimester cause neonatal respiratory depr
Mannitol	C	Use only if clearly needed and benefit outweig potential risk.
Maprotiline hydrochloride	B	Use only when need has been clearly established.
Mebendazole	C	Manufacturer advises to avoid, toxicity in animal Studies.
Mebeverine hydrochloride		Prescribe with caution.
Meclizine hydrochlo	B	Use only if potential benefit outweighs risk.
Medroxyprogestero acetate	X	Avoid , genital malformations and cardiac defects reported.
Mefenamic acid	C	See Acetylsalicylic acid. **3**
Mefloquine	B	Adequate contraception during prophylaxis and for 3 months after stopping (teratogenicity in animal studies).
Melatonin	N	Avoid.
Meloxicam	C	Avoid; use only if potential benefit outweighs risk.
Memantine hydrochloride	B	Use only if potential benefit outweighs risk.
Mercaptopurine	D	Avoid (teratogenic).
Meropenem	B	Use only if potential benefit outweighs risk.
Mesalazine		Negligible quantities cross placenta.
Mesna disulfide	B	Use only if potential benefit outweighs risk.
Metaraminol	C	May reduce placental perfusion, manufacturer advises use only if potential benefit outweighs risk.

Metformin	B	Avoid; insulin is substituted. **1, 2, 3**
Methionine	C	Use only when need has been clearly established.
Methotrexate	X	Avoid; teratogenic; fertility may be reduced during therapy which may be reversible.
Methyl prednisolon	C	Use when there are no alternatives and benefit outweighs risk.
Methyldopa	C	Use only if potential benefit outweighs risk.
Methylphenidate hydrochloride	C	Use only if potential benefit outweighs risk.
Metoclopramide hydrochloride	B	Use only when compelling reasons.
Metoprolol tartarate	C	Prescribe with caution.
Metronidazole	B	Avoid high doses; increased risk of teratogenicity if used during first trimester.
Miconazole	C	Avoid unless essential.
Miconazole nitrate		Absorbed from skin in small amounts; manufacturer advises caution.
Midazolam	D	Increased risk of teratogenicity , associated with the highest risk of major and minor congenital malformations
Mifepristone	X	Avoid.
Miglitol	B	Use only when need has been clearly established.
Milnacipran hydrochloride	C	Use only if potential benefit outweighs risk.
Minoxidil	C	Avoid , possible toxicity including reduced placental perfusion; neonatal hirsutism reported.
Mirtazapine	C	use with caution—limited experience.
Misoprostol	X	Avoid; teratogenic; potent stimulant of uterus.**1, 2, 3**
Mitomycin		Avoid (teratogenic in animal studies).
Mizolastine		Avoid.
Mometasone furoat	C	Use when there are no alternatives and benefit outweighs risk.
Montelukast	B	Avoid unless essential.

Morphine sulphate	C	Use only if potential benefit outweighs risk.
Moxifloxacin	C	Cause arthropathy in animal studies.
Moxonidine		Avoid—no information available.
Mupirocin	B	Use only when need has been clearly established.
Mycophenolate mof	D	Avoid; toxicity in animal studies; effective contraceptive measures must be taken during and for 6 weeks of treatment.
Nalbuphine hydrochloride	B	Use only if potential benefit outweighs risk.
Nalidixic acid	C	Shown to cause arthropathy in animal studies.
Naloxone	C	Use only if potential benefit outweighs risk.
Naltrexone	C	Use only if potential benefit outweighs risk.
Nandrolone	X	Avoid,masculinization of female fetus.**1, 2, 3**
Naphazoline nitrate	C	Prescribe with caution.
Naproxen	C	Prescribe with caution. **3**
Natamycin	C	Prescribe with caution.
Nateglinide	C	Avoid, toxicity in animal studies.
Nebivolol	C	Use only if potential benefit outweighs risk.
Nefopam hydrochlo		Avoid unless no safer treatment.
Nelfinavir	B	Use only if potential benefit outweighs risk.
Neomycin	D	Prescribe with caution. **2, 3**
Neostigmine	C	Neonatal myasthenia with large doses.**3**
Nepafenac	C	Use only if potential benefit outweighs risk.
Nevirapine	B	Use only when need has been clearly established.
Niacin	C	Use when there are no alternatives and benefit outweighs risk.

Nicorandil		Use only if potential benefit outweighs risk.
Nicotine	D	Use only if potential benefit outweighs risk.
Nifedipine	C	Prescribe with caution.
Nimodipine	C	Use only if potential benefit outweighs risk.
Nitazoxanide	B	Use only if potential benefit outweighs risk.
Nitrazepam		Prescribe with caution.
Nitrofurantoin	B	Avoid at term, may produce neonatal Hemolysis.
Nitroglycerin	C	Use only if potential benefit outweighs risk.
Nitrous oxide		May depress neonatal respiration if used during delivery.
Nizatidine	B	Avoid unless essential.
Noradrenaline/ norepinephrine	C	Avoid, may reduce placental perfusion.
Norethisterone		Masculinization of female fetuses and other defects reported.
Norgestrel	X	Use only if potential benefit outweighs risk.
Nortriptyline		Prescribe with caution. **3**
Ofloxacin	C	Should be avoided in pregnancy because they have been shown to cause arthropathy in animal studies; safer alternatives are available; however , a single dose of ciprofloxacin may be used for the prevention of a secondary case of meningococcal meningitis.
Olanzapine	C	Use only if potential benefit outweighs risk;neonatal lethargy, tremor, and hypertonia reported when used in third trimester.
Olmesartan medoxo	D	Avoid unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Olopatadine	C	Only recommended when there are no alternatives and benefit outweighs risk.

Omega-3 acid ethyl esters	C	use only if potential benefit outweighs risk—no information available.
Omeprazole	C	Not known to be harmful.
Ondansetron	B	avoid unless potential benefit outweighs risk.
Orlistat	X	Use with caution.
Oseltamivir	C	use only if potential benefit outweighs risk.
Oxaliplatin	D	Avoid, toxicity in animal studies; effective contraception required during and for 4 months after treatment in women and 6 months after treatment in men.
Oxaprozin	C	Avoid; only recommended when benefit outweighs risk.
Oxazepam	N	Risk of neonatal withdrawal symptoms when benzodiazepines are used during pregnancy. Avoid regular use and use only if a clear indication such as seizure control. High doses administered during late pregnancy or labour may cause neonatal hypothermia,hypotonia , and respiratory depression.
Oxybutynin hydrochloride	B	Avoid unless essential, toxicity in animal studies.
Oxcarbazipine	C	Teratogenic, if used in first trimester; neonatal bleeding occur if used in third trimester.
Oxiconazole	B	No controlled data in human pregnancy. Oxiconazole topical should only be used when need has been clearly established.
Oxymetazoline hydrochloride	C	Use when benefit outweighs risk.
Oxytetracycline		Should not be given to pregnant women. Effects on skeletal development when tetracyclines have been used in the first trimester in animal studies. Administration during the second or third trimester may cause discoloration of the child's teeth and maternal hepatotoxicity. However, when travel to malarious areas is unavoidable during pregnancy.
Oxytocin		Avoid.
Paclitaxel		Avoid (toxicity in animal studies); ensure effective contraception during and for at least

		months after treatment in men or women.
Palonosetron	B	Avoid , no information available.
Pancreatin		Not known to be harmful.
Pancuronium bromi	C	Non-depolarising neuromuscular blocking drugs are highly ionised at physiological pH and are therefore unlikely to cross the placenta in significant amounts.
Pantoprazole	B	Avoid unless potential benefit outweighs risk , fetotoxic in animals.
Paracetamol	C	not known to be harmful.
Paricalcitol	C	Avoid unless potential benefit outweighs risk.
Paroxetine	D	Increased risk of congenital malformations , especially if used in the first trimester.
Pegfilgrastim	C	There have been reports of toxicity in animal studies and not to use granulocyte-colony stimulating factors during pregnancy unless the potential benefit outweighs the risk.
Peginterferon alfa-2	C,X	Use when potential benefit outweighs risk.
Pemirolast potassiu	C	Only recommended for use during pregnancy when benefit outweighs risk.
Pentazocine hydrochloride	C	Use when need has been clearly established.
Pentoxifylline	C	Use when benefit outweighs risk.
Peppermint oil		Not known to be harmful.
Perindopril erbumin	C, D	Avoid unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Permethrin	B	Only use when benefit outweighs risk.
Pethidine		Respiratory depression and withdrawal symptoms can occur in the neonate if opioid analgesics are used during delivery; also gastric stasis and inhalation pneumonia has been reported in the mother if opioid analgesics are used during labour.
Pheniramine maleat	B	Unlikely to harm an unborn baby.

Phenobarbitone	C	Congenital abnormality occurs if used in first trimester; neonatal bleeding occurs if used in third trimester. **1, 2, 3**
Phenoxymethyl pen	B	Only be given when need has been clearly established.
Phenytoin hydrochl	D	Changes in plasma-protein binding make interpretation of plasma-phenytoin concentrations difficult, monitor unbound fraction.
Pholcodine		Avoid unless potential benefit outweighs risk.
Phytomenadione		Use if potential benefit outweighs risk.
Pilocarpine hydroch	C	Avoid; stimulation of smooth muscle; toxicity in animal studies.
Pioglitazone	C	Avoid.
Pindolol	D	See Atenolol.
Piracetam		Avoid.
Piroxicam	C	Avoid
Pitavastatin	X	Avoid
Pivmecillinam		Avoid; not known to be harmful.
Pizotifen		Avoid unless potential benefit outweighs risk.
Podophyllotoxin		Avoid.
Poly ethylene glycol 3350	C	Use when benefit outweighs risk.
Potassium chloride	C	Use only when benefit outweighs risk.
Potassium citrate	C	Use only when benefit outweighs risk.
Potassium guaiacol sulphonate	C	Use only when benefit outweighs risk.
Potassium iodide	D	Avoid.
Povidone		Use only when benefit outweighs risk.
Povidone iodine		Sufficient iodine may be absorbed to affect the fetal thyroid in the second and third

		trimester.
Pralidoxime chlorid	C	Use only when benefit outweighs risk.
Prazosin	C	No evidence of teratogenicity; use only if potential benefit outweighs risk.
Prednisolone	C	Use only when benefit outweighs risk
Pregabalin	C	Increased risk of teratogenicity, associated with the highest risk of major and minor congenital malformations.
Primaquine		Risk of neonatal haemolysis and methaemoglobinaemia in third trimester.
Procarbazine	X	al studies.
Prochlorperazine maleate		Use only when benefit outweighs risk.
Prochlorperazine mesilate		Extrapyramidal effects and withdrawal syndrome have been reported occasionally in the neonate when antipsychotic drugs are taken during the third trimester of pregnancy. Following maternal use of antipsychotic drugs in the third trimester, neonates should be monitored for symptoms including agitation, hypertonia, hypotonia, tremor, drowsiness, feeding problems, and respiratory distress.
Procyclidine hydrochloride		Use only if potential benefit outweighs risk.
Progesterone		Not known to be harmful.
Promethazine hydrochloride	C	Avoid.
Promethazine theoc	C	Avoid.
Propafenone hydrochloride	C	use only if potential benefit outweighs risk.
Propantheline brom	C	Avoid.
Propofol	B	May depress neonatal respiration if used during delivery; max. dose for maintenance of anaesthesia 6 mg/kg/hour.
Propranolol hydrochloride	C	May cause intra-uterine growth restriction, neonatal hypoglycaemia and bradycardia; the risk is greater in severe hypertension.If beta-blockers are used close to delivery,

		infants should be monitored for signs of beta-blockade.
Protamin sulphate	C	Use only when need has been clearly established.
Pseudoephedrine hydrochloride		defective closure of the abdominal wall (gastroschisis) reported very rarely in newborns after first trimester exposure.
Pyrazinamide	C	Use only if potential benefit outweighs risk.
Pyridostigmine	C	Use only if potential benefit outweighs risk.
Pyridoxine hydrochloride	A,C	Use only if potential benefit outweighs risk.
Pyrimethamine	C	Theoretical teratogenic risk in first trimester (folate antagonist); adequate folate supplements should be given to mother.
Quetiapine	C	Use only if potential benefit outweighs risk. Extrapyramidal effects and withdrawal syndrome have been reported.
Quinine dihydrochl	C	High doses are teratogenic in first trimester; but in malaria benefit of treatment outweighs risk.
Quinine sulphate	C	High doses are teratogenic in first trimester; but in malaria benefit of treatment outweighs risk.
Rabeprazole sodiu		Avoid—no information available.
Raloxifene hydroch		Avoid.
Ramipril		Should be avoided in pregnancy unless esse adversely affect fetal and neonatal blood pres renal function; skull defects and oligohydran been reported.
Ranitidine	B	Avoid unless essential, but not known to be harmful.
Ranolazine	C	Avoid unless essential— no information available.
Repaglinide	C	Avoid; insulin is substituted.
Retapamulin	B	Use only if potential benefit outweighs risk.
Ribavirin	X	Avoid; teratogenicity in animal studies.
Riboflavin	A,C	Use with caution.
Rifampicin		Teratogenic in animal studies in first trimester; risk of neonatal bleeding may be increased in third trimester.

Rifaximin	C	Avoid, toxicity in animal studies.
Rimexolone	C	Use only if potential benefit outweighs risk.
Risedronate sodium	C	Use only if potential benefit outweighs risk.
Risperidone	C	Use only if potential benefit outweighs risk.
Ritodrine hydrochlo	B	Not for use in first or third trimester.
Rituximab	C	Use only if potential benefit outweighs risk.
Rivaroxaban	C	Avoid.
Rivastigmine	B	Use only if potential benefit outweighs risk.
Rizatriptan	C	Avoid unless the potential benefit outweighs the risk.
Rofecoxib	C	Prescribe with caution.
Rocuronium bromid	C	Use only if potential benefit outweighs risk.
Roflumilast	C	Avoid.
Ropinirole	C	Avoid unless potential benefit outweighs risk.
Rosiglitazone	C	use only if potential benefit outweighs risk.
Rosuvastatin	X	Avoid.
Rupatadine		Take caution—limited information available.
Salmeterol	C	Use only if potential benefit outweighs risk.
Salmon calcitonin	C	Avoid unless potential benefit outweighs risk.
Salsalate	C	Use only if potential benefit outweighs risk.
Saxagliptin	B	Avoid unless essential , toxicity in animal studies.
Sennosides	C	Use only if potential benefit outweighs risk.
Sertraline	C	Avoid unless potential benefit outweighs risk.

Sevelamer hydrochloride	C	Use only if potential benefit outweighs risk.
Sibutramine hydrochloride	C	Use only if potential benefit outweighs risk.
Sildenafil	B	Use only if potential benefit outweighs risk.
Silver sulphadiazine	B	Use only if potential benefit outweighs risk.
simethicone		Use only if potential benefit outweighs risk.
Simvastatin	X	Avoid.
Sitagliptin	B	Avoid.
Sodium bicarbonate	C	Use only if potential benefit outweighs risk.
Sodium fusidate		Not known to be harmful; use only if potential benefit outweighs risk.
Sodium hyaluronate		Use only if potential benefit outweighs risk.
Sodium stibogluconate		Use only if potential benefit outweighs risk.
Sodium thiosulfate	C	Use only if potential benefit outweighs risk.
Sodium valproate	D, X	Avoid, increased risk of teratogenicity, associated with the highest risk of major and minor congenital malformations.
Somatropin		Discontinue if pregnancy occurs.
Solifenacin succinate	C	Caution—no information available.
Sorafenib	D	Avoid unless essential.
Sotalol hydrochloride	B	Beta-blockers may cause intra-uterine growth restriction, neonatal hypoglycaemia, and bradycardia; the risk is greater in severe hypertension.For the treatment of hypertension in pregnancy.
Sparfloxacin	C	Use only if potential benefit outweighs risk.

Spectinomycin	B	Take caution.
Spironolactone	C	Use only if potential benefit outweighs risk.
Streptokinase	C	Thrombolytic drugs can possibly lead to premature separation of the placenta in the first 18 weeks of pregnancy, risk of maternal haemorrhage throughout pregnancy and post-partum, and also a theoretical risk of fetal haemorrhage throughout pregnancy.
Streptomycin	D	Avoid unless essential; greatest risk of auditory or vestibular nerve damage in the infant.
Sulfasalazine	B	Theoretical risk of neonatal haemolysis in third trimester; adequate folate supplements should be given to mother.
Sulfinpyrazone		Caution—no information available.
Sulindac	C	Avoid unless the potential benefit outweighs the risk.
Sulphanilamide	C	Use only if potential benefit outweighs risk.
Sumatriptan	C	Use only if potential benefit outweighs risk.
Sunitinib	D	Avoid unless the potential benefit outweighs the risk.
Suxamethonium ch		Mildly prolonged maternal neuromuscular blockade may occur.
Tacrolimus	C	Exclude before treatment; avoid unless potential benefit outweighs risk, risk of premature delivery, intra-uterine growth restriction, and hyperkalaemia.
Tadalafil	B	Avoid
Tamoxifen	D	Avoid , possible effects on fetal development; effective contraception must be used during treatment and for 2 months after stopping.
Tamsulosin hydroc	B	Consult physician.
Tapentadol	C	Respiratory depression and withdrawal symptoms can occur in the neonate if opioid analgesics are used during delivery; also gastric stasis and inhalation pneumonia has been reported in the mother if opioid analgesics are used during labour.
Tazarotene	X	Avoid.

Tegaserod	B	Use only if potential benefit outweighs risk.
Teicoplanin		Use only if potential benefit outweighs risk.
Telmisartan	D	Should be avoided in pregnancy unless essential. They may adversely affect fetal and neonatal blood pressure control and renal function; skull defects and oligohydramnios have also been reported.
Temazepam	X	There is a risk of neonatal withdrawal symptoms when benzodiazepines are used during pregnancy. Avoid regular use and use only if a clear indication such as seizure control. High doses administered during late pregnancy or labour may cause neonatal hypothermia , hypotonia , and respiratory depression.
Temozolomide	D	Avoid (teratogenic and embryotoxic in animal studies); manufacturer advises adequate contraception during treatment; men should avoid fathering a child during and for at least 6 months after treatment.
Tenofovir disoproxi fumarate	B	Use only if potential benefit outweighs risk.
Tenoxicam		Avoid unless the potential benefit outweighs the risk.
Terazosin	C	No evidence of teratogenicity; use only when potential benefit outweighs risk.
Terbinafine		Avoid.
Terbutaline sulphat	B	Use only if potential benefit outweighs risk.
Testosterone		Avoid; causes masculinisation of female fetus.
Tetanus vaccines		Live vaccines should not be administered routinely to pregnant women because of the theoretical risk of fetal infection.
Tetracosactide		Avoid.
Tetracycline		Avoid; effects on skeletal development in animal studies; dental discoloration if used in second and third trimester. **1, 2, 3**
Theophylline	C	Prescribe with caution; neonatal irritability and apnoea. **3**
Thioridazine		Prescribe with caution.
Thiamine hydrochlo	A	Use only if potential benefit outweighs risk.

Thiopentone sodiur		May depress neonatal respiration when used during delivery.
Tibolone		Avoid , toxicity in animal studies.
Ticlopidine hydrochloride		Avoid unless essential.
Tigecycline	D	Should not be given to pregnant women. Effects on skeletal development have been documented when tetracyclines have been used in the first trimester in animal studies. Administration during the second or third trimester may cause discoloration of the child's teeth, and maternal hepatotoxicity has been reported with large parenteral doses.
Timolol maleate	C	Beta-blockers may cause intra-uterine growth restriction, neonatal hypoglycaemia and bradycardia; the risk is greater in severe hypertension.If beta-blockers are used close to delivery, infants should be monitored for signs of beta-blockade.
Tinidazole		Avoid in first trimester.
Tioconazole	C	Manufacturer advises avoid.
Tiotropium	C	Manufacturer advises use only if potential benefit outweighs risk.
Tizanidine	C	Avoid.
Tobramycin		Prescribe with caution.
Tolfenamic acid		Avoid the use of NSAIDs during pregnancy or avoiding them unless the potential benefit outweighs the risk. NSAIDs should be avoided during the third trimester because use is associated with a risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn. In addition , the onset of labour may be delayed and its duration may be increased.
Tolmetin	C	Avoid; use only if potential benefit outweighs risk.
Tolnaftate		Use only if potential benefit outweighs risk.
Tolterodine tartrate	C	Avoid.

Topiramate	D	Use only if potential benefit outweighs risk ;increased risk of cleft palate if taken in the first trimester of pregnancy.
Torasemide	B	Manufacturer advises avoid , toxicity in Animal studies.
Tramadol hydrochlo	C	Embryotoxic in animal studies, avoid.
Tranexamic acid		Use only if potential benefit outweighs risk.
Trastuzumab	D	Manufacturer advises avoid, oligohydramnios reported; effective contraception must be used during treatment and for 6 months after stopping.
Travoprost	C	Avoid.
Tretinoin		Teratogenic, effective concentration must be used for at least 1 month before oral treatment, during treatment and at 1 month after stopping also avoid topical treatment. **1, 2, 3**
Triamcinolone acet	C	use only if potential benefit outweighs risk.
Trifluoperazine		Prescribe with caution.
Trihexyphenidyl hydrochloride		Use only if potential benefit outweighs risk.
Trimethoprim	C	Avoid;teratogenic risk in first trimester (folate antagonist).
Trimipramine	C	Use only if potential benefit outweighs risk.
Tropicamide	C	Use only if potential benefit outweighs risk.
Ulipristal acetate	X	Manufacturer advises avoid , no information available.
Urokinase	B	Thrombolytic drugs can possibly lead to premature separation of the placenta in the first 18 weeks of pregnancy. There is also a risk of maternal haemorrhage throughout pregnancy and post-partum, and also a theoretical risk of fetal haemorrhage throughout pregnancy.
Ursodeoxycholic ac		No evidence of harm but manufacturer Advises avoid.
Valacyclovir	B	Use only if potential benefit outweighs risk.
Valsartan		Avoid.

Sodium valproate	D, X	Avoid, increased risk of teratogenicity, associated with the highest risk of major and minor congenital malformations.
Vancomycin	B	Use only if potential benefit outweighs risk.
Vasopressin		Oxytocic effect in third trimester.
Varenicline	C	Avoid, toxicity in animal studies.
Vecuronium bromid	C	Highly ionised at physiological pH and are therefore unlikely to cross the placenta in significant amounts.
Venlafaxine	C	Avoid unless potential benefit outweighs risk, toxicity in animal studies; risk of withdrawal effects in neonate.
Verapamil hydrochl	C	May reduce uterine blood flow with fetal Hypoxia; manufacturer advises avoid in first trimester Unless absolutely necessary; may inhibit labour.
Vildagliptin		Avoid , toxicity in animal studies.
Vinblastine	D	Avoid (teratogenicity and fetal loss in animal studies).
Vincristine	D	Avoid (teratogenicity and fetal loss in animal studies).
Vinorelbine	D	Avoid unless essential (teratogenicity, and fetal loss in animal studies); manufacturer advises effective contraception during and for 3 months after treatment; men must avoid fathering a child during and for at least 3 months after treatment.
Vinpocetine		Avoid.
Vitamin A	X	Excessive doses may be teratogenic.
Vitamin C	A	use only if potential benefit outweighs risk.
Vitamin E	A	Use only if potential benefit outweighs risk.
Voriconazole	D	Toxicity in animal studies. Manufacturer advises avoid unless potential benefit outweighs risk; effective contraception required during treatment.
Warfarin sodium	X	Teratogenic.
Xylometazoline		Manufacturer advises to avoid.

Zalcitabine	C	Use only if potential benefit outweighs risk.
Zafirlukast	B	Avoid.
Zaleplon		Avoid in first trimester; neonatal withdrawal. symptoms if used in third trimester.
Zidovudine	C	Use only if potential benefit outweighs risk.
Zinc oxide		Use only if potential benefit outweighs risk.
Zinc sulfate	C	Crosses placenta; risk theoretically minimal, but no information available.
Zinc sulphate mono	C	Use only if potential benefit outweighs risk.
Ziprasidone	C	Use only if potential benefit outweighs risk.
Zoledronic acid	D	Avoid , toxicity in animal studies.
Zolmitriptan	D	Limited experience of using $5HT_1$-receptor agonists during pregnancy; that they should be avoided unless the potential benefit outweighs the risk.
Zolpidem tartrate	C	Avoid regular use (risk of neonatal withdrawal symptoms); high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia, and respiratory depression.
Zopiclone		Avoid regular use (risk of neonatal withdrawal symptoms); high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia, and respiratory depression.

Appendix- 6

BREAST-FEEDING

When nursing mothers take some categorical drugs that affect the newborn, most of the drugs are found in breast milk. Some in too small quantity to be harmful for the neonate but some are found pharmacologically toxic to the infants. Some drugs also inhibit the infant's sucking reflex (e.g. phenobarbitone). Concentration of some drugs in milk may exceed those in (like iodides) the maternal plasma so that therapeutic doses in the mother may cause toxicity to the infant.

For some drugs information available is so insufficient that providing guidance is difficult. It is better to use only essential drugs by a breast-feeding mother.
The following table of information about drugs can be used as a guideline; absence of drugs from the table does not imply safety.

Chemotherapeutics, though harmful to infant, must be administered to the affected mother in certain cases like HIV, cancer etc. In such cases, breast-feeding of children must be suspended.

Drugs present in breast milk :

Drug	Comment
Abacavir	breast feeding recommended first six months if no safe alternative to breast milk.
Acarbose	Avoid.
ACE inhibitors.	Avoid.
Aceclofenac	Avoid; no information available.
Atenolol & Acebutolol	Grater amount found in the milk, avoid.
Acetazolamide	Can be used, very small amount found in the milk.
Acetylsalicylic acid or Aspirin	Avoid, because regular intake has a possible risk of Raye's syndrome; regular use of high doses could impair platelet function and produce hypoprothrombinaemia in infant if neonatal vitamin K stores low.
Acitretin	Avoid.
Aciclovir	Significant amount is found in milk after systemic administration.
Alendronate sodium	Avoid.
Allopurinol	Present in milk.
Alprazolam	Present in milk; avoid.
Alcohol	Large amount may affect infant and reduce milk consumption.
Amantadine	Should not be used
Amiodarone	Should not be used
Androgens	Avoid; may cause masculinisation in the female infant or precocious development in the male infant; high dose suppresses lactation.
Amiloride	Avoid, no information available
Antidepressants	Amount of tricyclic antidepressants (including related drugs such as mianserin and trazodone) too small to be harmful; avoid.

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Atracurium	Avoid, no information available.
Atropine	Use with caution, very small amount available in milk.
Azithromycin	Prescribe with caution; no harmful effect is known; use only if adequate alternatives not available.
Bendrofluazide	Amount too small to be harmful; large doses may suppress lactation.
Beta-blokers	Monitor infants; possible toxicity due to beta-blockade but amount of most beta-blockers excreted in milk too small to affect infant; acebutolol. Atenolol, nadolol and solatol are present in higher amounts than other beta-blockers; manufacturers advice to avoid celiprolol and nebivolol.
Bismuth Subcitrate/Subsalicylate	Avoid.
Benzoiazepines	Present in milk; avoid if possible.
Benzylpenicillin	trace amount present in milk; safe in usual dosage; monitor infant.
Betamethasone	Systemic effect in infant unlikely with maternal dose of less than equivalent of Prednisolone 40mg daily; monitor Infants adrenal function with higher dosage.
Bromazepam	See benzoiazepines.
Bupivacaine	Amount too small to be harmful.
Busulphan	Discontinue breast-feeding.
Calcipotriol	Avoid if possible; no information available.
Carbamazepine	Amount too small to be harmful; but 1-2 cases of reported skin rashes in infants.
Carbimazole	Amounts in milk may be sufficient to affect neonatal thyroid function, therefore lowest effective dose should be used.
Carbocisteine	Avoid.
Ceftriaxone	Excreted in low concentration; safe in usual dosage; monitor infant in higher dosage.
Clindamycin	Should avoid.
Clomiphene	May inhibit lactation; Avoid.
Clonidine	May decrease milk supply; Avoid.
Clozapine	Should not be used.
Carboplatin	Discontinue breast-feeding.
Chloramphenicol	Use replacement, may cause bone-marrow toxicity in infants; concentration in milk usually insufficient to cause Grey syndrome.
Chlorthalidone	May inhibit lactation; Avoid.
Chlorambucil	Discontinue breast-feeding.
Chloroquine	Amount too small to be harmful; inadequate for reliable protection against malaria.
Chlorpromazine	Drowsiness in infants reported.
Chlorpropamide	Caution; theoretical possibility of hypoglycemia in infants.
Cilazapril	Avoid; excreted in milk.
Cimetidine	Significant amount present in milk; till not known to be harmful; but better to avoid.
Citalopram	Can cause infant drowsiness; should avoid.
Ciprofloxacin	High concentrations in breast milk; avoid.
Cisatracurium	No information available.
Cisplatin	Discontinue breast-feeding.

Contraceptives (oral)	Combined OCP inhibit lactation; Should avoid.
Co-trimoxazole	Small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants.
Clarithromycin	Avoid; excreted in milk.
Dactinomycin	Discontinue breast-feeding.
Dalteparin	No information available.
Dapsone	Haemolytic anaemia; although significant amount in milk risk to infant very small.
Daunorubicin	Discontinue breast-feeding.
Diazepam	Present in milk, avoid if possible.
Diclofenac	Amount too small to be harmful.
Digoxin	Amount too small to be harmful.
Dihydroergotamine	Avoid, ergotism may occur in infants; repeated doses may inhibit lactation.
Diloxanide	Avoid.
Diltiazem	Avoid; significant amount present in milk.
Disopyramide	Present in milk; use only if essential and monitor infant for antimuscarinic effects.
Docetaxel	Discontinue breast-feeding.
Domperidone	Amount probably too small to be harmful.
Doxepin	Should avoid.
Doxorubicin	Discontinue breast-feeding.
Doxycycline	Avoid, or if necessary, discontinue breast-feeding.
Droperidol	Although amount excreted in milk probably too small to be harmful, animal studies indicate possible adverse effects of these drugs on developing nervous system, therefore avoid unless absolutely necessary.
Enoxaparin	Avoid, no information available.
Epoetin	Avoid, no information available.
Ergotamine	Avoid, ergotism may occur in infant; repeated doses may inhibit lactation.
Erythromycin	only a small amount is present in breast milk; safe in usual dosage; monitor infant.
Ethosuximide	Should avoid.
Etoposide	Discontinue breast-feeding.
Famotidine	Present in milk, not known to be harmful; avoid.
Felodipine	Appears in milk; avoid.
Fentanyl	Avoid.
Filgrastim	Avoid, no information available.
Fluconazole	Avoid; present in milk.
Fluorouracil	Discontinue breast-feeding.
Fluoxetine	Should Avoid.
Fluphenazine	Amount excreted in milk too small to be harmful. Animal studies showed harmful effect.
Flurazepam	See benzodiazepine.
Fluvastatin	Manufacturer advises to avoid.
Fosinopril	Present in milk; avoid.
Frusemide	Too small to be harmful.
Gemcetabine	Discontinue breast-feeding.
Gemfibrozil	Avoid; no information available.
Gentamicin	Avoid.
Glibenclamide	See sulphonylureas.
Gliclazide	See sulphonylureas.

Glimepiride	See sulphonylureas.
Glipizide	See sulphonylureas.
Haloperidol	Excreted in milk, but too small to be harmful.
Halothane	Excreted in milk.
Heparin	Avoid, risk of haemorrhage in infants.
Hydralazine	Present in milk but not known to be harmful. Monitor infants.
Hydrocortisone	Systemic effect in infant unlikely with maternal dose of less than equivalent of Prednisolone 40mg daily; monitor Infants adrenal function with higher dosage.
Hydrochlorothiazide	Amount too small to be harmful, large doses may suppress lactation.
Hydroxyzine	Avoid; significant amount found in milk.
Hyoscine butylbromide	Amount too small to be harmful.
Ibuprofen	Too small to be harmful, but better if avoided.
Idoxuridine	May possibly make taste of milk unpleasant.
Imipramine	May cause respiratory depression; avoid.
Indapamide	Avoid; no information available.
Indomethacin	Avoid; too small amount found in milk; convulsion reported in some infants.
Insulin	Amount too small to be harmful.
Interferons	Avoid; no information available.
Iodine	Stop breast-feeding; danger of neonatal hypothyroidism or goitre; appears to be concentrated in milk.
Irinotecan	Discontinue breast-feeding.
Isoniazide	Monitor infants for possible toxicities; theoretical risk of convulsion and neuropathy; prophylactic Pyridoxine is advisable for mother and infant.
Isotretinoin	Avoid.
Ivermectin	Avoid until infant is 1 week old.
Itraconazole	Small amount found in milk, not harmful.
Ketorolac	Avoid.
Ketotifen	Significant amount present in milk, not harmful but drowsiness in infants reported.
Lacidipine	Avoid; no information available.
Lamivudine	Breast-feeding not advised in HIV infection.
Lamotrigine	Small amount found in milk, not harmful.
Lignocaine	Amount too small to be harmful.
Lipid lowering agents	Should not be used.
Lisinopril	Caution to be taken; no information available.
Lithium	Present in milk, and risk of toxicity in infant.
Loperamide	Amount found in milk not harmful for infant.
Mebendazole	No information available.
Mebeverine	Amount in milk too small to be harmful.
Mefloquine	Present in breast milk but risk to infant is minimal.
Melphalan	Discontinue breast-feeding.
Mercaptopurine	Discontinue breast-feeding.
Meropenem	Avoid.
Methadone	Withdrawal symptoms in infant; breast-feeding permissible during maintenance but dose should be as low as possible and infant monitored to avoid sedation.
Methotrexate	Discontinue breast-feeding.
Metoclopramide	Although amount in milk is small, avoid unless essential.
Metronidazole	Significant amount in milk; do not take single large doses.

Mianserin	Risk of respiratory depression in infants.
Miconazole	Take caution; no information available.
Misoprostol	Avoid; no information available.
Mitomycin	Discontinue breast-feeding.
Morphine	Therapeutic doses unlikely to affect infants; withdrawal symptoms in infants of dependent mothers.
Mycophenolate	Avoid; no information available.
Nadolol	Should avoid.
Naloxone	Avoid; no information available.
Naproxen	Amount too small to be harmful.
Neostigmine	Amount too small to be harmful. Monitor infant.
Nifedipine	Amount too small to be harmful.
Nitrazepam	See benzodiazepam.
Nitrofurantoin	Only small amounts in milk but could be enough to produce G6PD-deficient infant.
Nortryptyline	Risk of respiratory depression in infants.
Ofloxacin	Avoid.
Olanzapine	Avoid; adverse reactions occur.
Omeprazole	Avoid; no information available.
Orlistat	Avoid; no information available.
Oxcarbazipine	See benzodiazepine.
Oxytetracycline	Avoid; teeth deformity in infants.
Paclitaxel	Discontinue breast-feeding.
Penicillamine	Trace amount in milk, use with caution.
Pethidine	Avoid.
Phenobarbital	Avoid.
Phenytoin	Small amount present in milk, avoid.
Piroxicam	should avoid.
Pilocarpine	Avoid; no information available.
Pindolol	Too small amount found in milk to be harmful; monitor infants.
Praziquantel	Avoid breast feeding during and 72 hours after treatment.
Prazosin	Amount probably too small to be harmful.
Primaquine	Avoid; risk of haemolysis in G-6PD deficit infant.
Procarbazine	Discontinue breast-feeding.
Propafenone	Avoid. No information available.
Propranolol	Monitor infant; possible toxicity due to beta-blockade but amount of most beta-blockers excreted in milk too small to affect infants.
Pyrazinamide	Amount too small to be harmful.
Pyrimethamine	Significant amount, avoid administration of other folate antagonists to infants.
Quinidine	Significant amount, but not known to be harmful.
Ranitidine	Significant amount present in breast milk but not known to be harmful.
Repaglinide	Avoid.
Reserpine	Should avoid.
Retinol	Theoretical risk of toxicities in infants of mother taking larger dose.
Rifampicin	Amount too small to be harmful.
Ritonavir	Breast-feeding not advised in HIV infections.
Recuronium	Avoid.
Rofecoxib	Avoid. Present in milk in animal studies.
Simvastatin	Avoid.

Sodium autothiomalate	Avoid.
Sodium valproate	Amount too small to be harmful.
Somatropin	Avoid, no information available.
Sotalol	Should avoid.
Sulphonylureas	Caution, theoretical possibility of hypoglycaemia in infants.
Sulphasalazine	Small amounts in milk. Theoretical risk of neonatal haemolysis especially in G6PD- deficient infants.
Sulpride	Significant amount in milk; avoid.
Tamoxifen	Avoid; no information available.
Terbinafne	Present in milk; avoid.
Tetracycline	Avoid; deformity and dental decolourisation in infants.
Theophylline	Irritability in infant reported; modified release preparations probably safe.
Thioridazine	Avoid.
Ticlopidine	Avoid.
Timotol	Avoid.
Tinidazole	Avoid.
Trimethoprime	Present in milk; short-term use not harmful.
Tretinoin	Avoid.
Trifluoperazine	Avoid.
Valsartan	Avoid.
Valproic acid	Amount too small to be harmful.
Vancomycin	Avoid; present in milk.
Verapamil	Amount probably too small to be harmful.
Venlaflaxine	Should avoid.
Vinblastine	Discontinue breast-feeding.
Vincristine	Discontinue breast-feeding.
Warfarin	See anticoagulant.
Zafirlukast	Avoid; present in milk.
Zalcitabine	Breast-feeding not advised in HIV infections.
Zaleplon	Avoid.
Zidovudine	Breast-feeding not advised in HIV infections.

Appendix-7

POISONING

A BRIEF OVERVIEW

Poisoning occurs when any substance interferes with normal body functions after it is swallowed, inhaled, injected, or absorbed. In 80% of the cases, the victim is a child under the age of five. Curiosity, inability to read warning labels, a desire to imitate adults, and inadequate supervision lead to childhood poisonings. The elderly are the second most likely group to be poisoned. Mental confusion, poor eyesight, and the use of multiple drugs are the leading reasons why this group has a high rate of accidental poisoning. A substantial number of poisonings also occur as homicide, suicide attempts or drug overdoses.

There are basically two major types of poisons. One group consists of products that are never meant to be ingested or inhaled, such as shampoo, paint thinner, pesticides, toxic planteaves, and carbon monoxide. The other group contains products that can be ingested in small quantities, but which are harmful if taken in large amounts, such as pharmaceuticals, medicinal herbs, or alcohol. Other types of poisons include the bacterial toxins that cause food poisoning, such as *Escherichia coli*; heavy metals, such as the lead found in the paint on older houses; and the venom found in the bites and stings of some animals and insects.

On the basis of severity, the types of poisoning are 1) **Acute poisoning** – excessive single dose, or several smaller doses of a poison taken over a short interval of time; 2) **Chronic poisoning** – smaller doses over a period of time, resulting in gradual worsening; 3) **Sub-acute poisoning** – the poisoning lies between acute and chronic poisoning, resulting in gradual worsening and 4) **Fulminate poisoning** – a very high or massive dose of poison at a time results death with or without any sign and symptom and patient become collapse suddenly. There have some nature of poisoning which are- a) **Homicidal** – killing of a human being by another human being by administering poisonous substance deliberately without other one's notice. b) **Suicidal** – when poisoning is created by himself/ herself to end his/ her life; c) **Accidental** – any poisonous substance taken/administered unknowingly by the person or children. Eg. Household poisons- nail polish remover, acetone etc; and d) **Occupational** – poisoning occurs as professional workers. Eg. insecticides, noxious fumes.

The effects of poisons are as varied as the poisons themselves; however, the exact mechanisms of only a few are understood. Some poisons interfere with the metabolism. Others destroy the liver or kidneys, such as heavy metals and some pain relief medications, including acetaminophen and nonsteroidal anti-inflammatory drugs. A poison may severely depress the central nervous system, leading to coma and eventual respiratory and circulatory failure. Potential poisons in this category include anesthetics (e.g. ether and chloroform), opiates (e.g., morphine and codeine), and barbiturates. Some poisons directly affect the respiratory and circulatory system. Carbon monoxide causes death by binding with hemoglobin that would normally transport oxygen throughout the body. Certain corrosive vapors trigger the body to flood the lungs with fluids, effectively drowning the person. Cyanide interferes with respiration at the cellular level. Another group of poisons interferes with the electrochemical impulses that travel between neurons in the nervous system. Yet another group, including cocaine, ergot, strychnine, and some snake venoms, causes

potentially fatal seizures. Severity of symptoms can range from headache and nausea to convulsions and death. The type of poison, the amount and time of exposure, and the age, size, and health of the victim are all factors which determine the severity of symptoms and the chances for recovery

Some general principles for diagnosing and treating poisoning are discussed first. Highlights of symptoms and treatment for individual chemicals and drugs, or groups of substances follow alphabetically. Poisoning from snakebites and other life-forms are discussed.

GENERAL PRINCIPLES OF TREATMENT:

DIAGNOSIS

Poisoning should be considered in the differential diagnosis of any unexplained symptoms or signs, especially in children < 5 yr. Similarly, in the young adult, any disparity between expected history and clinical findings should suggest poisoning. Often the type and speed of onset of the total clinical picture will conform or refute a suspicion of poisoning. Occasionally, the absence of a specific finding will be as important as its presence. Any pertinent history should be secured and the person and premises inspected for traces of drugs, i.e. imprint identifications on solid medication forms, alcohol, etc., particularly for the unconscious patient.

IMMEDIATE CARE/ FIRST AID MEASURES

1. Remove patient from further exposure to pain.
2. Determine adequacy of cardiac and respiratory function and begin resuscitation if needed.
3. Determine quickly what has happened. Identify the substance ingested, its route of entry into the body, and its toxicity potential. *Save any containers and appropriate specimens of the product or of emetic returns*.
4. Determine the need for medical care, recognizing that many substances eed no further treatment. At all times, it should be recalled that over treatment per se may be a hazard. Unless contraindicated, immediately dilute and remove the toxic substance from the body. A person who has ingested a toxic substance may also have spilled it on the skin and may be inhaling fumes as well.
5. Maintain body temperature and blood pressure.
6. Fluid balance should be maintained.

Ingested poison: Emesis will usually remove more of the toxic substance than will gastric lavage. Immediately induce vomiting with ipecac syrup 15 to 30 mL (1 to 2 tbsp for children and adults taken with water or soft drinks (orally: 15 mL/kg for infants: 1 qt [1 L] for adults); and keep the patient actively moving if possible. The dose of ipecac may be repeated in 15 min if necessary. If ipecac is not available, give soapy water, anionic or non-anionic detergent (hand-washing liquid detergent) plus water and induce vomiting by inserting a finger or blunt instrument into the patient's throat. Avoid being bitten. Place a child in the head-down position. Save a portion of the vomitus for analysis. (*CAUTION : Do not induce vomiting if the patient is comatose, is having convulsions [or is likely to], or has ingested petroleum distillates or corrosive substances. Emesis of petroleum distillates is hardly ever indicated unless some other compound has been dissolved in the distillates that requires evacuation [eg. parathion*]).

When **gastric lavage** is carried out (do not use lavage if the patient is convulsing or if the ingested substance is corrosive), use the largest tube appropriate for the patient. For comatose or sedated patients > 2 yr of age, use a cuffed endotracheal tube to

prevent aspiration. For those < 2, no cuff is needed on the endotracheal tube because of the snug fit. Have the patient in a head-low position. For adults, physiologic (0.9%) sodium chloride solution or tap water may be used; for children, 0.45% sodium chloride solution is recommended. Introduce lavage fluids in 20 to 30 mL aliquots and remove the stomach contents by siphon or syringe after each installation. Continue the rinsing procedure until washings return free of toxin. After the return is clear, instill a specific antidote if one is available; otherwise instill a slurry of activated charcoal (see below).

The use of **cathartics** remains controversial; some evidence suggests that they may actually enhance absorption rather than promote excretion. If a cathartic is used, it is best limited to sodium sulfate 30gm dissolved in 250 mL water, with proportionally reduced amounts for children.

When taken internally, **activated charcoal** with its molecular configuration and large surface area adsorbs significant amounts of many poisons, precluding their absorption from the gut. The earlier the charcoal is used, the more effective it is. From 5 to 10 times the amount of charcoal as that of poison suspected of being ingested should be used. For children < 5 yr the usual dose is 25 gm; for older children and adults, 50 to 100 gm.

Specific antidotes: While not numerous, specific antidotes are remarkably effective eg., naloxone in opioid overdoses, atropine and pralidoxime in organo-phosphate encounters, methylene blue for methemoglobinemia, N- acetylcysteine for acetaminophen, protamine sulphate for heparine, flumazenil for benzodiazepine.

Inhaled poison: The patient should be removed from the contaminated environment, his/her respiration supported and other personnel protected from contamination.

Skin and eye contamination: Contaminated clothing (including shoes and socks) should be removed. The skin should be thoroughly washed and the eyes flushed with water. Helpers should also be taken care of being protected from contamination.

CNS stimulation by the poison may require **sedation**. Usually, diazepam or a barbiturate is used. In pure amphetamine poisoning, chlorpromazine is the drug of choice. To terminate convulsions, diazepam (5 to 10 mg for adults; 0.1 to 0.2 mg/kg for children) is given slowly IV. Phenobarbital (100 to 200 mg for adults and 4 to 7 mg/kg for children) may be used IV or IM to either terminate or prevent the recurrence of a convulsion.

CONTINUING CARE

Symptomatic and supportive treatment depends on symptoms and signs and on anticipation of the clinical course, based upon identification of the poison. Continuation of the appropriate measures already begun and attempts to enhance excretion of poison already absorbed are basic considerations. Stimulants are unlikely to be effective and are generally *contraindicated*. **Severe CNS depression** requires support of the circulation and ventilation. Endotracheal intubation and rarely tracheostomy may be necessary. In suspected or known narcotic poisoning, naloxone-an potent opiod antagonist should be used.

Cerebral edema is common in poisoning due to sedatives, carbon monoxide, lead, and other CNS depressants. A 20% mannitol solution (5 to 10 mL/kg) is given slowly IV over a 30- to 60 min period. Corticosteroids are also used (dexamethansone 1 mg/sq m of BSA q 6 h by IV drip). The use of intracranial monitoring with hyperventilation to alter the degree of cerebral edema enjoys widespread favor. The use of “barbiturate coma” in cerebral edema associated with hypoxic episodes has been advocated but the practice must be considered experimentally.

Renal failure may occur in poisoning, and dialysis may be required. Elimination of poisons sometimes can be hastened either by augmenting normal excretory pathways or by using artificial means such as dialysis, depending upon the nature of the poisoning, the availability of the faculties and the condition of the patient. Flushing out the poison by simply increasing urine volume is rarely helpful. Alkalinization or acidification of the urine can occasionally be helpful (eg. in acute salicylate ingestions, giving 2 to 3 mEq/kg of sodium bicarbonate IV will augment excretion significantly). In general, weak acids are captured in alkalinized urine and weak bases in acidified urine.

Over the past decade, **hemo**- and peritoneal dialysis have been augmented by the development of "**lipid dialysis**" aimed at removal of lipid-soluble substances from the blood and **hemoperfusion**, to provide an even more rapid and efficient clearance of toxic substances from the blood. However, these techniques are useless if the involved substance has a large "apparent volume of distribution" – i.e. if it is stored in fatty tissue or extensively bound to tissue protein. In select circumstances these techniques may be effective, but in many instances their yield is negligible. Thus while digoxin is rapidly cleared from the blood via hemoperfusion, such a small amount (3 to 5%) of the total body digoxin is present in the blood that hemoperfusion is ineffective.

TREATMENT OF COMMON POISONING:

ACETAMINOPHEN or PARACETAMOL

SYMPTOMS

Early: Often asymptomatic; mild nausea, vomiting, diaphoresis, pallor, beginning signs of hepatotoxicity; oliguria; Later (at 24-48h): Nausea & protracted vomiting, right upper quadrant pain, jaundice, coagulation defects, hypoglycemia, encepthalopathy, hepatic failure; renal failure, myocardiopathy may occur.

TREATMENTS

Emesis: gastric lavage. Monitor plasma drug levels for prognosis;

If > 160-200 µg/ mL at 4 h. hepatic necrosis may occur; if plasma level > 300 µg/ mL at 4 h. hepatic damage is almost certain. If given before 18 h. oral N-acetylcysteine (Mucomyst®) 140 mg/ kg to start and 70 mg/ kg q 4 h for 4 to 18 doses have been effective in preventing significant hepatotoxicity.

ASPIRIN AND SALICYLATES

SYMPTOMS

Nausea, vomitting, dizziness, tinnitus, headache, confusion, hyperventellation, tachycardia, fever. In severe case: delirium, hallucination, convulsion, coma and respiratory crisis may occur.

TREATMENTS

Supportive treatment: Fluid/ electrolyte management: Rehydrate with 0.9 % saline at the rate of 10-20 cc / hr over 1-2 hrs until urine flow is 3-6 cc/kg/ hr. For preventing absorption: Ipecac, Gastric lavage, charcoal and cathertic administration. For enhancing elimination, perform forced alkaline diuresis, hemodialysis, hemoperfusion

BARBITURATES

Amobarbital, Pentobarbital, Phenobarbital, Secobarbital

SYMPTOMS

Headache, confusion, ptosis, excitement, delirium, loss of corneal reflex, respiratory failure, coma

TREATMENT

Empty stomach up to 24 h after ingestion. If immediately after, use ipeace emetic; if sedated, use lavage with cuffed endotracheal tube. Consider saline cathartic (sodium sulphate 15-30gm); good nursing care; support respirations, give O_2; correct any dehydration. Rarely hemodialysis or peritoneal lavage, especially for long-acting barbiturates.

NAPHTHALENE

SYMPTOMS

On contact, dermatitis and corneal ulceration occur. Inhalation results in headache, confusion, vomiting, dyspnea. On ingestion, abdominal cramps, nausea, vomiting, headache, confusion; dysuria; intravascular hemolysis; convulsions occurs. Hemolytic anemia results in persons with G6PD deficiency

TREATMENT

For poisoning due to contact, remove clothing if formerly stored with naphthalene, flush skin and eyes. If ingested, perform Ipecac emesis, gastric lavage; blood transfusion for severe hemolysis; alkalize urine for hemoglobinuria; for severe hermolysis, blood transfusions is necessary; control convulsions

NARCOTICS

Alpharodine, codeine, heroin, meperidine, methadone, morphine, opium, propoxyphene.

SYMPTOMS

Pinpoint pupils, drowsiness, shallow respirations, spasticity and respiratory failure.

TREATMENT

Do not give emetics. Gastric lavage, respiratory support. Naloxone 5 μg/ kg IV to awaken & improve respiration; if patient does not respond, give 2-20 mg naloxone (dosage must be repeated as many as 10- 20 times); fluids IV to support circulation.

PESTICIDES

PARAQUAT preparations are available to farmers and horticulturists. It has local and systemic effects. Splashes in the eyes irritate and ulcerate the cornea and conjunctiva. Washing of the eye and installiation of antibacterial eye drops, should promote healing. Skin irritation, blistering and ulceration can occur from prolonged contact.

Nausea, vomitting and diarrhoea follow ingestion of concentrated paraquat solutions. Painful ulceration of the mucous membranes may appear within 36-48 hours.

The single most useful measure of immediate treatment is the oral administration of activated charcoal. The first dose of 100 gm is given with magnesium sulfate followed

by activated charcoal 50 gm every 4 hours. Fluid and eletrolyte balance to be maintained. Oxygen therapy in early stages may make paraquat more toxic.

ORGANOPHOSPOROUS INSECTICIDES

These are usually supplied as powders or as dissolved in organic solvents. All are absorbed through the bronchi and intact skin as well as through the gut and inhibit cholinesterase activity, thereby prolonging and intensifying the effects of acetylcholine.

TREATMENT

The patient should be removed from source of poisoning and the contaminated clothing should be removed immediately. Emptying the stomach with gastric lavage should prevent further absorption, contaminated skin should be washed. In severe poisoning the airway is to be established. Artificial respiration is to be started with air or oxygen if necessary. The excess bronchial secretions are to be removed. Atropine injection IV or IM 2 mg is to be given. It should be repeated every 20-30 minutes until signs of atropinisation (hot dry skin, dry mouth, widely dilated pupils and flat pulse). Up to 12 mg of atropine can be given safely during the first 2 hours of treatment.

Pralidoxime mesilate, a cholinesterase reactivator is indicated, as an adjunct to atropine, in moderate or severe poisoning but is only effective if given within 24 hours. A dose of 30 mg/ kg diluted with 10-15 ml water for injections by slow intravenous injections should produce improvement in muscle power within 30 minutes.

Pralidoxime mesilate avilable as: Protopam (Ayerst), Tab. 500mg ; Inj. 1 gm/ vial.

PARAFFIN, PETROL AND OTHER PETROLIUM PRODUCTS

(Including pain thinners, organic solvents etc.)

Gastric lavage should be performed, using activated charcoal. Before lavage is carried out a cuffed endotracheal tube should be inserted to prevent pulmonary aspiration.

ETHANOL

Unabsorbed ethanol to be removed by gastric lavage. Activated charcoal is to be given to reduce absorption of any remaining ethanol. Adequate airway should be maintained. If patient is in coma, naloxone IV 0.01 mg/ kg to be given. Normal body temperature to be maintained.

In acute alcoholic mania, Inj. diazepam 10 mg IV slowly to be given, followed by 5 mg slow IV every 5-10 minutes until mania is controlled. The blood glucose should be measured and injection glucose IV to be given if indicated.

CARBON MONOXIDE

The patient should be removed from further exposure. 100 % oxygen is given by mask for several hours. Blood pressure and body temperature is to be maintained. Mannitol 20% IV is given to reduce cerebral oedema and prednisolone is to be given by slow IV. To control convulsions, IV diazepam should be given slowly.

VENOMOUS BITES AND STINGS POISONOUS SNAKES

A good number of snake varieties are poisonous. Among the poisonous snakes, members of *Crotalidae, Elapidae* and a few species of *Colubridae* families are important. Small scale studies indicate that, about 25% snakebite is poisonous and the highest bite rates are in the hilly areas of the country. Severity of any venomous snakebites depends on the size and variety of the snake, the amount and toxicity of the venom injected and underlying medical conditions of the victim, among other factors.

CHEMISTRY, PHARMACOLOGY, AND PATHOLOGY

Snake venoms are complex mixtures, chiefly proteins, many having enzymatic activity. Although the enzymes contribute to the deleterious effect of the venom, some of the more important toxic components are smaller polypeptides, which are more toxic than the crude venom. Most venom components appear to have specific chemical and physiologic receptor sites.

Envenomation may be further complicated by the release of autopharmacologic substances (eg. histamine, serotonin) that can make diagnosis and treatment difficult, *Arbitrary grouping of snake venoms into categories such as " neurotoxins," "hemotoxins," "cardiotoxins" is pharmacologically superficial and can lead to grave errors in clinical judgment.* A so-called neurotoxic venom can produce marked cardiovascular changes or direct hematologic effects. The so-called hemotoxin venoms can also produce changes in the nervous system, or in vascular dynamics. A patient with snake venom poisoning must be considered as a victim of a complex poisoning .

SYMPTOMS, SIGNS AND DIAGNOSIS

Venomous snake bites are medical emergencies, requiring immediate attention and considerable judgment. Before any treatment is begun, it must be determined whether the snake was venomous and whether envenomation occurred, since a venomous snake may bite and not inject venom. When no envenomation occurs, or the bite inflicted by a nonvenomous snake, it should be treated as a puncture wound.

Symptoms and signs very considerably, depending on the species of snake, the amount of venom injected and other factors. If there is evidence of poisoning soon after a bite, the possible consequences must not be underestimated.

Contrary to popular opinion, severe pain is not a constant finding; it may be mild or absent.

Untreated the edema progresses rapidly and may involve the entire extremity within hours. There may be lymphangitis and enlarged, tender, regional lymph nodes, Skin temperature over the injured part and body temperature are usually elevated. Although the patient may complain of chills. Weakness, a rapid and weak pulse, syncope, sweating, nausea and vomiting may be present. BP often drops and shock may develop early. Respiratory distress may occur.

There may be hemorrhage from the gums, hematemesis, melena, and hematuria. Bleeding and clotting times are prolonged and platelet counts may fall sharply in moderate or severe envenomations.

Laboratory Tests

In all but trivial cases, a CBC (including platelets), coagulation profile (PT, PTT, fibrinogen), blood typing, and urinanalysis are essential. Other tests, such as ESR, serum electrolytes, BUN, creatinine, and RBC fragility tests, may be useful. An ECG is indicated in all severe cases.

TREATMENT

When bitten by poisonous snakes and if the patient is within 30 to 40 min of a medical facility, he/she should be put at rest, reassured, kept warm, and transported there as quickly as possible. The injured part should be loosely immobilized in a functional position just below heart level, and all rings, watches and constrictive clothing removed. If the patient is > 40 min from medical care, single incision can be made through the fang marks (no longer than ¼ inch and no deeper than 1/8 inch) within the first 5 min. Suction, using Sawyer's "extractor", applied directly over the incisions or

even over the fang punctures is of value only during the first 30 to 60 min following the bite. The wound should be cleansed and covered with a sterile dressing.

If antivenin is needed, a skin test for horse serum sensitivity should be performed as described in the antivenin brochure. If the patient is mildly sensitive to horse serum and the poisoning is serious, diphenhydramine IV may be indicated before given the antivenin. When a patient is 3+ or 4+ sensitive and life or limb are at stake, the patient should be placed in a critical or intensive care unit, carefully monitored, and antivenin given in the presence of a physician. A tourniquet, O_2, epinephrine, and other drugs and equipment for treating for treating anaphylaxis should be available during antivenin therapy.

BEES, WASPS, HORNETS, ANTS

The venoms of these insects (order *Hymenoptera*) contain, among other components peptides and nonenzymatic proteins (eg, apamin and melittin and/or kinins), enzymes (eg, phospholipase A and B and hyaluronidase), and amines (eg, histamine and 5-hudroxytryptamine).

While it may take over 100 bees to inflict a lethal does of venom in most adults, one sting can cause a fatal anaphylactic reaction in a hypersensitive person.

TREATMENT

The stings of many hymenoptera may remain in the skin and should be removed by teasing or scraping rather than pulling. An ice cube placed over the sting will reduce pain; an antihistamine – analgesic – corticosteroid balm is often useful. Persons with known hypersensitivity to such stings should carry a kit containing an antihistamine and epinephrine when in endemic areas. Desensitization can be carried out using insect whole-body antigens or preferably, whole-venom antigens.

OTHER BITING ARTHROPODS

Among the more common biting and sometimes blood sucking arthropods the ticks and mites, mosquitoes; fleas; lice; bedbugs are most prominent. The composition of the saliva of these arthropods varies considerably, and the lesions produced by the bites of these animals vary from a small papule to a large ulcer with swelling and acute pain. Dermatitis may also occur. Most serious bites are complicated by sensitivity reaction or infection. In hypersensitive persons, bites can be fatal.

TREATMENT

The offending arthropod should be quickly removed. For ticks and some of the bugs, this is best accomplished by direct application of a petroleum products or other irritant to the animal or by slowly withdrawing the arthropod while twisting it slowly with forceps. Care should be taken not to leave the capitulum in the wound, as it may induce chronic inflammation or migrate into deeper tissues and give rise to a granuloma. The bite should be cleansed and a corticosteroid lotion applied.

TICKS AND MITES

Ticks are vectors of many diseases. In addition to the reactions noted above under BITING ARTHROPODS, ticks are also involved in poisonings. In North America, some species of Dermacentor and Amblyomma cause tick paralysis, Symptoms and signs include anorexia, lethargy, muscle weakness, incoordination, nystagmus, and ascending flaccid paralysis. Bulbar or respiratory paralysis may develop.

Mite infestations are quite common and are responsible for “chiggers” (intensely pruritic dermatitis caused by the mite larva, or chigger) , various forms of scabies, demodicidosis and a number of other diseases. The bites produce varying degrees of local tissue reaction with or without sensitization.

TREATMENT SCHEDULE FOR BITE BY TICKS AND MITES

Treatment of tick paralysis is symptomatic. O2 and respiratory assistance may be needed. An antitoxin is presently under study. Pajaroello tick lesions should be cleansed, soaked in 1:20 Burow's solution, debrided, and painted with the aqueous triple dye as used for viper bites. Corticosteroids are of value in severe reactions. Infections are common during the ulcer stage but rarely require more than local antiseptic measure.

CENTIPEDES AND MILLIPEDES

Some of the large centipedes of the genus *Scolopendra* can inflict bite with some localized swelling and erythema .Lymphangitis and lymphadenitis are common. Necrosis is rare and infection almost unknown. Symptoms and signs seldom persist for 48 h. Millipedes do not bite but when handled may secrete a toxin that can cause local skin irritation and in severe cases, tissue changes.

TREATMENT

An ice cube will control the pain of most centipede bites. Toxic secretions of millipedes should be washed from the skin with copious amounts of soap and water; alcohol should not be used. A topical corticosteroid should be applied if a skin reaction develops. Eye injuries require immediate irrigation and the application of a corticosteroid – analgesic ointment.

SCORPIONS

Most of the scorpions except *Centruroides exilicauda (sculpturatus)* are relatively harmless , their stings usually causing no more than some localized pain with minimal swelling , some lymphangitis with regional lymph gland swelling and increased skin temperature and tenderness around the wound. Children become tense, restless, and abnormal and random head, neck, and eye movements. In adults, tachycardia, hypertension, increased respirations, weakness and motor disturbances may predomainate. Respiratory difficulties may occur in both children and adults often complicated by excessive salivation.

TREATMENT

An ice cube over the wound area reduces pain. Hypertension can be controlled with diazoxide in doses of 5 mg/kg by slow IV push. For convulsions, diazepam is given IV 0.1 to 0.2 mg/kg up to 10 mg in adults and repeated q 15 min prn ; in children the total dose is 10 mg. Muscle spasms usually respond to calcium gluconate, methocarbamol, or diazepam. Complete bed rest is indicated and no food for the first 8 to 12 h. Antivenin should be use in all severe cases.

Appendix-8

IMMUNIZATION SCHEDULE

Appendix- 8a :

IMMUNIZATION SCHEDULE FOR CHILDREN 0-11 MONTHS AND 15 MOTHS WITH DOSAGE AND MODE OF ADMINISTRATION OF VACCINE

Disease	Vaccine	Quantity for each dose	Number of dose	Interval between doses	Age of starting	Site of Vaccination	Route of administration
Tuberculosis	BCG	0.05 ml	1	-	After birth	Upper part of left arm	Intradermal
Diphtheria, Pertussis & Tetanus, Hepatitis B, Haemophilus Influenza-B	Pentavalent Vaccine (DPT, Hepatitis-B, Hib)	0.5 ml	3	4 weeks	6 weeks 10 weeks 14 weeks	Outer part of left mid-thigh	Intra-muscular (IM)
Pneumococcal Pneumonia	PCV	0.5 ml	3	4/8 weeks	6 weeks 10 weeks 18 weeks	Outer part of right mid-thigh	Intra-muscular (IM)
Poliomyelitis	OPV	2 drops	3*	4 weeks	6 weeks 10 weeks 14 weeks	Oral	Oral route (by dropper)
	IPV	0.5 ml	1	-	14 weeks	Outer part of right mid-thigh	Intra-muscular (IM)
Measles & Rubella	MR	0.5 ml	1	-	Just after completion of 9 months	Outer part of right mid-thigh	Sub-Cutaneous
Measles	Measles vaccine	0.5 ml	1	-	Just after completion of 15 months	Outer part of left mid-thigh	Sub-Cutaneous

* After addition of IPV, OPV vaccine will be given in total three doses. 4th dose is not to be given with MR vaccine.
Four doses of OPV vaccine should be given before the addition of IPV vaccine. Moreover additional OPV dose can be given within 14 days of the birth.
Note: As per immunization schedule,
During vaccination, if minimum interval is not followed the vaccine will be ineffective.

See also section 13.1.3 and for more details EPI Programme, DGHS, Ministry of Health & Family Welfare, Govt. of Bangladesh

Appendix- 8b :

IMMUNIZATION SCHEDULE FOR GIRLS OF 15 YEARS AND WOMEN OF 15-49 YEARS WITH DOSAGE AND MODE OF ADMINISTRATION OF VACCINE

Disease	Vaccine	Quantity for each dose	Number of dose	Right Time for starting Vaccination	Site of Vaccination	Route of administration
Measles & Rubella	MR	0.5 ml.	1	During the time of first Dose TT Vaccination of the 15 years Girl	Upper part of arm	Sub-Cutaneous
Tetanus	TT (Tetanus Toxoid)	0.5 ml.	5 doses	**TT-1**: 15 years Old	Upper part of arm	Intra-muscular (IM)
				TT-2: 28 days after the TT-1 vaccination		
				TT-3: 6 months after the TT-2 vaccination		
				TT-4: One year after the TT-3 vaccination		
				TT-5: One year after the TT-4 vaccination		

Appendix–9

ESSENTIAL DRUG LIST

LIST OF 209 ESSENTIAL DRUGS

Sl.	Name of drugs	Dosage form
1	**Abacavir (ABC)**	Oral Liquid, Tablet
2	**Acetazolamide**	Tablet
3	**Acetylsalicylic acid**	Suppository, Tablet
4	**Aciclovir**	Powder for injection, Tablet
5	**Albendazole**	Tablet (chewable)
6	**Allopurinol**	Tablet
7	**Aluminium hydroxide + Magnesium hydroxide**	Oral liquid, Tablet
8	**Amitriptyline**	Tablet
9	**Amlodipine Besylate**	Tablet
10	**Amoxicillin**	Capsule or Tablet, Powder for oral liquid, Powder for injection
11	**Ampicillin**	Powder for Injection
12	**Anti-D immunoglobulin (human)**	Injection
13	**Antitetanus immunoglobulin (human)**	Injection
14	**Artemether + Lumefantrine***	Tablet
15	**Artesunate**	Injection, Tablet
16	**Ascorbic Acid**	Tablet
17	**Atenolol**	Tablet
18	**Atropine**	Injection, Solution (eye drops)
19	**Barium Sulfate**	Aqueous suspension
20	**BCG vaccine**	Injection
21	**Benzathine benzylpenicillin**	Powder for injection
22	**Benzoic acid + Salicylic acid**	Ointment or cream
23	**Benzyl benzoate**	Lotion
24	**Benzyl penicillin**	Powder for injection
25	**Betamethasone**	Ointment or cream
26	**Bleomycin**	Powder for injection
27	**Bupivacaine**	Injection
28	**Calcium gluconate**	Injection
29	**Carbamazepine**	Oral liquid, Tablet (chewable), Tablet (scored)

30	**Charcoal, activated**	Powder
31	**Chlorambucil**	Tablet
32	**Chloramphenicol**	Eye drops, Eye ointment
33	**Chlorhexidine**	Solution
34	**Chloroquine**	Oral liquid, Tablet
35	**Chlorpheniramine**	Injection , Tablet
36	**Chlorpromazine**	Injection, Oral liquid, Tablet
37	**Ciprofloxacin**	Tablet or powder for suspension
38	**Cisplatin**	Injection
39	**Clofazimine**	Capsule
40	**Clotrimazole**	Vaginal cream, Vaginal tablet
41	**Cloxacillin**	Capsule, Powder for injection, Power for oral liquid,
42	**Condoms**	
43	**Cyclophosphamide**	Powder for injection, Tablet
44	**Dapsone**	Tablet
45	**Dexamethasone**	Injection
46	**Dextran 70**	Injectable solution
47	**Diazepam**	Injection, Tablet, Tablet (scored)
48	**Didanosine (ddl)**	Buffered powder for oral liquid, Capsule (unbuffered enteric coated), Tablet (buffered chewable, dispersible)
49	**Diethylcarbamazine**	Tablet
50	**Digoxin**	Injection, Oral liquid, Tablet
51	**Diloxanide**	Tablet
52	**Diphtheria antitoxin**	Injection
53	**Diptheria vaccine**	Injection
54	**Dopamine**	Injection
55	**Doxorubicin**	Powder for injection
56	**Doxycycline**	Capsule or Tablet, Tablet (dispersible)
57	**DPT vaccine**	Oral + Injection
58	**Efavirenz (EFV or EFZ)**	Capsule, Oral liquid, Tablet
59	**Enalapril**	Tablet
60	**Epinephrine (adrenaline)**	Injection, Solution (eye drops)
61	**Ergocalciferol**	Capsule or Tablet, Oral liquid
62	**Ergometrine**	Injection
63	**Erythromycin**	Capsule or Tablet, Powder for injection, Powder for oral liquid
64	**Ethambutol**	Tablet

65	**Ethinylestradiol + Levonorgestrel**	Tablet
66	**Ferrous salt**	Oral liquid, Tablet
67	**Ferrous salt + Folic acid**	Capsule, Tablet
68	**Fluconazole**	Capsule, Oral liquid
69	**Fluorescein**	Eye drops
70	**Fluorouracil**	Injection, Ointment
71	**Fluphenazine**	Injection
72	**Folic acid**	Tablet
73	**Furosemide**	Injection, Tablet
74	**Gentamycin**	Injection, Solution (eye drops)
75	**Gentamycin + Hydrocortisone**	Ear drop
76	**Glibenclamide**	Tablet
77	**Gliclazide**	Tablet
78	**Glucose**	Injectable solution
79	**Glucose with sodium chloride**	Injectable solution
80	**Glyceryl trinitrate**	Tablet (sublingual)
81	**Griseofulvin**	Capsule or Tablet
82	**Haloperidol**	Injection, Tablet
83	**Halothane**	Inhalation
84	**Heparin sodium**	Injection
85	**Hepatitis B vaccine**	Injection
86	**Homatropine**	Solution (eye drops)
87	**Human normal immunoglobulin**	Intramuscular administration, Intravenous administration
88	**Hydrochlorothiazide**	Tablet (scored)
89	**Hydrocortisone**	Powder for injection, Ointment or cream, Suppository
90	**Hyoscine butylbromide**	Tablet**,** Injection
91	**Ibuprofen**	Tablet
92	**Indinavir (IDV)**	Capsule
93	**Insulin Injection (Soluble)**	Injection
94	**Isoniazide**	Tablet, Tablet (scored)
95	**Isoniazide + Ethambutol**	Tablet
96	**Isosorbide dinitrate**	Tablet (sublingual)
97	**Ketamine**	Injection
98	**Lamivudine (3TC)**	Oral liquid, Tablet,
99	**Levamisole**	Tablet
100	**Levodopa + Carbidopa**	Tablet
101	**Levothyroxine**	Tablet

102	**Lidocaine**	Injection, Topical
103	**Lithium Carbonate**	Capsule or tablet
104	**Lopinavir + Ritonavir (LPV/r)**	Capsule, Oral liquid
105	**Magnesium hydroxide**	Oral liquid
106	**Magnesium sulfate***	Injection
107	**Mannitol**	Injectable solution
108	**Measles vaccine**	Injection
109	**Mebendazole**	Tablet (chewable)
110	**Mefloquine**	Tablet
111	**Metformin**	Tablet
112	**Methotrexate**	Powder for injection, Tablet
113	**Methyldopa**	Tablet : 250 mg
114	**Methylrosanilinium chloride (gentian violet)**	Aqueous solution, Tincture
115	**Metoclopramide**	Injection, Tablet
116	**Metronidazole**	Injection, Oral liquid, Suppository, Tablet
117	**Miconazole**	Ointment/Ceam
118	**Miltefosine**	Capsule/Oral liquid
119	**Misoprostol**	Tablet
120	**Morphine**	Injection, Oral liquid, Tablet, Tablet (prolonged release)
121	**Naloxone**	Injection
122	**Nelfinavir (NFV)**	Oral powder, Tablet
123	**Neomycin Sulfate + Bacitracin**	Ointment
124	**Neostigmine**	Injection, Tablet
125	**Nevirapine (NVP)**	Oral liquid, Tablet
126	**Nicotinamide**	Tablet
127	**Nifedipine**	Immediate release capsule
128	**Nitrofurantoin**	Tablet
129	**Nitrous oxide**	Inhalation
130	**Nystatin**	Oral Suspension
131	**Omeprazole**	Capsule
132	**Oral rehydration salts**	Powder
133	**Oseltamivir**	Tablet
134	**Oxygen**	Inhalation
135	**Oxytocin**	Injection
136	**Paracetamol**	Oral liquid, Suppository, Tablet
137	**Paromomycin**	Solution for intramuscular injection
138	**Peritoneal Dialysis Solution**	Intraperitoneal dialysis solution (of appropriate composition)

139	**Permethrin**	Cream, Lotion
140	**Pertussis vaccine**	Injection
141	**Pethidine hydrochloride**	Injection
142	**Phenobarbital**	Injection, Oral liquid, Tablet
143	**Phenoxymethylpenicillin**	Powder for oral liquid, Tablet,
144	**Phenytoin**	Capsule, Injection, Oral liquid, Tablet, Tablet (chewable)
145	**Pilocarpine**	Solution (eye drops)
146	**Poliomyelitis vaccine**	Oral
147	**Polyvalent anti snake venom**	Injection
148	**Potassium chloride**	Tablet, Solution
149	**Povidone Iodine**	Solution
150	**Prednisolone**	Tablet, Solution (eye drops)
151	**Primaquine**	Tablet
152	**Procainamide**	Injection
153	**Procaine benzylpenicllin**	Powder for injection
154	**Procarbazine**	Capsule
155	**Proguanil**	Tablet
156	**Promethazine**	Oral liquid, Injection, Oral liquid, Tablet
157	**Propranolol**	Tablet
158	**Protamine sulfate**	Injection
159	**Pyrazinamide**	Tablet, Tablet (dispersible), Tablet (scored)
160	**Pyridoxine**	Tablet
161	**Pyrimethamine**	Tablet
162	**Quinine**	Injection, Tablet
163	**Rabies immunoglobulin**	Injection
164	**Rabies vaccine**	Injection
165	**Retinol**	Capsule, Tablet, Oral oily solution, Water-miscible injection
166	**Riboflavin**	Tablet
167	**Rifampicin**	Capsule or Tablet
168	**Rifampicin + Isoniazid**	Tablet
169	**Rifampicin + Isoniazid + Ethambutol**	Tablet
170	**Rifampicin + Isoniazid + Pyrazinamide**	Tablet
171	**Rifampicin + Isoniazid + Pyrazinamide + Ethambutol**	Tablet
172	**Ritonavir**	Oral liquid, Oral solid dosage form
173	**Salbutamol**	Injection, Oral liquid, Respirator solution for use in nebulizers, Tablet

174	**Salicylic acid**	Solution
175	**Saquinavir (SQV)**	Capsule
176	**Senna**	Tablet
177	**Silver sulfadiazine**	Cream
178	**Sodium chloride**	Injectable solution
179	**Sodium Chloride 3%**	I/V fluid
180	**Sodium Chloride quartet strength (0.225%) + Dextrose 5%**	I/V fluid
181	**Sodium Hydrogen Carbonate**	Injectable solution, Soution
182	**Sodium stibogluconate**	Injection
183	**Sodium thiosulfate**	Solution
184	**Spironolactone**	Tablet
185	**Stavudine (d4t)**	Capsule, Powder for oral liquid
186	**Streptomycin**	Powder for injection
187	**Sulfadoxine + Pyrimethamine**	Tablet
188	**Sulfamethoxazole + Trimethoprim**	Oral liquid, Tablet, Injection
189	**Suxamethonium**	Injection, Powder for injection
190	**Tamoxifen**	Tablet
191	**Tenofovir disoproxil fumarate (TDF)**	Tablet
192	**Tetanus vaccine**	Injection
193	**Tetracycline**	Eye ointment
194	**Thiamine**	Tablet
195	**Thiopental**	Powder for injection
196	**Trimethoprim**	Tablet
197	**Tropicamide**	Eye drops
198	**Tuberculin, purified protein derivative (PPD)**	Injection
199	**Valproic acid**	Oral liquid, Tablet (crushable), Tablet (enteric coated)
200	**Vecuronium**	Injection
201	**Verapamil**	Injection, Tablet
202	**Vinblastine**	Powder for injection
203	**Vincristine**	Powder for injection
204	**Vitamin B-Complex (Vitamin B1- 5 mg + Vitamin B2- 2 mg + Vitamin B6 - 2 mg + Nicotinamide 20 mg)**	Tablet
205	**Warfarin**	Tablet
206	**Water for Injection**	Ampoule
207	**Xylometazoline Hydrochloride**	Nasal drops
208	**Zidovudine (ZDV or AZT)**	Capsule, Oral liquid, Solution for IV infusion injection, Tablet

209	**Zinc sulphate**	Oral liquid, Tablet

Appendix-10

LIST OF CONTROLLED DRUGS

Controlled drugs are classified in this list according to the First Schedule of the Narcotics Control Act, 1990. Note that the said Schedule contains also the names of other narcotic and psychotropic substances that are not used either in their crude forms or otherwise in the preparation of pharmaceutical or medicinal products. The penalties applicable for offences involving the different classes of the listed drugs are graded broadly according to the degree of harmfulness attributable to a drug when it is misused. For details of such offences, see the Narcotics Control Act, 1990.

1. A-Class Controlled Drugs

Alfentanil; buprenorphine; cocaine and its salts; codeine phosphate; dextromoramide; dihydrocodeine tartrate; diphenoxylate; ethylmorphine; fentanyl; heroin (diamorphine) hydrochloride; hydromorphone hydrochloride; meptazinol; methadone hydrochloride; morphine and its salts; pentazocine; pethidine hydrochloride; phenazocine hydrobromide; pholcodeine; tetrahydro cannabinol or cannabis resin in any form; and remifentanil.

2. B-Class Controlled Drugs

(a) Amphetamine/ methylamphetamine and related other drugs (these drugs are prohibited in Bangladesh for medicinal purposes); barbiturates (e.g. amylobarbitone, butobarbitone, methyl phenobarbitone, phenobarbitone, phenobarbitone sodium, quinalbarbitone/ secobarbital, etc.)

(b) Ethyl alcohol and all kinds of wine, spirit, liquor and beer; rectified spirit; any medicine or liquid containing more than 5% of ethyl alcohol.

(c) Herbal cannabis in any form; LSD or any other drug containing LSD.

3. C-Class Controlled Drugs

Benzodiazepines (e.g. alprazolam. bromazepam, chlorazepate, chlordiazepoxide, diazepam, flurazepam, loprazolam, lorazepam, lormetazepam, nitrazepam, oxazepam etc.); denatured spirit or methylated spirit; meprobamate; other tranquilizer or hypnotic drugs not included in B-Class.

Appendix-11

ADVERSE DRUG REACTIONS MONITORING (ADRM) and PHARMACOVIGILLANCE

Drug classes frequently involved in Adverse Drug Reactions (ADRs) related admissions include drugs of abuse, anticonvulsants, antibiotics, respiratory drugs, and pain medications. ADRs can also occur in hospitalized patients and require an increase in length of stay and treatment with medical and pharmacologic interventions.

Drug Reactions Defined
Confusion exists regarding the terms *adverse drug reaction*, *side effect* and *drug allergy*.

The World Health Organization (WHO) endorses an ADR definition that many health care practitioners have also adopted; it reads as follows: ***"any response to a drug which is noxious and unintended, and which occurs at doses used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function".***

An ADR may therefore include any of the following:
(a) an exaggerated drug response,
(b) an unwanted effect on an organ system different from that being treated,
(c) an allergic or hypersensitivity reaction,
(d) an idiosyncratic reaction, or
(e) a drug interaction that causes either an increased or diminished response.

A *side effect* and a drug allergy are both types of ADRs. A side effect is an example of a dose-related, predictable reaction to a drug. It is typically accepted that a side effect of a drug is known to occur in a given percentage of the population and has been observed with regular frequency. A *drug allergy* is an example of a non-dose-related, unpredictable adverse effect to a drug.

Any reaction to a new drug (e.g., a drug on the market 3 years or less), whether or not included in the product labeling and regardless of its severity, should be reported. Reporting for biologic agents (e.g., vaccines) as well as devices, and any reactions for these agents or products should be reported as well. Table-1 below shows the reportable adverse drug reactions.

Table 1: Reportable Adverse Drug Reactions.

- For "new" drugs – report all suspected reactions, including minor ones. (In many countries drugs are still considered "new" up to five years after marketing authorization);
- For established or well-known drugs – report all serious or unexpected (unusual) suspected ADRs;
- Report if an increased frequency of a given reaction is observed;
- Report all suspected ADRs associated with drug-drug, drug-food or drug-food supplements (including herbal and complementary products) interactions;
- Report ADRs in special fields of interest such as drug abuse and drug use in pregnancy and during lactation;

• Report when suspected ADRs are associated with drug withdrawals; • Report ADRs occurring from overdose or medication error; • Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.
An event is serious and should be reported when it: 1. resulted in death. 2. was life-threatening. 3. required prolonged hospitalization 4. directly resulted in disability. 5. resulted in congenital anomaly.

How to recognize ADRs

Since ADRs may act through the same physiological and pathological pathways as different diseases, they are difficult and sometimes impossible to distinguish. However, the following step-wise approach may be helpful in assessing possible drug-related ADRs:

1. Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised;
2. Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient;
3. Do a thorough physical examination with appropriate laboratory investigations, when possible;
4. A full drug and medical history should be done, when possible;
5. Determine the time interval between the beginning of drug treatment and the onset of the event;
6. Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient's status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events.
7. Analyse the alternative causes (other than the drug) that could on their own have caused the reaction;
8. Use relevant up-to-date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction.
9. Report any suspected ADR to the person nominated (if any) for ADR reporting in the hospital or directly to the ADRM Cell of the Directorate of Drugs Administration.

Drug Induced Diseases

Disease management, collective management of all aspects of a patient's disease, rather than isolated drug treatment of a disease is rapidly becoming the accepted practice in health care. Adverse drug monitoring and management should be thought of in a similar fashion. It is impossible to consider the desired outcomes of drug therapy without taking into consideration all adverse, as well as beneficial, consequences of treatment. The remaining sections of this chapter will focus on major organ systems most commonly associated with adverse pharmacologic reactions. Throughout the remainder of this chapter, the reader may be referred to other chapters in this book that describe in detail the mechanism of specific drug-induced diseases.

Hypersensitivity Reactions: True hypersensitivity reactions are immunologically mediated through a series of reproducible steps. Hypersensitivity reactions are most

frequently associated with β-lactam antibiotics, which include penicillins and cephalosporins. While allergic reactions to penicillin have been reported to occur in 0.7 to 8% of the general population, anaphylaxis only occurs in 0.01% of identified treatment courses.

Hypersensitivity reactions may manifest as acute urticaria, rhinitis, bronchial asthma, and angioedema. Depending on the severity of the reaction, there may also be peripheral circulatory collapse; therefore, immediate medical care should be sought. The offending agent should be removed. Epinephrine should be administered 0.1—0.2 mg IV over 2 to 3 minutes. This dose may be repeated every 15 to 20 minutes as needed up to 3 doses. Oxygen should be administered if available. Since the patient may be experiencing vascular collapse, fluid therapy should be initiated as needed to maintain blood pressure. If the patient is unresponsive to fluid replacement, a dopamine infusion may be necessary at a rate of 2 to 15 mg/kg. β-Agonists, diphenhydramine, and hydrocortisone should also be administered after the emergent situation is controlled.

Hepatotoxicity*:* Drug-induced hepatotoxicity has been associated with over 600 drugs. Hepatotoxicity can be difficult to diagnose because the literature consists primarily of case reports and because injury can present acutely or after prolonged drug administration. Table-2 illustrates some of the risk factors associated with developing hepatotoxic reactions. Table-3 lists a number of drugs that have been implicated in causing chronic active hepatitis. Acute liver injury can be cytotoxic or cholestatic. Cytotoxic injury involves direct injury to the hepatocytes with necrosis that can be localized or diffuse throughout the liver. Aminotransferase levels can be elevated to up to 500 times the normal levels. Prominent signs and symptoms include fatigue, anorexia, nausea, and jaundice. Drug-induced cytotoxic injury can progress to fulminant hepatic failure. Isoniazid, methyldopa, and phenytoin have been associated with direct cytotoxic reactions that have led to mortality rates of 10% or higher. Cholestatic injury results in a characteristic decrease in bile flow. Hepatic injury of this type leads to jaundice and pruritus, and aminotransferase levels are only moderately elevated. Cholestatic hepatic injury has a much better prognosis as compared to cytotoxic injury with a mortality rate of less than 1%.

Table 2 : Risk Factors Associated with Developing Hepatotoxic Reactions

	Factor	**Example**
Age	Adult **>** Children	Isoniazid, halothane
	Elderly> others	NSAIDs
	Children **>** Adults	Valproic acid, aspirin
Sex	Female **>** Male	Methyldopa, Drug-induced chronic active hepatitis
Drugs	Alcohol & Phenobarbital	Can induce Cytochrome p 450 system and enhance the toxicity of agents converted to active metabolites
Pathological State	AIDS	Increased susceptibility to hepatotoxic effects of Sulfamethoxazole-Trimethoprim
	Diabetes	Enhances toxicity of carbon tetrachloride
	Hyperthyroidism	Enhances toxicity of carbon tetrachloride

Adapted from Zimmerman HJ. Hepatotoxicity. Disease-a-Month 39:675 787. 1993.

Table 3 . Drugs Implicated in Causing Chronic Active Hepatitis		
Acetaminophen	Isoniazid	Papaverine
Dantrolene	Nitrofurantoin	Propylthiouracil
Diclofenac	Methyldopa	Sulfonamides
Adapted from Zimmerman HJ. Hepatotoxicity. Disease-a-Month 39:675 787. 1993.		

Pancreatitis: Pancreatitis can also be characterized as being either acute or chronic. A large number of medications can cause acute pancreatitis. Clinical symptoms of pancreatitis include acute abdominal pain and increased blood and urine pancreatic enzyme concentrations. Morphologic changes in the pancreas itself are minor or absent. Table-4 given below.

Table 4: Examples of Drugs Suspected in Drug-Induced Pancreatitis		
Asparginase	Furosemide	Sulindac
Azathioprine	Mercaptopurine	Tetracyclines
Didanosine	Pentamidine	Thiazides
Estrogens	Sulfonamides	Valporic Acid

Nephrotoxicity: Drug-induced nephrotoxicity depends on the concentration of drug presented to the kidney and the biochemical or physiologic effect of the drug on the affected tissue. Factors that influence the concentration of given drugs in the kidney include mechanisms for the transport of drugs across the tubular epithelium, the rate of water versus drug reabsorption, plasma protein binding, and rate of urine flow. A list of drugs and chemicals associated with each of these lesions is provided in Table-5.

Table 5: Drugs Associated with Nephrotoxicity			
Acute tubular necrosis	***Antibiotics***	**Acute tubulointerstitial disease**	***Penicillins***
	Aminoglycosides		Amoxicillin
	Amphotericin B		Carbenicillin
	Bacitracin		Methicillin
	Cephalosporins		Nafcillin
	Polymixins		Oxacillin
	Sulfonamides		Penicillin
	Metals		***Other antibiotics***
	Antimony		Cephalosporins
	Bismuth		Cotrimoxazole
	Mercurials		Erythromycin
	Platinum		p-Aminosalicylate
	Chelates		Polymixins
	Dimercaprol		Rifampin
	EDTA		Sulfonamides
	Contrast media		***NSAIDs***
	Miscellaneous		Fenoprofen
	Acetaminophen		Ibuprofen
	Aminocaproic acid		Indomethacin
	Carbamazepine		Mefenamic acid

	Cisplatin		Phenylbutazone Tolmetin
	Cyclosporine		***Miscellaneous***
	Methotrexate		Allopurinol
	Methoxyflurane		Azathioprine
	Phenazopyridine		Captopril
	Streptozocin		Cimetidine
Glomerulo-nephritis	Allopurinol		Cloflbrate
	Captopril		Furosemide
	Cyclophosphamide		Phenytoin
	Daunorubicin		Thiazides
	Fenoprofen		
	Hydralazine	**Chronic tubulointerstitial disease**	Acetaminophen
	Rifampin		Aspirin
	Sulfonamides		Lithium
	Thiazides		Methyl-CCNU
	Trimethadone		Phenacetin

Gastrointestinal Diseases: Nausea and vomiting are among the most frequent drug-induced symptoms and they occur more often in women. Almost any orally administered drug can produce these symptoms by a direct irritant effect on the gastric or small-bowel mucosa, or by central stimulation of the chemoreceptor zones and vomiting center in the medulla. The most common drugs causing these reactions included potassium chloride, heparin, docusate and aluminum and magnesium hydroxide suspension. The most clinically significant ADRs affecting the upper gastrointestinal tract result from the use of nonsteroidal anti-inflammatory drugs (NSAIDs), partly because of their widespread use in this country. There are two types of gastrointestinal toxicity associated with NSAIDs: dyspepsia and ulceration of the gastric mucosa. Ulcerogenic properties of NSAIDs have received intensive study both in the laboratory and epidemiologically. The anti-inflammatory activity of these agents is derived from their ability to inhibit cyclooxygenases (prostaglandin synthetases), which, unfortunately, results in an impairment of the gastrointestinal mucosa to resist acid attack.

Hematologic Disorders: Drug-induced hematologic disorders encompass a wide variety of disorders, only some of which are mechanistically understood. Hematologic disorders such as, aplastic anemia, agranulocytosis, hemolytic anemia, megoblastic anemia, and thrombocytopenia have been associated with drug-induced etiologies.
Aplastic anemia is the most serious drug-induced blood disorder, and it has been estimated that drugs are responsible for nearly one-half of all cases of aplastic anemia. The first clinical manifestations of aplastic anemia usually are related to hemorrhage. Pancytopenia is observed in a majority of the patients on initial examination, and a hypocellular bone-marrow biopsy may be obtained at some time in the course of the illness. Many drugs can cause suppression of bone-marrow activity or aplasia in a dose-dependent manner, as is the case with cytotoxic drugs. For many other drugs, aplastic anemia can occur suddenly in the form of an idiosyncratic reaction, unrelated to the dose. Cytostatic drugs are used in the treatment of neoplastic disorders because of their action on dividing cells. All of these agents, which include alkylating agents, antibiotics, antimetabolites and vinca alkaloids, in large doses, can produce bone-marrow aplasia.

In agranulocytosis resulting from allergic mechanisms, signs and symptoms appear in a few days to weeks following administration. There is an abrupt onset of high fever, rigors and occasional episodes of localized infections. Drugs associated with this type of reaction include sulfonamides, sulfonylureas, phenothiazines, antithyroid agents, phenylbutazone and semisynthetic penicillins. Drugs that can produce a lupus-like syndrome and result in agranulocytosis are procainamide, hydralazine, isoniazid, rifampicin and propylthiouracil.

Cardiovascular Effects: Adverse drug reactions involving the cardiovascular system are not specifically limited to those agents used to treat cardiovascular disease. For example, bronchodilator therapy and sympathomimetic effects of various cough and cold remedies often negatively affect cardiac rate and rhythm regulation. Many antiarrhythmic agents may also be proarrhythmic. Tricyclic antidepressants in an overdose situation cause ECG changes that can be life-threatening. In addition to certain cardiac medications, bradycardia can also be induced by agents such as carbamazepine, methyldopa, and H_2 antagonists. Some agents used in chemotherapy regimens, such as the anthracyclines, have a dose limiting side effect of causing congestive cardiomyopathy. Additionally, some diuretics and β-blockers may adversely affect lipid risk profiles.

Pulmonary Effects: Pulmonary injury secondary to pharmacologic treatment has been shown to occur with the administration of over 150 medications. Table-6 lists agents known to cause pulmonary disease.

Table 6: Agents Known to Cause Pulmonary Disease

Cardiovascular	**Anti-inflammatory**	**Chemotherapeutic Agents**
Amiodarone	Aspirin	Azathioprine
ACE inhibitors	Ifosfamide	Bleomycin
Anti-coagulants	Methotrexate	Busulphan
β-Blockers	NSAIDs	Chlorambucil
Dipyridamole	Penicillamine	Cyclophosphamide
Tocainide	***Miscellaneous***	Etoposide
Antibiotics	Bromocriptine	Melphalan
Amphotericin B	Dantrolene	Mitomycin
Nitrofurantoin	Oral Contraceptives	Nitrosoureas
Sulfasalazine	Hydrochlorothiazide	Procarbazine
Pentamidine	Tricyclic Antidepressants	Vinblastine

Adapted from Rosenow ECIII. Drug-induced pulmonary disease. Disease-a-Month. 5:258—310, 1994.

Ototoxicity: Ototoxicity from drug therapy may be manifested in two ways, depending on the portion of the inner ear affected. Vestibular toxicity can result in dizziness or vertigo, while cochlear toxicity usually results in hearing loss. Manifestations of ototoxicity may range from mild tinnitus or dizziness to total bilateral irreversible hearing loss and/or permanent disabling vertigo. Aminoglycosides such as neomycin, streptomycin, gentamicin, amikacin and netilmicin are considered to be the most ototoxic, in terms of permanent damage. These drugs destroy the outer hair cells in the cochlea in such a way that high-frequency hearing loss occurs first; lower and midrange frequencies or conversational tones are affected later. Topically administered aminoglycoside antibiotics can be absorbed sufficiently to result in ototoxicity. Oral or peritoneal administration or topical use of neomycin for wound

irrigation has also resulted in ototoxicity. Similarly ototoxicity has followed the application of a 0.1% gentamicin cream to the skin. Loop diuretics, ethacrynic acid, furosemide and bumetanide all possess the potential to produce ototoxicity. There have been numerous case reports of transient effects of ethacrynic acid on auditory function and reports of permanent deafness, even after oral administration. High intravenous doses of furosemide may cause vertigo and transient hearing loss, particularly in patients with renal impairment. Even in the absence of renal failure, oral doses of furosemide have been reported to result in permanent hearing impairment.

Ocular Toxicity: The list of drugs that are toxic to the eye is extensive. Nearly every structure of the eye has been affected adversely by drugs. Decreased tear production has been shown to have damaging effects on the eye. Tear secretion can be diminished by anticholinergic and by ganglionic blocking drugs. A decrease in tear production occasionally has been noted in patients receiving phenothiazines. Patients using chloroquine, or related aminoquinolines, for diseases such as systemic lupus erythematous and rheumatoid arthritis take high doses for prolonged periods and are at risk of developing ocular toxicity. Ocular damage normally does not occur with lower dosages used in the suppression and treatment of malaria. Both chloroquine and hydroxychloroquine produce numerous forms of ocular toxicity, which include whitening of the lashes, extraocular muscle palsy, corneal deposits, decreased corneal sensitivity and retinal damage. Elevated intraocular pressure is a well-documented side effect of both local and systemic corticosteroid therapy. The increased intraocular pressure occurs a few weeks after topical application and a few months after systemic therapy. Severe increases in intraocular pressure, similar to those seen in acute glaucoma, have resulted in cupping of the optic discs and visual field defects similar to those seen in open-angle glaucoma. Corticosteroid-induced glaucoma develops more commonly in patients with a family history of glaucoma.

Sexual Dysfunction:
Normal sexual function is mediated by various physiologic mechanisms including neurogenic, psychogenic, vascular, and hormonal factors. It is expected, then, that medications that interfere with any of these systems may also interfere with sexual Function. Sexual dysfunction is often associated with antihypertensive and antipsychotic medications.
Thiazide diuretics, peripheral and central sympatholytics, and β-blockers have all have been associated with a decline in sexual function. The adverse events range from loss of libido to impotence, ejaculatory failure, and anorgasmia, with impotence being the most frequently reported. Calcium channel blockers and ACE inhibitors appear to have a relatively decreased potential for causing sexual dysfunction. Antipsychotic or antidepressant medications are also associated with a variety of effects on sexual function (e.g., impotence, priapism, anorgasmia, and diminished libido); however, ejaculatory failure is the most frequently reported.
Additional medications that have been associated with sexual dysfunction, although less frequently than the aforementioned agents, are the H_2 antagonists, metoclopramide, anticonvulsants (e.g., carbamazepine, phenytoin, phenobarbital, and primidone), and opioids when used chronically.

HISTORY OF ADVERSE DRUG REACTIONS MONITORING (ADRM)

Background

In 1962, in the wake of the thalidomide disaster, World Health Assembly requested WHO to establish an international system of monitoring adverse reactions to drugs using information derived from national centres. Before an effective international

system could become operative, a common reporting form had to be developed, agreed guidelines for entering information had to be formulated, common terminologies and classifications had to be prepared and compatible systems for transmitting, storing, retrieving and disseminating data had to be created. Upon the successful completion of these tasks the operational activities sub serving the international data base were relocated in 1978 to a WHO collaborating centre situated in Uppsala, Sweden.

ADRM and Pharmacovigillance in Bangladesh

Questions with regard to the safety and efficacy of drugs, particularly those which concern ADRs in Bangladesh, were left unanswered mainly due to the lack of a systematic mechanism of monitoring. Under the guidance of WHO, an Adverse Drug Reaction Monitoring (ADRM) Cell was established in the Directorate of Drug Administration, now known as Directorate General of Drug Administration (DGDA) in 1996. Initially the Cell circulated posters bearing awareness slogans of drug use throughout the country, organized awareness meetings among the chemists of different area and also published awareness instructions in the daily newspapers and broadcasted these awareness slogans on Radio Bangladesh. The Cell has been trying since its inception to introduce a systematic mechanism for ADR monitoring in Bangladesh and for collection, analysis and compilation of ADRs, spontaneously reported by the medical and pharmaceutical professional of all health services outlets of the country. With this end in view, DGDA has been organizing ADR Monitoring Workshops/meetings in the Medical Colleges and Hospitals of the country and distributing printed ADR reporting forms to the doctors for spontaneous reporting of ADR cases since 2000. On 6 July 1997, the Ministry of Health & Family Welfare (MOHFW) formed a 10-Member ADR Advisory Committee (ADRAC) to evaluate, analyze and make recommendations for solving problems of medicinal hazards due to ADRs.

ADRM Cell Declared as the National Drug Monitoring Centre

In recent years, ADRM Cell and ADRAC have become dormant. In 2013, the United States Agency for International Development (USAID)'s Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program that is implemented by Management Sciences for Health (MSH) provided support to DGDA in reviving the Cell and Committee in the Directorate as part of health systems strengthening. As a result, ADRM Cell and ADRAC have become fully functional, with meetings taking place at regular intervals. When the Cell took up its responsibilities, it applied to MOHFW, requesting recognition as the National Drug Monitoring Centre (NDMC) for Bangladesh, and on 3 September 2013 the Ministry issued a notification declaring ADRM Cell as the NDMC for the country. ADRM Cell is responsible for the collection and collation of adverse event reports received from healthcare facilities, hospitals and pharmaceutical companies. In addition, they are responsible for the maintenance and analysis of adverse event database, including data entry / quality assurance and to share adverse event information with WHO Uppsala Monitoring Centre (WHO-UMC). The ADR Advisory Committee is responsible for providing technical assistance on causality assessment, risk assessment / management, and case investigation, in order make recommendations for DGDA to take regulatory actions. The National Centre will also collaborate with WHO-UMC to further strengthen their capacity and for ensuring medicine safety and of good quality for the people of Bangladesh. The overall Bangladesh health system is improved when necessary actions are taken in response to ADR cases, thereby enhancing the provision of quality medicine to the people of the country.

DGDA Awarded 120th Membership of WHO-UMC

In light of the achievements of the Adverse Drug Reaction Monitoring Cell including it being declared as the National Drug Monitoring Centre by the Ministry, DGDA has been awarded 120th Membership from the WHO-UMC in 2014. As a member of WHO-UMC, DGDA has access to VigiBase, the WHO global individual case safety reports (ICSR) database. DGDA has also adopted UMC web-based tool, VigiFlow that currently serves as the national database and allows ICSRs received within the country to be committed to VigiBase. As a member of WHO-UMC, Bangladesh has international recognition, access to international network – gaining knowledge and expertise of member countries, training materials and resources, as well as, early information about potential safety data – based on analysis of worldwide data. The overall Bangladesh health system is improved when necessary actions are taken in response to ADR cases, thereby enhancing the provision of quality medicines to the people of the country.

What to Report

The National Drug Monitoring Centre shall encourage reporting of all suspected adverse drug related events, whether it is seemingly insignificant or common adverse reactions, as it may highlight widespread prescribing problem. The reporter should made aware not to wait until he feels certain that a causal link can be considered proven or disproven. In any case of doubt it is better to report than not to report.

A case report in pharmacovigilance can be defined as: A notification relating to a patient with an adverse medical event (or laboratory test abnormality) suspected to be induced by a medicine. It should also be a comprehensive and complete medical description of the case.
An updated and standardized suspected adverse event reporting form has been developed and adopted by Bangladesh to report all cases of ADRs. The ADR form is available at DGDA and on the website in a fillable pdf format. ADR case report should (as a minimum to aim at) contain information on the following elements:

1. The patient : name or initials, age, sex, contact information, and brief medical history
2. Suspected Adverse event: type of event, description (nature, localization, severity, characteristics), results of investigations and tests, start/end date, course and outcome.
3. Suspected drug(s) :name (brand or generic name, manufacturer) dose, dosage form, frequency, Batch number, start/stop date, indication for use, seriousness of event, outcomes attributed, other relevant history.
4. All concomitant drugs information (including self medication): names, doses, routes, indication, frequency, start/stop dates.
5. Risk factors (e.g., impaired renal faction, previous exposure to suspected drug, previous allergies)
6. Name and address of the reporter (to be considered confidential and to be used only for date verification, completion and case follow-up)

APPENDIX-11 : ADRM

Who Should Report

Government/Private Hospitals/Clinics/Pharmaceutical Companies: Every hospitals and clinics must decide for itself how the reporting system should be operated and by whom. The arrangements will depend on the hospital's/clinic's own organisation and traditions. Conversely, during the launch of Bangladesh as a National Pharmacovigilance Program on September 2, 2013, DGDA identified Focal Point persons at 20 public and private hospitals, which has subsequently be increased to 30 in 2014 that would be responsible for collecting ADRs and submitting to DGDA. The remaining hospitals and pharmaceutical companies are encouraged to do the same. Generally the physicians themselves act as reporters, completing the reporting form, keeping a record and sending them to the Focal Point person at the hospital, who will forward the report to: **ADRM Cell, Directorate General of Drug Administration, 105-106, Motijheel Commercial Area, Dhaka-1000, Bangladesh.**

The hospital pharmacist may act as a reporter, completing the forms in consultation with the reporting physician. Patients/Consumers may also act as reporters and contact the pharmaceutical companies regarding any suspect adverse event or ADRM Cell directly.

A reporter should report

(a) Apparent ADRs previously unknown to the reporter
(b) Serious ADRs
(c) All suspected ADRs to new drugs
(d) Cases of suspected dependence
(e) Cases of drug interactions

Collaboration with WHO

After evaluation of ADR reports by the Adverse Drug Reactions Advisory Committee (ADRAC), **the ADRM Cell of the Directorate General of Drug Administration, 105-106, Motijheel Commercial Area, Dhaka-1000, Bangladesh** would provide the essential ADRs data to WHO collaborating center for International Drug Monitoring & Exchange of Drug Information.

NB : A Light green- coloured card for reporting Adverse Drug Reactions is available from the above address and also included in this book (inside back cover).

Appendix-12

CLINICAL PATHOLOGY AND OTHER BIOMEDICAL TABLE

Part A: Laboratory Reference Values for Adults: * Blood (B), Plasma (P), Serum (S)		
Test	**Conventional units**	**SI units**
Aminotransferase		
Alanine (ALT) SGPT	10-40 U/L (37°C)	0.22–0.68 mckat/L (37°C)
Aspartate (AST) SGOT	10-59 U/L	0.17–1.00 -2 to +3 kat/L (37°C)
-1 antitrypsin (P)	78–200 mg/dL	0.78–2.00 g/L
Albumin (P)	3.5–5.2 g/dL	35–52 g/L
Aldolase (S)	1.0–7.5 U/L (30°C)	0.02–0.13 mckat/L (30°C)
Alkaline phosphatase (P)	38–126 U/L (37°C)	0.65–2.14 mckat/L
Amylase (P)	27–131 U/L	0.46–2.23 mckat/L
Ammonia (B)	9–33 mcmol/L	9–33 mcmol/L
Angiotensin converting enzyme (ACE) (S)	12-35 u/L	
Acetone and acetoacetate(S)	0.3–2.0 mg/dL	0.05–0.34 mmol/L
Acid phosphatase (S)	<3.0 ng/mL	<3.0 mcg/L
Ascorbic acid (P)	0.4–1.5 mg/dL	23-85 micromol/L
Bicarbonate (S)	22–29 mEq/L	22–29 mmol/L
Bilirubin (S) Total	0.2-1.2 mg/dL	2-20 micromol/L
Direct (conjugated)	0.1-0.4 mg/dL	<7 micromol/L
Indirect (unconjugated)	0.2-0.7 mg/dL	<12 micromol/L
Blood volume	8.5-9% of body weight (kg)	80-85 ml/kg
Blood urea nitrogen (BUN) (S or P)	8-25 mg/dl	2.9-8.9 mmol/L
Calcium (S) Total	8.5-10.3 mg/dL	2.1-2.6 mmol/L
Ionized	4.25-5.25 mg/dL	1.05-1.3 mmol/L
Carcinoembryonic antigen (CEA)(S)	0-2.5 ng/ml	0-2.5microgram/l
CO_2 content (S)	24-30 mEq/L	24-30 mmol/L
CO (B)	0.5–1.5% total Hb	0.005–0.015 HbCO fraction
Carotenoids (S)	50-300 microgram/dL	0.9-5.58 micromol/L
Ceruloplasmin (S)	27-37 mg/dL	1.8-2.5 pmol/L
Chloride (S)	96-106 mEq/L	96-106 mmol/L
Cholesterol (S)	120-220 mg/dL	3.1-5.68 mmol/L
Creatine kinase (S) female male	 10-80 u/L 15-105 u/L	 0.17–1.36 mckat/L (30°C) 0.26–1.79 mckat/L (30°C)

APPENDIX-12

Part A: Laboratory Reference Values for Adults: * Blood (B), Plasma (P), Serum (S)		
Test	**Conventional units**	**SI units**
Creatine kinase (MB) (S)	0–7 ng/mL	0–7 mcg/L
Copper (S)	70-155 pg/dL	11-24 micromol/L
Complement C3 (S)	64-166 mg/dl	640-1660 mg/L
Complement C4 (S)	15-45 mg/dl	150-450 mg/L
Cryoglobulins (S)	<0.12 mg/dl	
Creatinine (S)	<1.5 mg/dL	<133 micromol /L
Cyanocobalamin (S)	200pgm/mL	148 pmol/L
Digoxin (S) Therapeutic Toxic	 0.8-2 ng/ml >2.5 ng/ml	 1.0-2.6 nmol/L >3.2 nmol/L
Erythropoietin (EPO) (S)	5-20 mU/ml	5-20 u/L
Ethanol	Not normally detectable 65-87 mmol/L (marked intoxication) 87-109 mmol/L (stupor) >109 mmol/L Coma	>21.7 mmol/L (Depression of CNS) >86.8 mmol/L (Fatalities reported)
□-fetoprotein (AFP) (S)	0-15 ng/ml	0-15 microgram/L
Ferritin (S) Female Male	 4-161 ng/ml 16-300 ngm/ml	 4-161 microgram/L 16-300 microgram/L
Children to 15 years	7-140 ngm/ml	
Folic acid (S)	2-20 ngm/ml	4.5-45 nmol/L
Folic acid (RBC) (B)	165-760 ng/ml	370-1720 nmol/L
Glucose, fasting (S or P)	65-110 mg/dl	3.6-6.1 mmol/L
Gamma glutamyl transferase (GGT) (P)	2-30 u/l male 1-24 u/l female	0.03–0.51 mckat/L (37°C) 0.02–0.41 mckat/L (37°C)
Glycated haemoglobin (HbA1) (P)	4.2% – 5.9%	0.042–0.059
Haptoglobin (S)	46-316 mg/dl	0.5-3.2 g/L
Haemoglobin electrophoresis (B)	HbA->95% HbA_2 1.5-3.5%	>0.95 Hb fraction 0.015–0.035 Hb fraction
Haemoglobin, fetal (HbF) (B)	Adult <2% (varies with age)	<0.02 Hb fraction
β-hydroxybutyrate (S)	0.5-3 mg/dl	0.05-0.3 mmol/L
Insulin, immunoreactive (S)	6-35 microunit/ml	42-243 pmol/L
Insulin-like growth factor-1(P)	123-463 ng/ml	123-463 microgram/L
Iron (S)	50-150 mcg/dl	9-27 micromol/L
Iron binding capacity (S)	250-410 mcg/dl	45-73 micromol/L
Iron Percent saturation	20-55%	0.2-0.55

Part A: Laboratory Reference Values for Adults: * Blood (B), Plasma (P), Serum (S)		
Test	**Conventional units**	**SI units**
Immunoglobulin A (P)	70–400 mg/dL	0.7-4 g/L
Immunoglobulin G (P)	700–1600 mg/dL	7–16 g/L
Immunoglobulin M (P) Male Female	 30-220 mg/dL 40-250 mg/dL	 0.3-2.2g/L 0.4-2.5g/L
Lactic acid (lactate) (B) Venous Arterial	 4.5-20 mg/dl 4.5-14.4 mg/dl	 0.5–2.2 mmol/L 0.5–1.6 mmol/L
Lactate dehydrogenase (LDH) (total)(S)	100-190U/L	1.7–3.2 mckat/L
Lead (B)	0-50 pg/dl	0-2.4 pmol/l
Lipase (S)	23–300 U/L (37°C)	0.39–5.1 mckat/L (37°C)
Lithium (S) Therapeutic Toxic	 0.5-1.4 mEq/L 2.0 mEq/L	 0.5-1.4 mmol/L >2.0 mmol/L
Lipid fractions (S or P)	HDL- Cholesterol >50 mg/dl, LDL-Cholesterol-<130mg/dl, VLDL-Cholesterol <40 mg/dl	**(to convert into mmol/l, multiply by 0.026)
Magnesium (S)	1.8-3 mg/dl	0.7-1.1 mmol/L
5'-Nucleotidase (S)	2-17 u/L	0.034–0.29 mckat/L
Osmolality (S)	280-296 mosm/kg water	280-296 mmol/kg water
Oxygen saturation (B) Arterial PO_2 (PaO_2) PCO_2	96-100% of capacity 80-100 mmHg 35-45 mmHg	 10-13.3 kPa 4.7-6 kPa
pH (Arterial, B)	7.35-7.45	7.35-7.45
Phosphorous (Inorganic) (S)	3-4.5 mg/dl	1-1.5 mmol/L
Potassium (S or P)	3.5-5 mEq/L	3.5-5 mmol/L
Protein (S) Total (S) Albumin (S) Globulin (S) A/G Ratio Fibrinogen (P)	 6-8 gm/dl 3.5-5.5 gm/dl 2.2-4.2 gm/dl 1.1-2.4 0.2-0.6 gm/dl	 60-80 g/L 35-55 g/L 22-42 g/L 11-24 g/L 2-6 g/L
Prostate-specific antigen (PSA) (S)	0-4 ng/ml	0-4 microgram/L
Protein S (P) (antigen)	76-178%	
Pyruvate (B)	0.6-1 mg/dl	70-114 micromol/L
Sodium (S or P)	136-145 mEq/L	136-145 mmol/L
Specific gravity (B) Specific gravity (S)	1.056 1.0254-1.0288	 same
Sulphate (S)	2.9-3.5 mg/dl	0.3-0.36 micromol/L
Transferrin (S)	200-400 mg/dl	23-45 micromol/L
Triglycerides (S)	<165 mg/dl	1.9 mmol/L

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Part A: Laboratory Reference Values for Adults: * Blood (B), Plasma (P), Serum (S)		
Test	**Conventional units**	**SI units**
Troponin-I	<1.5 ng/ml	
Thyroglobulin (S)	3-42 ng/ml	3-42 microgram/L
Thrombin time (P)	24-35 seconds	
Urea (P)		2.5-6.6 mmol/L
Uric acid (S or P)	Male 3-9 mg/dl Female 2.5-7.5 mg/dl	0.18-0.54 mmol/L 0.15-0.45 mmol/L
Electrophoresis Globulin		
$\alpha 1$	0.1-0.4 gm/dl	1-4 gm/L
$\alpha 2$	0.4-1.1 gm/dl	4-11 gm/L
β	0.5-1.6 gm/dl	5-16 gm/L
γ	0.5-1.4 gm/dl	5-14 gm/L
Vitamin A (S)	20-60 pg/dl	0.7-2.1 micromol/L
Vitamin B 12 (S)	140-820 pg/ml	100-600 pmol/L
Vitamin D derivatives (S) 1,25-dihydroxy 25- hydroxy	 20-45 pg/ml 25-40 ng/ml	 48-108 pmol/L 62.5-100 nmol/L
Zinc (S)	50-150 microgram/dl	7.65-22.95 micromol/L

A.2. Reference value for hormones in serum or plasma		
Test	**Conventional units**	**SI units**
Adrenal		
Aldosterone (P) Supine	2-9 ng/dl	56-250 pmol/L
Cortisol (S)	8.00AM 5-20 microgram/dl 8.00 PM <10 microgram/dl	0.14-0.55 micromol/L 0.28 micromol/L
Deoxycortisol (S)	After metyrapone >7 microgram/dl	>0.2 micromol/L
Dopamine(P)	<135pg/ml	
Epinephrine (P)	<0.1 ng/ml	<0.55nmol/L
Norepinephrine (P) supine	<500 pg/ml	<3 nmol/L
Follicle-stimulating hormone (FSH)	Male 1.5-9 u/L Female: 3-15 u/L (early follicular), Upto 17 mIU/mL (mid-cycle), 19–100 mIU/mL (postmenopausal)	1.4–15.4 IU/L (male) 1–10 IU/L (female-follicular phase), 6–17 IU/L (Mid cycle), 19–100 IU/L (postmanopausal)
Gastrin	<100 pg/mL	<100 ng/L
Growth Hormone (GH)	Male <5 ng/mL Female <10 ng/mL	Male, <5 mcg/L, Female<10 mcg/L
Gonad:		
Testosterone, free (S)	Male 10-30 ng/dl Female 0.3-2 ng/dl	

A.2. Reference value for hormones in serum or plasma		
Test	**Conventional units**	**SI units**
Testosterone, Total (S)	Prepubertal <100ng/dl Adult male 280–1100 ng/dL Adult female 20-80 ng/dl Luteal phase upto 120 ng/dl	0.52–38.17 nmol/L (adult male), 0.52–2.43 nmol/L (adult female)
Estradiol (E2)(S)	Male 12-50 pg/ml Female menstrual cycle 1-10 days 24-68 pg/ml, 11-20 days 50-300pg/ml, 21-30 days 73-149 pg/ml (By RIA)	Male: 37-184 pmol/L Female: Varies with menstrual cycle
Progesterone (S)	Male : 13–97 ng/dL Female: Follicular phase 15–70 ng/dL Luteal phase 200–2500 ng/dL Pregnancy Varies with gestational week	Male: 0.4–3.1 nmol/L Female: Follicular Phase: 0.5–2.2 nmol/L Luteal Phase: 6.4–79.5 nmol/L Pregnancy: Same
Islets:		
Insulin (S)	4-25 microunit/ml	29-181 pmol/L
C-peptide (S)	0.78–1.89 ng/mL	0.26–0.62 nmol/L
Glucagon(S) fasting	20-100 pg/ml	
Parathyroid hormone (PTH)	10-55 ng/L	
Lutenising hormone	Female: Follicular phase 1.68–15.0 mIU/mL 1.68–15.0 IU/L Mid-cycle peak 21.9–56.6 mIU/mL 21.9–56.6 IU/L Luteal phase 0.61–16.3 mIU/mL 0.61–16.3 IU/L Postmenopausal 14.2–52.5 mIU/mL 14.2–52.3 IU/L Male: 1.24–7.8 mIU/mL	Female: Follicular phase: 1.68–15.0 IU/L Mid-cycle peak : 21.9–56.6 IU/L Luteal phase: 0.61–16.3 IU/L Postmenopausal: 14.2–52.3 IU/L Male: 1.24–7.8 IU/L
Prolactin (S)	1-25 ng/ml	0.4-10 nmol/L
Somatomedin C (P)	0.4-2 U/ml	
ADH (P)	Serum osmolality 285: mosm/kg 0-2pg/ml, Serum osmolality>290/kg: 2-12+pg/mL	
Placenta Estriol (E3) (S)	Male and nonpregnant female <0.2 microgram/dl	<7nmol/L (by RIA)
Placenta Chorionic gonadotropin	Beta subunit male <9 mIU/ml, female pregnant after implantation >10 mIU/ml.	
Thyroid		
Thyroxine, free (FT4) (S)	0.8-2.4 ng/dl	10-30 pmol /L
Thyroxine, Total (TT4) (S)	5-12 microgram/dl	65-156 nmol/L (by RIA)

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A.2. Reference value for hormones in serum or plasma		
Test	**Conventional units**	**SI units**
Triidothyronine (T3) (S)	80-220 ng/dl	1.2-3.3 nmol/L
Reverse Triidothyronine (rT3)	30-80 ng/dl	0.45-1.2 nmol/L
Throid stimulating hormone(TSH) (S)	<10 microU/ml	<10 mU/L
Calcitonin (S)	<100 pg/ml	<29.2pmol/L

A.3. Reference value for urine		
Test	**Conventional units**	**SI units**
Acetone plus acetoacetate	negative	
Amylase	1-17 u/h	1-17 u/h
Calcium	100-300 mg/day	2.5-7.5 mmol/d
Copper	0-50 pg/d	0-0.8 pmol/d
Cortisol		9-50 micromol/mol creatinine
Creatinine		10-20 mmol/24 hour
Hemosiderin	Negative	
Hemoglobin and myoglobin	Negative	
Lead	<120 pg/d	<0.39 pmol/L
Osmolality	Random: 100-900 mosm/kg H_2O	Random: 100-900 mmol/kg H2O
Oxalate	80-490 (M) mmol/24 hour 40-320 (F) mmol/24 hour	
Phosphate	15-50 mmol/d	
Porphyrins		
Delta-aminolevulinic acid	1.5-7.5 mg/24 hour	11-57 micromol/d
Porphobilinogen	<2 mg/24 hour	<8.8 micromol/d
Protein	<150 mg/day	<150mg/day
Potassium	25-100mmol/24 hour	
Sodium	100-200 mmol/24 hour	
Urobilinogen	0-2.5 mg/24 hour	70-470 micromol/d
Urate	1.2-3 mmol/24 hour	
Urea	170-600 mmol/24 hour	
Vanilylmandelic acid (VMA)	1-9 mg/d	5-45 micromol/d

A.4. Reference values for Cerebrospinal fluid		
Test	**Conventional units**	**SI units**
Cells	0–10 lymphocytes/mm^3 0 RBC/mm^3	0–10lymphocytes/mm^3 0 RBC/mm^3
Chloride	118–132 mmol/L (20 mmol/L higher than serum)	Same
Glucose	40–70 mg/dL	2.2–3.9 mmol/L
Total protein	8–32 mg/dL	80–320 mg/L
Glutamine	6-16 mg/dL	60-160 mg/L

Part B. Conditions in which normal chemistry values may increase or decrease		
Analyte	**Increase**	**Decrease**
Alanine aminotransferase (ALT or SGPT)	It is an enzyme found primarily in the liver but also found in heart and other tissue. The value increases in hepatitis, cirrhosis of liver, obstructive jaundice, alcoholism, chemical pollutants, myocardial infarction.	Decreased ALT in combination with increased cholesterol levels is seen in cases of a congested liver. Vitamin B6 deficiency.
Aspartate aminotransferase (AST or SGOT)	It is an enzyme found primarily in liver, heart, kidney, pancreas and muscle. It increases in myocardial infarction, heart failure, myocarditis, pericarditis, myositis, muscular dystrophy, trauma, hepatic disease, pancreatitis, renal infarct, cerebral damage, seizure.	Vitamin B deficiency, pregnancy.
Alkaline phosphatase	Produced in the cells of the bone and liver with some activity in the kidney, intestine, and placenta. Growing children have higher levels of this enzyme also. It increases in bone growth, bone metastases, Paget's disease, ricket, healing fracture, bone injury, pregnancy, hepatic disease, obstructive jaundice.	Low levels are sometime found in protein deficiency, malnutrition, pernicious anaemia and a number of vitamin deficiencies.

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Part B. Conditions in which normal chemistry values may increase or decrease		
Analyte	**Increase**	**Decrease**
Lactic dehydrogenase (LDH)	It is an intracellular enzyme found particularly in kidney, heart, skeletal muscle, brain, liver, and lungs. It can be useful in confirming myocardial or pulmonary infarction only in relation to other tests. It is raised in haemolytic anaemia, leukemia, lymphoma, hepatic disease, renal infarction, trauma, seizures, cerebral damage	Malnutrition, hypoglycaemia, adrenal exhaustion etc.
Bilirubin, Total	A byproduct of the breakdown of haemoglobin in the liver. It is excreted into bile; it gives the bile its pigmentation. It is raised in liver disease, obstructive jaundice, haemolytic anaemia, pulmonary infarct, neonatal jaundice.	Inefficient liver, excessive fat digestion.
Albumin	It is the major constituent of serum protein (usually over 50%). It is manufactured by liver from amino acids taken from diet. It helps in osmotic pressure regulation, nutrient transport and waste removal. High values are rarely found and are primarily due to dehydration.	Low levels are found in poor diets, diarrhea, fever, infections, liver disease, burn, edema. hypocalcaemia, multiple myeloma.
Globulin	A larger protein than albumin is important for its immunologic responses, particularly its gamma component. It has many diverse functions like carrier of some hormones, lipids, metals, and antibodies. T is elevated in chronic infections, liver disease, rheumatoid arthritis, myeloma.	Lower levels may be found in immune compromised patients, poor diet, malabsorption, liver and kidney disease.

Part B. Conditions in which normal chemistry values may increase or decrease		
Analyte	**Increase**	**Decrease**
Calcium	The most abundant mineral in the body and is involved in bone metabolism, protein absorption, muscular contraction, transmission of nerve impulse, blood clotting and cardiac function. It increases in hyperparathyroidism, bone metastases, myeloma, sarcoidosis, hypervitaminosis D.	It decreases in hypoparathyroidism, renal failure, malabsorption, pancreatitis, vitamin D deficiency, overhydration.
Phosphorous	Abundant element found in most tissue and cells in the body and is involved in calcium transport, buffering action and osmotic pressure. It is closely related to calcium with an inverse relationship. It is increased in renal failure hypoparathyroidism, diabetic acidosis, acromegaly.	Hyperparathyroidism, osteomalacia, cirrhosis, hypokalemia. Excess IV glucose.
Potassium	It is the major intracellular cation in the blood. It along with the help of sodium maintains osmotic balance and also involved in acid-base balance. It helps in nerve and muscle action. It is increased in hyperkalemic acidosis, cardiac arrhythmia, diabetic acidosis, hypoadrenalism.	Cirrhosis, malnutrition, vomiting, metabolic alkalosis, diarrhea, diuretics, hyperadrenalism, familial periodic paralysis.
Sodium	Most abundant cation in blood and its chief base. It is required to maintain osmotic pressure, acid-base impulse, and transmission of nerve impulse. It is increased in dehydration, diabetes insipidus, excessive salt ingestion.	Excess ADH, nephrosis, myxedema, congestive heart failure, diarrhea, vomiting, diuretics.
Chloride	Maintain cellular integrity through its influence on osmotic pressure. It also helps in acid-base balance and water balance. It is increased in acidosis.	

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Part B. Conditions in which normal chemistry values may increase or decrease		
Analyte	**Increase**	**Decrease**
Cholesterol	It is a fat that is a structural component of cell membrane and plasma lipoproteins and is required for synthesis of steroid hormones, glucocorticoids and bile acids. Mostly synthesized in liver, some is absorbed through diet. HDL is desired as opposed to the LDL. Elevated levels are found in atherosclerosis, diabetes, obstructive jaundice, hypothyroidism, pregnancy.	Low levels are found in hyperthyroidism, depression, malnutrition, anaemia, infections, heart failure, malignancies.
Tryglycerides	It is stored in adipose tissue as glycerol, fatty acids and monoglycerides are reconverted as tryglycerides by liver.90% of dietary intake and 95% of fat stored in tissue are tryglycerides. Elevated levels are found in atherosclerosis, hypothyroidism, liver disease, pancreatitis, myocardial infarction, metabolic disorder, toxaemia, nephrotic syndrome, hereditary.	Low levels are found in chronic obstructive pulmonary disease, brain infarction, hyperthyroidism, malnutrition and malabsorption.
Creatinine	It is the waste product of muscle catabolism. Elevated levels are found in kidney disease, muscle degeneration, drugs.	Low levels are found in kidney damage, protein starvation, liver disease, pregnancy.
Blood urea nitrogen	The nitrogen component of urea, is the end product of protein catabolism. Elevated levels are found in excessive protein intake, kidney damage, low fluid intake, intestinal bleeding, exercise, heart failure.	Lower levels may be found in poor diet, malabsorption, liver damage, low nitrogen intake.
Uric acid	It is the end product of purine metabolism. Elevated levels are found in gout, infections, kidney disease, alcoholism, high protein diet, diuretics, leukemia, lymphoma, polycythemia, psoriasis, toxaemia of pregnancy.	Lower levels may be found in diet low in purine, liver damage, uricosuric drugs, allopurinol, large doses of vitamin C.

Part B. Conditions in which normal chemistry values may increase or decrease		
Analyte	**Increase**	**Decrease**
Glucose (fasting)	Primary source of energy is elevated in diabetes, obesity, pancreatitis, steroid, stress, IV glucose, thiazides, Cushing syndrome, acromegaly, hyperthyroidism.	Lower levels may be found in excess insulin, insulinoma, liver disease, hypothyroidism, alcoholism, malabsorption.

Part: C. Clinical chemistry for paediatric range		
Test	**Reference range**	**Age**
C1. Blood chemistry		
Albumin g/dl	2.6-4.1(M) 2.7-4.3 (F) 2.8-4.6 2.9-4.2 2.8-4.8 3.3-4.8 3.2-4.7 2.9-4.2	1-30 days 31-days-6 months 6 months-1 year 1-18 years
Alkaline phosphatase (S) u/L	 72-307 133-340 103-429 49-210 99-453 53-186 38-110 38-110	0-6 years 6-9 9-15 (male) 15-18 (male) 9-13 (F) 13-15(F) 15-18(F) 18 years and older
Alanine transaminase, u/L	 13-45	 Newborn
AST (Aspartate transaminase, U/L	20-60 20-40 14-40 5-40	0-6 years 6-10 10-18 18 years and older
Amylase (S) U/L	5-65 27-131	Newborn Adult
Ammonia micromol/L	20-100 20-60	<1 month >1month
Bicarbonate (arterial)	17-24 mmol/L 19-24 16-24 22-26	Newborn Infant 2 months-2 year Adult
Bilirubin (total) (S)	24-149 micromol/L 58-197 micromol/L 26-205 micromol/L	0-1 day 1-2 days 3-5 days
Bilirubin Direct (S)	1-25 micromol/L <10 micromol/L	<2 weeks >2 weeks
Carbon dioxide mEq/L	15-20 18-27	Cord blood Child
Calcium (ionized) mg/dL	 4.2-5.9	 Neonatal

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Part: C. Clinical chemistry for paediatric range		
Test	**Reference range**	**Age**
Calcium (S) (Total) (mg/dl)	8.5-10.6 (M) 8.4-10.6 (F) 8.7-10.5 8.9-10.5 8.8-10.6 8.5-10.5 8.7-10.3 8.5-10.3 8.5-10.2 8.4-10.0 8.4-10.3 8.6-9.8	Birth – 30 days 31 days- 1 year 1-6 years 7-12 years 13-15 years 16-18 years
Cholesterol Total (S or P) mmol/L	1.3-2.6 1.8-3.2 2.6-4.5 2.6-5.5	<1 month 1 month-2 years 2-10 years >10 years
Creatinine (mg/dl)	0.5-1.2(M) 0.5-0.9 (F) 0.4-0.7 0.4-0.7 0.5-0.8 0.5-0.8 0.6-1.0 0.6-1.0 0.6-1.2 0.7-1.1 0.8-1.4 0.8-1.2	Birth-30 days 31days-3 years 4-6 7-12 13-15 16-18
CK (creatine kinase)(S) U/L	10-200 15-105 10-80 20-110 16-18	Newborn Adult M Adult F >60 years M >60 years F
Total protein g/dl	4.6-7 4.4-7.6 5.1-7.3 5.6-7.5 6-8	Newborn 1 week 7 month-1 year 1-2 year >3years
Glucose (S) fasting mmol/L	1.1-3.3 1.7-3.3 2.2-3.3 2.8-4.5 3.3-5.6 4.1-5.9	Premature Neonate Newborn- 1day Newborn>1day Child Adult
GGT (Gamma glutamyl transpeptidase)	8-154 U/L 7-103 9-76 6-52 5-40 5-24 <45	0-1 wk 1-2 2-4 4-6 6-7 7wk-16 years >16 years
Lactate mmol/L	0.7-2.0	All ages
Magnesium mmol/L	0.71-0.96	All ages
Osmolality mmol/kg	265-295	All ages
Sodium (S or P) mmol/L	130-140 133-146 139-146 138-145 136-145	Premature Newborn Infant Child Thereafter

Part: C. Clinical chemistry for paediatric range		
Test	**Reference range**	**Age**
Potassium (S)) mmol/L	3.7-5.9 4.1-5.3 3.4-4.7 3.5-5.1	Newborn Infant Child Thereafter
Chloride (S or P) mmol/L	98-113 98-107	Newborn (0-30 days) Thereafter
Urea	1-6 mmol/L	All ages
Uric acid mg/dL	2-7 2-6.5 2-7	0-2 years 2-12 years 12-14 years
Phosphorous mg/dL	4.2-9 3.8-6.2 3.5-6.8	Newborn 1 year 2-5 years
Triglyceride (fasting)	0.5-1.4 mmol/L 0.6-1.7	<5 years > 5 years
C.2. Reference values for cerebrospinal fluid in paediatric age ranges		
Glucose	>3.0 mmol/L	
Protein	<1.20 g/L 0.20-0.80 0.15-0.4	Full term newborn <1 month >1 month
C.3. Thyroid function test in paediatric age ranges		
TSH (S) Micro IU/mL	Male Female 0.52-16.0 0.72-13.1 0.55-7.10 0.46-8.10 0.37-6.0 0.36-5.80 0.40-5.00	 0-30 days 1month-5 years 5-18 years 18 years and older.
Total T4 (microgram/dL)	Male Female 3.0-14.3 3.0-13.3 5.2-16.3 4.6-13.3 5.5-11.4 6.3-12.8 5.3-10.5 5.3-10.8 4.5-10.3 4.9-10.0 4.9-8.8 5.1-10 5.0-12.0	 0-30 days 1-12 months 1-5 years 5-10 years 10-15 years 15-18 years 18 years and older.
Free T4 (ng/dL)	Male Female 0.8-2.8 0.9-1.9 0.5-2.3 0.6-1.9 0.8-2.0 0.9-1.9 0.9-1.6 1.0-1.7 0.8-1.7 0.9-1.6 0.9-1.6 0.8-1.5 0.9-1.6 0.9-1.5 0.8-1.6	 0-2 days 3-30 days 1-12 months 1-5 years 5-10 years 10-15 years 15-18 years 18 years and older.

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C.4. Pediatric haematology						
Value	**At birth**	**Day-3**	**1 month**	**2-6 months**	**2-6 years**	**6-12 years**
Red blood cell count ($\times 10^{12}$/l	6.0±1.0	5.3± 1.3	4.2±1.2	3.8±0.8	4.6±0.7	4.6±0. 6
Haemoglobin (g/L)	165±30	185±40	140±30	115±20	125±15	135±2 0
Packed cell volume	0.54±0. 10	0.56±0. 11	0.43±0. 12	0.35±0.07	0.37±0. 03	0.40± 0.05
Mean cell volume (MCV) (fl)	110±10	108±13	104±19	91±17	81±6	86±8
Mean cell haemoglobin (MCH) (pg)	34±3	34±3	34±6	30±5	27±3	29±4
Mean cell haemoglobin con. (MCHC) (g/l)	330±30	330±40	330±40	330±30	340±30	340±3 0
Reticulocytes (%)	2-5	1-4.5	0.3-1	0.4-1	0.2-2	0.2-2
WBC ($\times 10^9$/l)	18±8	15±8	12±7	12±6	10±5	9±4
Neutrophils ($\times 10^9$/l)	5-13	3-5	3-9	1.5-9	1.5-8	2-8
Lymphocytes ($\times 10^9$/l)	3-10	2-8	3-16	4-10	6-9	1-5
Monocytes ($\times 10^9$/l)	0.7-1.5	0.5-1	0.3-1	0.1-1	0.1-1	0.1-1
Eosinophils ($\times 10^9$/l)	0.2-1	0.1-2.5	0.2-1	0.2-1	0.2-1	0.1-1

C.5. Miscellaneous haematological tests	
Tests	**Normal range**
Prothrombin time (P)	11-15 seconds for children >6 months
International normalized ratio (INR)	1.0-1.3 for children >6 months
Activated partial thromboplastin time (P) (APTT)	27-39 seconds for children >6 months
Fibrinogen (P)	Above 1.5 g/L for children >6 months
D-Dimer (P)	<0.2 mg/L for children >6 months
Ferritin (S)	10-150 microgram/L for children >6 months
Iron	110-270 ug/dl Birth- 4 months 30-70 ug/dl 4 months-1 year 20-124 ug/dl 2-3 years 53-119 ug/dl 3-10 years
Iron binding capacity	59-175 ug/dl birth-4 months 250-400 ug/dl 4 months-10 years
Percent saturation	65% Newborn 25% 4-10 months 30% 3-10 years

Appendix-13

PHARMACEUTICAL ABBREVIATIONS

Communication of dosage instructions to patients

Physicians and Pharmacists have to devote considerable time and effort to the development and utilization of safe and cost-effective drug therapy. In order to gain maximum benefit from the use of drugs while minimizing their side effects, prescribers and pharmacists must maintain effective communications not only among themselves, but with their patients as well. The directions for drug use and other information which prescribers indicate on prescription orders must be transferred on the labels and explained by the pharmacists to the patients for safe and effective drug therapy. In order to assure that this information is conveyed clearly and effectively to the patients, the following guidelines have to be followed by the professionals.

Notes for prescribers

1. Whenever possible, specific times of the day for drug administration should be indicated (for example, Take one capsule at 8:00 am, 2:00 pm, and 8:00 pm is more preferable as compared Take one capsule three times daily).
2. The use of potentially confusing abbreviations, ie, qid, tid, bd, etc, is discouraged.
3. Vague instructions such as “take as necessary” or “take as directed” which are confusing to the patient’s should be avoided.
4. If dosing at specific intervals around-the-clock is therapeutically important, this should specifically be stated on the prescription by indicating appropriate times for drug administration.
5. The symptom, indication, or the intended effect for which the drug is being used should be included in the instructions whenever possible (for example, Take one tablet at 6:00 am and 6.00 pm for high blood pressure, or Take one tablet at 7:00 am, 11:00 am, 4:00 pm, and 8.00 pm for cough).
6. The Metric System of weights and measures should be used.
7. The prescription order should indicate whether or not the prescription should be refilled and, if so, the number of refill(s) and the period of time for such renewal is recommended.
8. The prescriber should print his/her name, telephone number and registration number on the prescription blank.

Notes for Pharmacists

1. Instructions to the patient regarding directions for use of medication should be concise and precise, but readily understandable to the patient. The pharmacist should give verbal reinforcement and clarification of instructions to the patient when appropriate.

2. For those dosage forms where confusion may develop as to how the medication is to be administered, the pharmacist should clearly indicate the intended route of administration on the prescription label.

3. Where special storage conditions are required, the pharmacist should indicate appropriate instructions for storage on the prescription label and explain to the patient.

TABLE: Common Abbreviations of Prescriptions, Medical and Pharmaceutical orders.

APPENDIX-13 : PHARMACEUTICAL ABBREVIATIONS

ABBREVIATION	MEANING
a.d.	Right ear
a.s	left ear
Aa	of each
abd	abdomen
ac	before meals
ad lib	At pleasure, freely
ad	To, up to
amp	Ampoule of medication
aq	Water
as	directed
ATC	Around the clock
au	each ear
BCP	birth control pill
bid	Twice a day
BM	Bowel movement.
BP	Blood pressure
BPH	benign prostatic hypertrophy
BS	Blood sugar
BSA	Body surface area
CAD	coronary artery disease
caps	Capsule
cc	cubic centimeter [milliliter]
CHF	congestive heart failure
COPD	chronic obstructive pulmonary
CP	chest pain
DC	discontinue medication
dil	dilute
disp	dispense
div	divide
DJD	degenerative joint disease
DM	diabetes mellitus
dtd	Let such doses be given
DW	distilled water
DX	diagnosis
elix	elixir
Ft	Make,
GI	Gastrointestinal
grGrain	Sx symptom
gtt	A drop
GU	Genitourinary
HA	headache
HBP	High blood pressure
HR	heart rate

HRT	hormone replacement therapy
hs	at bedtime
HTN	Hypertension
ID	Intradermal injection
IM	intramuscular injection
inj	An injection
IU	international units
IV	Intravenous injection
JRA	juvenile rheumatoid arthritis
kg	kilogram
L	liter ud
let	it be made
m or min	Minimum
wk	week
m	Mix
mcg	microgram
mEq	milliecluivalent
mg	milligram
mL	milliliter
mOsmol	milliosmole
N&V	Nausea and vomiting
noct	At night
non rep/NR	Do not repeat
OA	osteoarthritis
od	Right eye
os	Left eye
ou	Each eye
p	pulse
pc	After eating
PEFR	peak expiratory flow rate
po	by mouth
postop	after surgery
pr	rectally
prn	when necessary
pulv	A powder
PVD	peripheral vascular disease
q	every
qd	every day
qh	every hour
qid	four times daily
qod	every other day
qs ad	a sufficient quantity to
qs	as much as is sufficient disease (prepared)
RA	rheumatoid arthritis
Rect	Use rectally

s	without
Sig	write on label
SL	sublingual
SOB	shortness of breath
Sol	Solution
ss	One-half
stat	immediately
supp	Suppository
Susp	Suspension
Syr	Syrup
TB	tuberculosis
tbsp	tablespoon
TED	thromboembolic disease
TIA	transient ischernic attack
tid	three times a day
tiw	three times a week
top	(Use) topically
tsp	teaspoon
Tx	treatment
U	unit
UC	ulcerative colitis
ung	ointment
URI	upper respiratory infection
ut dict	as directed
UTI	urinary tract infection
WA	while awake
Pf	prefilled syringe

Appendix-14

MEDICINAL GASES

The following is a brief descriptions of the medical gases in common use, together with some details of their administration, health hazard information, contraindication, and color coding of cylinders.

1. OXYGEN (O_2)

Uses : Oxygen is used extensively in medical practice to increase oxygenation in patients with acute and chronic lung disease and cardiac disorders, for resuscitation, and for the treatment of victims of poisoning. It is always administered during anaesthesia. Oxygen therapy is also used in several applications: to supplement the breathing of patients whose respiratory system has become comprised from ailments such as bronchitis, or emphysema; to treat patients who are suffering from hemorrhage, shock, convulsions or other trauma; to administer atomized, liquid medication into the lungs; or as a treatment itself, due to pure oxygen's vasoconstrictive properties.

Administration: Oxygen is administered by mask, tent, endotracheal tube, nasal catheter and by special equipment for prolong treatment. Masks are used for controlled flows which may give concentrations over 60% by volume. Tents are used when the concentration need not to exceed 50% by volume. Respiratory facemasks are used to provide oxygen concentrations of approximately 30% of inhaled air.

Humidification of the gas may be needed when nasal catheters are used with a flow rate of over 3 liters/minute. Dependent on whether masks, tents or nasal catheters are used the flow rate is determined by the clinician. The dosage is adapted to the patient on the basis of the clinical course of the illness and generally ranges from 1 to 10 litres of gas per minute. In circumstances where oxygen is being mixed with other gases (anesthetics and analgesics) it is essential that the proportion of oxygen in the inspired mixture never falls below the concentration in air.

Health Hazard Information: At normal atmospheric pressures, oxygen is non-toxic up to about 20 hours exposure. At increasing pressures, oxygen becomes toxic to the lungs and central nervous system. Oxygen toxicity may result from the long-term exposure to partially reduced oxygen products which alter the metabolic function and structure of lung cells.

Contraindications: Newly born and premature infants should be given oxygen only if absolutely necessary because of the risk of the development of retinal damage. Patients who have chronic respiratory disease with carbon dioxide retention may develop apnoea if given oxygen, due to the reduction in stimulation of the respiratory system by carbon dioxide. Careful monitoring of these patients for hypoventilation is required during oxygen therapy.

Color code of cylinders : Black body, white shoulder.

2. CARBON DIOXIDE (CO_2)

Uses: Carbon dioxide stimulates the respiratory centre directly and if its concentration is raised from the normal concentration in air, the rate and depth of respiration are increased. At 3 percent concentration the depth is doubled while at 5 percent it is trebled with a great increase in respiration rate. Its use is not without danger and, therefore, it is reserved mainly for emergencies; for example, to induce and improve respiration rate in new-born infants, drowning persons, and cases of poisoning by carbon monoxide, morphine, hypnotics and other depressants. Generally, concentrations of 5 to 7 percent mixed with oxygen are used. Solid carbon dioxide is used in tissue freezing techniques. Carbon dioxide is also used: to increase the depth of anaesthesia rapidly, when volatile agents are being administered, it increases depth of respiration and helps to overcome breathholding and bronchial spasm, to increase cerebral blood flow in arteriosclerotic patients undergoing surgery, in gynaecological investigation for insufflation into fallopian tubes and abdominal cavities.

Administration: Carbon dioxide should only be administered by medical personnel trained in the appropriate techniques. Cylinders should only be used in conjunction with medical carbon dioxide gas pressure regulators. Special medical equipment will be used if it is being used to inflate parts of the body during keyhole surgery or gynaecological procedures.

Health Hazard Information: Carbon dioxide regulates the rate of breathing. The occupational exposure limit is 5000 ppm. As the concentration of carbon dioxide rises it affects the rate of breathing, at 2% the rate is noticeably above normal, at 10% breathing is very rapid and headache, vomiting and death may occur in an unfit person, 15% will cause unconsciousness in a few minutes, 25% leads to rapid circulatory insufficiency and death.
Pregnancy and breast feeding: The use of Medical Carbon Dioxide is not recommended during pregnancy but is unlikely to influence lactation.

Contraindications: Carbon dioxide is contraindicated:
-In acidosis
-In respiratory obstruction, the administration of carbon dioxide may be dangerous since any further increase in respiratory effort increases negative intra-thoracic pressure
-During resuscitation, where it can be dangerous and should be avoided.

Color code of cylinders: Grey body, grey shoulder.

3. NITROUS OXIDE (N_2O)

Uses: Nitrous oxide is a non irritating anaesthetic gas, used as a carrier for the volatile anaesthetics, it may be used to insufflate body cavities and in cryosurgery as a refrigerant. It can also be used as an analgesic and in dental work to provide short-term analgesia for tooth extraction and other brief procedures, administered with 50% oxygen.

Administration: Nitrous oxide should only be administered by medical personnel trained in the appropriate techniques. Cylinders should only be used in conjunction with medical nitrous oxide gas pressure regulators. Nitrous oxide should not be used for more than a total of 24 hours, or more frequently than every 4 days, without close clinical supervision and haematological monitoring.

Health Hazard Information: Nitrous oxide does not support life and when used for anaesthesia an adequate oxygen concentration must be ensured. Because it is much more soluble than nitrogen, nitrous oxide will diffuse into air filled body cavities much faster than nitrogen will diffuse out, increasing the pressure within them. Administration of nitrous oxide will, if continued for some hours, result in some inactivation of vitamin B_{12}, which is a co-factor of methionine synthase. Folate metabolism is consequently interfered with and DNA synthesis is impaired following prolonged administration of nitrous oxide. If administration is frequent, say every 2 days, this can result in megaloblastic changes in bone marrow, myeloneuropathy and sub acute combined degeneration of the spinal cord. Addiction can also occur. After a substantial period of time signs similar to those of sub acute combined degeneration of the spinal chord may develop. The suggested limits for continuous exposure range between 25-400 ppm. Nitrous oxide should never be given with less than 21% oxygen, but a maximum of 30% oxygen should be used during anaesthesia (except when used in combination with a volatile anaesthetic agent) and more at altitude and in the presence of disorders affecting oxygenation.

Absolute Contraindications:

- High and low atmospheric pressures.
- Unconsciousness.
- The first sixteen weeks of pregnancy.
- Artificial, traumatic or spontaneous pneumothorax.
- Gross abdominal distension
- During myringoplasty
- Air embolism

Care is required in the following conditions:

- Sedated patients.
- The very young and old due to mask fitting difficulties.
- Bowel obstruction.
- Having Vitamin B12 deficiency.

Color code of cylinders: Blue body, blue shoulder

4. HELIUM (He)

Uses: Helium is used in physiological investigations. The low density of helium compared to nitrogen enables it to provide a substitute for air when mixed with oxygen which is easier to breath in obstructive or dystrophic chest disease. It is indicated to assist flow of oxygen into the alveoli and to reduce the work of breathing in patients with severe airway obstruction. It is also used in some cryogenic applications.

Administration: By mask or endotracheal tube; cylinders should only be used in conjunction with medical oxygen gas pressure regulators. It may also be administered via nasal prongs if sufficiently high flow rate is employed to prevent air entrainment. It can be administered to spontaneously breathing patients or in combination with various forms of invasive and non-invasive ventilatory modes.
Health Hazard Information: Helium is an inert gas and will not support life. An adequate concentration of oxygen must be ensured when helium is administered. The risk for cooling should be taken into account, especially in smaller children. When using devices not designed for helium-oxygen mixtures, set ventilator tidal volumes and measured flow rates may not be accurate due to the physical properties of helium.
Contraindications: Not reported.
Color code of cylinders: Brown body, brown shoulder.

5. CYCLOPROPANE (C_3H_6)

Uses: Cyclopropane is a potent anaesthetic producing good muscular relaxation. It is non-irritating and induction and recovery are rapid. Mixtures of 4, 8 and 20 to 25 percent with oxygen produce analgesia, light analgesia and surgical analgesia respectively.

Administration: Cyclopropane should only be administered by anesthetists trained in the use of Cyclopropane. Because of the flammability and expense of cyclopropane, it is usually used in a closed (rebreathing) system, in which an absorbent chemical, such as soda lime, removes exhaled carbon dioxide, and theanesthetic is recirculated.
Health Hazard Information: Cardiac irregularities are possible if atropine or catechelomines are used with cyclopropane, nausea, vomiting and a degree of hypotension are common post-operative symptoms.
Contraindications: Not reported.
Color code of cylinders: Orange body, orange shoulder.

6. OXYGEN + CARBON DIOXIDE

Uses: Oxygen/carbon dioxide mixtures are used as a stimulant to the respiratory centre.
Administration: Usually by mask or endotracheal tube. Cylinders should only be used in conjunction with medical oxygen gas pressure regulators.
Health Hazard Information: Oxygen/carbon dioxide mixtures have similar toxicity to oxygen, but at normal atmospheric pressures the mixtures will induce a marked increase in breathing rate. The mixture should not be used at pressures above normal atmospheric pressure.
Contraindications: Newly born and premature infants should be given oxygen only if absolutely necessary because of the risk of the development of retinal damage.
Color code of cylinders: Black body, white and green shoulder.

7. HELIUM + OXYGEN

Uses: The low density of helium compared to nitrogen enables it to provide a substitute for air when mixed with oxygen which is easier to breath in obstructive or dystrophic chest diseases.
Administration: By mask or endotracheal tube; cylinders should only be used in conjunction with medical oxygen gas pressure regulators.
Health Hazard Information: Not reported.
Contraindications: Not reported.
Color code of cylinders: Brown and green.

8. **Nitric Oxide (NO)**
Uses: Nitric oxide is a powerful vasodilator, essential signaling molecule, and also a free radical. Since it dilates blood vessels, it is commonly prescribed to patients who suffer from circulation or heart ailments; however, it is prescribed as nitroglycerin and amyl nitrate pills which are metabolized into NO. In fact, the only instance for a NO gas prescription, which needs to be implemented in equal parts with oxygen, is for neonatal patients who suffer from pulmonary hypertension or post-meconium aspiration.
Administration: Nitric oxide is a gas available in concentrations of only 100 ppm and 800 ppm. The nitric oxide administration apparatus is to be used in conjunction with a ventilator or other breathing gas administration system. The concentration of nitric oxide is maintained approximately constant during the inspiratory flow regardless of the variation in flow rate within the inspiratory portion of the respiratory cycle. The concentration of inspired nitric oxide can be set, typically in the range of 0 to 80 parts per million (ppm). The administration apparatus includes a pressure regulator and connectors with fittings which are specific for nitric oxide gas cylinders, typically containing 400 or 800 ppm nitric oxide in nitrogen

Health Hazard Information: Overdosage with inhaled nitric oxide will be seen by elevations in methemoglobin and pulmonary toxicities associated with inspired nitric oxide. Elevated NO may cause acute lung injury.

Contraindications: Inhaled nitric oxide is contraindicated in the treatment of neonates known to be dependent on right-to-left shunting of blood.

Color code of cylinders: Nitric oxide lines and cylinders are frequently labeled with teal and black labels.

9. Medical air
Medical air cylinders are supplied to the following specification:
- oxygen content 20.9% Oxygen ± 0.5%
- nitrogen balance.

Uses: Medical air is used: as a replacement for atmospheric air when the atmosphere is contaminated by noxious fumes, vapours or gases, in anaesthesia as a carrier gas for volatile anaesthetic agents, as a power source for pneumatic equipment in ventilators and incubators to provide uncontaminated and controlled air flows.

Administration: For breathing purposes medical air is administered by various means, commonly by self contained or compressed air line breathing apparatus.In anaesthesia, medical air is administered via a cylinder and valve assembly through a face mask or endotracheal tube.

Health Hazard Information: Medical air should never be administered to a patient if, when it is mixed with other gases, the oxygen content is less than 21%. Care is needed in the handling and use of medical air cylinders.

Contraindications: Medical air is contraindicated where oxygen or other gaseous combinations would be indicated (airways obstruction, pneumonia, and a myriad of cardio-respiratory conditions).

Color code of cylinders: Yellow

Appendix-15

NUCLEAR MEDICINE AND RADIOPHARMACEUTICALS

Introduction:

Nuclear Medicine is a medical specialty devoted to diagnostic, therapeutic and research applications of radionuclides utilizing nuclear gamma and positron emission and sometimes beta-ray which are used specially in therapy.

Radiopharmaceuticals have been defined as radioactive drugs that, when used for the purpose of diagnosis or therapy, typically elicit no physiological response from the patient.

The design of these compounds is based solely upon physiological function of the target organ. Unlike radiographic procedures, which depend almost entirely upon tissue density differences, external imaging of radiopharmaceuticals is essentially independent of the density of the target organ. The mechanism of localization of a radiopharmaceutical in a particular target organ can be as simple as the physical trapping of particles or as sophisticated as an antigen-antibody reaction or chemisorption of an inorganic phosphate on the hydroxyapatite crystals deposited in an acute myocardial infarction.

Properties of the ideal diagnostic radiopharmaceuticals

1. Pure gamma emitter.
2. 100 < gamma energy < 250 keV.
3. Effective half-life = 1.5 X test duration.
4. High target to non target ratio.
5. Minimal radiation dose to patient and Nuclear Medicine personnel
6. Patient safety.
7. Chemical reactivity.
8. Inexpensive, readily available radiopharmaceutical.
9. Simple preparation and quality control if manufactured in house.

Diagnostic approaches of Nuclear Medicine include both in vivo and in vitro procedures:

In vivo technique is the most common type of procedure, where radiopharmaceuticals/ radionuclides/ radiotracers are administered to the patients. Then patients are imaged from outside using the instruments- planar Gamma Camera and SPECT (Single Photon Emission Computed Tomography) by mapping radiotracer distribution in different target organs of the body. Characteristics of commonly used radiopharmaceuticals are shown in Table-I.

PET (Positron Emission Tomography) images offer potentially more functional demonstration (cellular activity at molecular level) rather than simply anatomical information. A PET scan allows the physician to distinguish between living and dead tissue or between benign and malignant disease.
18 fludeoxyglucose (FDG) is mostly used radiotracer in PET studies. ^{18} Fl is produced by cyclotron and half life is 110 min. The uptake of ^{18} F -FDG by tissues reflects the tissue uptake of glucose which correlates with certain type of tissue metabolism.

PET/CT:

PET/CT are both state of art imaging tools that allow physicians to pinpoint the location of cancer within the body before making treatment recommendations. The highly sensitive PET scan images the biology of disorders at the molecular level, while CT scan provides a detailed picture of the body's internal anatomy. The PET/CT scan combines the strengths of these two well-established imaging modalities into a single scan. A PET/CT scan can also help physicians monitor the treatment of disease and identify recurrence of disease. This PET/CT has become the fastest growing imaging modality since its introduction to clinical medicine in 2001.

SPECT/CT:

Hybrid SPECT/CT demonstrate added value to single imaging modality. With SPECT/CT scanners, lesions visualized by functional imaging can be correlated with anatomic structures. The addition of anatomic information increases the sensitivity as well as the specificity of scintigraphic findings.

In vitro procedure includes Radioimmunoassay (RIA) and Immuno-radiometric assay (IRMA), which are used to measure different hormone levels in serum such as free triiodothyronine (FT_3), free tetraiodothyronine (FT_4), Thyroid stimulating hormone (TSH), follicularstimulating hormone (FSH), Luteinizing hormone (LH), calcitonin and prolactin and antibodies. Sometimes radionuclides are introduced to the patients and samples of breath, urine and faeces are taken from the patient. Measurements of radioactivity in samples are made by gamma- or beta-sample counting techniques.

Therapeutic aspects of nuclear medicine mostly deal with radioiodine (^{131}I) treatment of primary hyperthyroidism and carcinoma of thyroid. Low-energy beta-emitting radionuclides (^{153}samarium-ethylenediaminetetrameth-ylenephosphonate (EDTMP) and ^{89}strontium (^{89}Sr) are used to relieve metastatic bone pain. ^{90} Sr are for the treatment pterygium. Furthermore, radionuclides are being used for cardiac stenting, synovectomy, liver cancer, ovarian and prostatic cancer. Radioimmunotherapy is the promising aspect of therapeutic Nuclear Medicine. In non-Hodgkins lymphoma radioimmunotherapy (Zevalin) has been approved by the FDA of USA since 2002.

Table I- Characteristics of commonly used radionuclides.				
Radionuclide	Mode of production	Type of decay	Principles of photon emissions (kev)	Half-life
^{99m}Tc	Generator	IT	140	6 h
^{131}I	Reactor	Gamma, Beta	360, 640	8 day
^{123}I	Cyclotron	Ec	160	13 h
^{125}I	Reactor	Gamma	35	60 day
^{67}Ga	Cyclotron	EC	92, 182, 300, 390	78 day
^{201}Tl	Cyclotron	EC	68-80b	73.5 h
^{111}In	Cyclotron	EC	173, 247	2.8 day
^{133}Xe	Reactor	Beta	81	5.3 day
^{81m}Kr	Generator	IT	191	13 s
^{18}F	Cyclotron	Positron	635	110 min
EC- Electron capture, IT- isomeric transition, b- Characteristic X-rays				

Organ specific imaging procedures:

Some Nuclear Medicine imaging for different organs are described very shortly below which will provide introductory knowledge about Nuclear Medicine. Organ specific radiopharmaceuticals are given in Table-II and Table-III.

Thyroid gland

The oldest but most frequently performed nuclear medicine procedure is thyroid scan by ^{99m} Tc (Technetium), ^{131} I (Iodine) or ^{123} I. Thyroid scan gives information about radiotracer uptake by thyroid gland and details about nodular goiter. Previously radioiodine uptake was used to evaluate thyroiditis, hypothyroidism and calculation of therapy dose for hyperthyroidism. But radioiodine uptake is no more use in most of the nuclear medicine departments. Commonly 37 or 74 MBq of ^{99m} Tc is injected intravenously and scan is taken after 20 minutes.
Most of the therapeutic nuclear medicine in our country deals with radioiodine treatment in primary hyperthyroid patients by giving 370 MBq-555 MBq ^{131}I as outdoor patient.. About 1110 MBq -7400 MBq dose of ^{131}I are usually given to differentiated thyroid carcinoma patient after total thyroidectomy at National Institute of Nuclear Medicine and Allied Sciences (NINMAS) and other Institutes of Nuclear Medicine under Bangladesh Atomic Energy Commission. These patients are followed up life long at the concerned institutes.

Skeletal System

Whole body bone scan represents main bulk of study in most of the nuclear medicine departments. This is a highly sensitive test to survey the entire skeletal system with less radiation in comparison to X-ray imaging. ^{99m}/Tc phosphonate radiopharmaceuticals are highly sensitive to bone turnover and therefore are useful in the early detection of bone and joint abnormalities. About 740 MBq of ^{99m} Tc phosphonate is introduced intravenously to the patients and different spot views are taken after 2-3 hours.

Renal System

Morphology and functional status of renal system can be well evaluated by ^{99m}Tc DMSA (Dimercaptosuccinate acid) scan and renogram by ^{99m}Tc DTPA (Diethylene triamine pentaacetic acid). These techniques are useful in diagnosing renal scar, obstructive uropathy and parenchymal disease of kidneys.

Cardiovascular System

Several nuclear medicinal techniques are available for the diagnosis and management of cardiovascular diseases. Myocardial perfusion study using Thallium-201 (^{201}Tl), ^{99m}Tc sestamibi, ^{99m}Tc teboroxime, ^{99m}Tc tetrofosmin are used to diagnose coronary artery disease. Radionuclide ventriculography by ^{99m}Tc labeled RBCs is used to evaluate by global and regional ventricular function before and after intervention.

Brain

In the late 1960s & early 1970s conventional brain scintigraphy by blood brain barrier agent, ^{99m}Tc DTPA was the method of choice. Now a days CT (Computed tomography) and MRI (Magnetic Resonance Imaging) have been playing important role in anatomical imaging. Rather, the role of nuclear medicine imaging for central nervous system has been redefined as functional brain imaging. ^{99m}Tc HMPAO (Hexamethyl propylene amine oxime) is currently the best agent to estimate regional cerebral blood flow (rCBF). SPECT imaging of ^{99m}Tc HMPAO is useful in cerebrovascular disease and psychiatric disorders. PET using both blood flow and metabolic agents ^{18}F FDG produces images of physiologic and biochemical processes in the brain that has both important research and clinical impacts. Radionuclide cisternography is a simple method to investigate differentiation of communicating and non-communicating hydrocephalous, CSF (cerebrospinal fluid) leaks and demonstration of CSF shunt patency.

Liver and Biliary Scan

Colloid liver scan is used to examine the liver, spleen and bone marrow. Now a days liver scan is rarely performed. Readily available ultrasound scan has replaced this procedure to see the liver focal lesions. Hepatobiliary imaging using several amino-diacetic acid compounds labeled with ^{99m}Tc has been used to investigate biliary excretion and the pathway from liver to small intestine. Indications of this scintigraphy are- cholecystitis, biliary atresia in newborn to assess the hepatic uptake, bile duct patency, cystic duct patency, and sphincter of Oddi dysfunction.

Lungs

Pulmonary imaging comprises ventilation scan & perfusion scan. Ventilation scan is usually performed by ^{81m}Kr (Krypton) gas / ^{133}Xe (Xenon) gas or Technegas (^{99m}Tc –labelled carbon particles). Perfusion imaging is done by ^{99m}Tc labeled ^{99m}Tc MAA (macroaggregate albumin). Combined ventilation/ perfusion (V/Q) study is mostly applied to diagnose the medical emergency condition pulmonary embolism. Conditions associated with V/Q mismatch are acute and chronic pulmonary embolism, bronchogenic carcinoma, mediastinal and hilar adenopathy, hypoplasia of pulmonary artery and vasculitis. V/Q matched abnormalities are seen in chronic obstructive pulmonary disease, bronchitis, blebs, congestive heart failure, pulmonary oedema, pleural effusion, asthma, pulmonary trauma and bronchogenic carcinoma.

Gastrointestinal tract

Gastric emptying studies by ^{99m}Tc DTPA combined with meal are most often performed on patients who have an unsatisfactory result from peptic ulcer surgery and in studying the physiology of the stomach. The milk scan using ^{99m}Tc –sulphur colloid in 100 ml milk or orange juiceis applied orally to diagnose gastro-oesophageal reflux in children. Meckels' diverticulum, the commonest congenital anomaly of gastrointestinal tract could be evaluated by simple imaging technique by ^{99m}Tc-pertechnetate.

Tumour Imaging

Tumour imaging is the growing area of Nuclear Medicine application. Many radionuclide studies are performed for the detection of primary and metastatic tumours. These studies are divided into tumour specific imaging and tumour-non-specific imaging. Tumour specific imaging include ^{131}I whole body scan, ^{131}I MIBG (metaiodobenzylguanidine) radiolabeled monoclonal antibodies and peptides. Radionuclides those are not tumour specific are gallium –67 (^{67}Ga), thallium-201 (^{201}Tl) and ^{99m}Tc sestamibi. ^{18}F FDG PET imaging also heps in diagnosis of primary tumour and to assess metastases and prognosis of treatment.

Lymphoscintigraphy and sentinel lymphnodes

Lymphoscintigraphy is performed by injecting a small quantity of ^{99m}Tc labeled nanocolloid subcutaneously usually unilateral lymphoedema and lymphnodes metastases are diagnosed by this imaging procedure. 'Sentinel' node detection has become popular in recent years and routinely used in some Nuclear Medicine Departments to diagnose early stage of breast carcinoma and melanoma. This procedure is useful to surgeons to take decision about extent of operation.

Infection

There has been considerable improvement in the scintigraphic imaging of inflammation and infection over the last few years. Radiolabelled white blood cells have been used as an important diagnostic modality in the diagnosis of infection. The radionuclides available for leucocyte labeling for localization of infection are ^{111}In, ^{99m}Tc and ^{67}Ga.

Radiation safety issue:

As was the case with diagnostic radiopharmaceuticals, the goal is a *minimal radiation dose* absorbed by both the patient, who is probably having a one-time therapeutic procedure, and the Physician or Nuclear Medicine Technologist, who is routinely exposed to radioactive patients on a daily basis. The usual rules of the TDS concept apply: one should minimize TIME, maximize DISTANCE, and use the appropriate amount of SHIELDING. There should be specific rules governing the *release of patients from the hospital after administration of a therapeutic radiopharmaceutical.*

Precautions for radiopharmaceuticals handling:

There are many precautions one must take during the preparation and use of radiopharmaceuticals, in general, and Tc-99m radiopharmaceuticals, in particular. Since most radiopharmaceuticals are intended to be administered intravenously, it is imperative to use aseptic technique in order to maintain sterility of the product. The vial septum must be wiped with 70% isopropanol prior to puncturing the septum with a needle. This is really a cleansing step rather than a true sterilization step since the alcohol doesn't remain on the septum long enough to kill all pathogens that might be present.

Air must NEVER be injected into any radiopharmaceutical vial, especially one containing a Tc-99m product. The oxygen contained in only 0.1 ml of air is enough to completely destroy the stannous ion used in many commercially available cold kits as a reducing agent. In addition, room air is not sterile so it is possible to introduce pathogens into the vial by using a preliminary injection of air to increase internal pressure in the vial and ease the removal of the contents.

Prior to reconstituting a cold kit with Tc-99m pertechnetate, oxidant-free pertechnetate must be diluted to the required final volume with 0.9% NaCl solution. Ideally, oxidant-free saline (Low Dissolved Oxygen Saline) should be used for the dilution step. Reconstitution of a cold kit with a small volume of pertechnetate followed a few minutes later by dilution with saline solution can cause dissociation of certain weak chelates, resulting in the formation of significant amounts of Free Tc. This is not a problem with sulfur colloid or other insoluble Tc-99m compounds.

Patient safety

Patient safety is also critical. Ideally, the therapeutic radiopharmaceutical should exhibit no toxicity to the patient. While most commonly used compounds are inherently safe and provide wide margins of safety, we routinely inject drugs that are potentially toxic. Thallous ion (Tl^{1+}), for example, is known to be a potent cardiotoxin and yet we routinely inject Tl-201 thallous chloride intravenously into our patients. This is an acceptable practice since the specific activity (activity per unit mass) of carrier-free Tl-201 is very high and the amount of Tl-201 contained in the typical 3 mCi dose (only 42 ng) is very small.

One of the concerns regarding treating a patient with I-131 NaI therapy solution is whether the patient is allergic to iodine. A calculation will show that 10 mCi of carrier-free I-131 contains only 80 ng of elemental iodine, far too small an amount to have a physiological effect on the patient.

Table II Commonly used radiopharmeceuticals for different organs.

Target organ	Radiopharmaceuticals	Indications	Dose (MBq)
Skeletal System	^{99m}Tc HDP (disodium oxidronate) ^{99m}Tc MDP (Methylene diphosphonate)	Metastatic lesions, size and extent of primary bone tumour, osteomyelitis and fractures.	350-750
Kidneys	^{99m}Tc DTPA (diethylenetriamine pentacetic acid) ^{99m}Tc MAG (mercaptylacetyltriglycerine) ^{99m}Tc DMSA (dimercaptosuccinic acid)	Parenchymal function, evaluation of obstruction. Congenital anomaly, Tumour, Cortical scarring.	200-750 40-80
Thyroid	^{99m}Tc pertechnetate	Thyroid scan to see size of gland and uptake in nodule.	40-80
Thyroid	^{131}I	Therapy for hyperthyroidism. Carcinoma of thyroid.	~ 555 ~1700-5550
Cardiovascular system	^{99m}Tc sestamibi ^{99m}Tc Tetrofosmin ^{99m}Tc teboroxime ^{201}TL ^{99m}Tc RBC	Evaluation of ischaemia, infarction wall motion. Cardiac output.	370-1100 74-111
Lungs	^{99m}Tc Technegas ^{133}Xe ^{81m}Kr	Pulmonary embolism Tumour	40-74 370
Brain	^{99m}Tc DTPA ^{99m}Tc HMPAO (hexamethylpropylele oxime)	Primary or secondary tumour, psychiatric problems	~740 555
Liver scan Biliary system	^{99m}Tc Tin colloid ^{99m}Tc hepatic iminodiacetic acid	Tumour. Biliary atersia, Acute cholecystitis.	40-80 40-80
Tumour	^{67}Ga (Gallium citrate)	Tumour	100
Infection	^{111}In White blood cell	Infection	12
Lymphoscintigraphy	^{99m}Tc nanocolloid	Lymphoedema, Metastases & 'sentinel node'detection	40

Clinical Utility

Radiopharmaceuticals have been used clinically for a wide variety of studies which generally fall into three categories. (Table III).

1. Static studies.
2. Dynamic studies.
3. In vivo non-imaging studies.

Table III. Clinical use of Radiopharmaceuticals			
Study Type	Tracer	Region	Pathology
Static Studies With Radiotracers			
Bone Scan	Tc-MDP, Tc-HDP	Whole Body	Bone tumors, fractures, Paget's disease, spread of metastatic disease
Liver/Spleen Scan	Tc-SC, Tc-MIAA	Abdomen	Tumors, cysts, hepatocellular disease
Brain Scan	Tc-HMPAO	Brain	Tumors, trauma, dementia
Tumor Scan	Ga-67 citrate	Whole Body	Malignant Tumors
Dynamic Studies With Radiotracers			
Study Type	Tracer	Region	Pathology
Cardioangiography	Tc-RBC, Tc-HSA	Chest	Aneurysms, congenital heart defects; myocardial dyskinesia; cardiomegaly
Cerebral Blood Flow	TcO4	Head/neck	Cerebral death, AVM
Cholecystography	Tc-DISIDA	Abdomen	Obstructive disease
Cisternogram	In-111 DTPA	Head/neck	Blockage/slowed CSF flow
Dynamic kidney	Tc-DTPA	Back	Obstructive disease
Gastric emptying	Tc-ovalbumin	Abdomen	Abnormal GE Rates In-DTPA regurgitation
Pulmonary vent	Xe-133 gas	Upper back	obstructed airways
Renogram	I-131 hippuran	Back	renal dysfunction
Venogram	Tc-MAA	Legs	thrombosis
Voiding cystogram	Tc-sulfur colloid	Abdomen	reflux of urine incomplete bladder emptying
In Vivo Non-Imaging Tracer Kinetic Studies			
CO2 breath test	C-14 CO2	breath	glucose intolerance
Iron turnover	Fe-59 chloride	whole body	abnormal ferrokinetics
Ocular P-32 uptake	P-32 Na3PO4	eyes	ocular melanoma
Platelet survival	In-111 platelets	blood	abnormal platelet loss

Radioactive iodine (RAIU)	*I-NaI	thyroid	abnormal uptake test, hyperthyroidism
RBC Survival	Cr-51 RBC's	blood	hemolytic anemias
Schilling Test	Co-57 B12	urine	pernicious anemia, Vitamin B12 malabsorption syndromes
Splenic Sequestration	Cr-51 RBC's	spleen	hypersplenism

Categories of Radiopharmaceuticals

Radiopharmaceuticals fall into several different categories:

- ready-to-use radiopharmaceuticals
- instant kits for preparation of Tc99m products
- kits requiring heating
- products requiring significant manipulation.

Examples of each of these categories are listed in the Table IV.

Table IV. Categories of Radiopharmaceuticals	
Prepared Products	**Tc-99m Kits requiring heating**
I-123 capsules	MAG3
I-131 hippuran	sestamibi
Ga-67 citrate	sulfur colloid
Tl-201 chloride	teboroxime
Xe-133 gas	**Products requiring significant manipulation**
Tc-99m pertechnetate	Cr-RBC's
Instant Tc-99m kits	Tc-99m RBC's
Disofenin	Tc-99m WBC's
DTPA	In-111 WBC's,
GH	In-111 Platelets
HDP	Xe-133 in saline
MDP	I-123 mIBG
mebrofenin	
MIAA	
MAA	
PYP	

Appendix-16

PARENTERAL DOSES (FOR ADULTS AND CHILDREN) OF DRUGS FOR MEDICAL EMERGENCIES

Drugs which are required immediate administration within minutes post or during a medical emergency. Medicines which have the potential to sustain life and/or prevent further complications.

DRUG	USE	DOSAGE
Adrenaline (1 mg/ml, i.e. 1:1,000)	Anaphylaxis or acute angioedema	Give intramuscularly (not intravenously): adults and 12-18 years olds: 500 microgram (0.25 ml) 6 months- 6 years: 120 microgram (0.12 ml) under 6 months: 50 microgram (0.05 ml)
Aminophylline	Reversible airways obstruction, severe acute asthma	Given Intravenously : Adults: 300 micrograms/kg/hour; CHILD under 12 years :1mg/kg/hour, adjusted according to plasma-theophylline concentration
Amiodarone	Arrhythmia (ventricular tachycardia)	Given Intravenously : initially 5 mg/kg over 20–120 minutes with ECG monitoring; subsequent infusion given if necessary according to response up to max. 1.2 g in 24 hours
Atropine (600 microgram/ml)	Bradycardia (arrhythmia) plus hypotension in myocardial infarction	adults: 0.3-1 mg intravenously; the dose may be repeated every 3-5 times if the first dose is not effective
Benzylpenicillin (600 mg vial for reconstitution with sodium chloride or water for injection)	Suspected bacterial meningitis or meningococcal septicemia	Give intravenously (or intramuscularly if venous access is not available) as a single dose: adults and children 10 years and over: 1.2 g 1-9 years: 600 mg under 1 year: 300 mg
Calcium Gluconate	In severe acute hypocalcaemia or hypocalcaemic tetany,	An initial slow intravenous injection of 10–20mL of calcium gluconate injection 10% (providing approximately 2.25–4.5 mmol of calcium) in adult with plasma Ca and ECG monitoring.
Cefotaxime (1 g vial for reconstitution with water for injection)	Suspected bacterial meningitis or meningococcal septicemia, in patients allergic to penicillin (on history of anaphylaxis)	Give intravenously or IM as a single dose: adults and children 12 years and over: 1 g children up to 12 years: 50 mg/kg
Chloramphenicol (1 g vial for reconstitution with water for injection)	Suspected bacterial meningitis or meningococcal septicemia, if there is a history of anaphylaxis due to penicillin	adults and children: 12.5-25 mg/kg intravenously
Chlorphenamine (10 mg/ml)	As an adjunct after adrenaline in the	Give by slow intravenous injection over 1 min:

	treatment of anaphylaxis or acute angioedema	adults and children over 12 years: 10-20 mg 6-12 years: 5-10 mg 1-6 years: 2.5-5 mg 1 month-1 year: 250 microgram/kg (max 2.5 mg)
Cyclizine (50 mg/ml)	Vomiting due to vestibular disorders or with diamorphine (except in myocardial infarction)	adults: 50 mg IM or intravenously children over 1 month: 0.5-1 mg/kg intravenously (max single dose: 6-18 years, 50 mg: 1 month 6 years, 25 mg)
Diamorphine (5 mg or 10 mg powder for reconstitution with water for injection)	Severe pain (e.g. myocardial infarction) and acute left ventricular failure	Give by slow (1 mg/min) intravenous injection (particularly with shock or peripheral vasoconstriction): adults : 1.25-5 mg 12-18 years: 2.5-5 mg 1-12 years: 75-100 microgram/kg 6-12 months: 75 microgram/kg 3-6 months: 25 microgram/kg 1-3 months: 20 microgram/kg Or, IM (not in myocardial infarction) or subcutaneously (but not if tissue perfusion is impaired or if there is edema) in a dose of 5-10 mg in adults, or 5 mg in children aged 12-18 years
Diazepam (5mg/ml Injection)	Severe acute anxiety, control of acute panic attacks, and acute alcohol withdrawal, acute drug induced dystonic reactions,	Given by intramuscular injection or slow intravenous injection: for severe acute anxiety, control of acute panic attacks, and acute alcohol withdrawal, 10 mg, repeated if necessary after not less than 4 hours Given by slow intravenous injection: for acute drug induced dystonic reactions, 5–10mg repeated as necessary after at least 10 minutes; CHILD: 1 month–12 Years: 100 micrograms/kg repeated as necessary after at least 10 minutes
Diclofenac (25 mg/ml)	Analgesia (e.g. ureteric colic, bone pain, acute back pain)	adults: 75 mg IM deep into the gluteal muscle
Dobutamine	inotropic support in infarction, cardiac surgery, cardiomyopathies, septic shock, and cardiogenic shock; cardiac stress testing	Given by intravenous infusion, 2.5–10 micrograms/kg/minute, adjusted according to response
Dopamine	cardiogenic shock	Given by intravenous infusion, 2–5 micrograms/kg/minute initially
Flumazenil (100 microgram/ml)	To reverse respiratory depression caused by benzodiazepines	adults: 200 microgram intravenously over 15 seconds, then 100 microgram at 1 min intervals, if needed (max. 1 mg)
Furosemide (100 mg/ml)	To relieve pulmonary edema associated with acute left ventricular failure	adults: 20-50 mg by slow intravenous injection

Glucagons (1 mg/ml)	Hypoglycaemia-first-line use, except in those who have been hypoglycaemic for some time and may have exhausted their supplies of liver glycogen	Give subcutaneously, IM or intravenously: adult: 1 mg children 2-18 years: 0.5-1 mg (i.e. weight <25 kg, 0.5 mg: >25 kg/1 mg) 1 month- 2 years: 500 microgram under 1 month: 20 microgram/kg
Glucose (10% and 20% solution)	Hypoglycaemia-second line use in unconscious patients	Give intravenously into a large vein over 3 min: adults: up to 50 ml to 20% infusion children:2-5 ml/kg of 10% infusion
Haloperidol (5 mg/ml)	Very agitated or violent patients with psychiatric illness	adults: 2-10 mg IM
Hydrocortisone (100 mg powder as sodium succinate)	Acute severe asthma	Give intravenously over at least 1 min: adults: 100 mg children: 4 mg/kg (max 100 mg)
	Severe or recurrent anaphylaxis	Give by slow intravenous injection: adults: 100-300 mg children: 1 month-18 years: 4-8 mg/kg (max 200 mg)
	Hypoadrenalism	Give by slow intravenous or IM injection: adults and children 12 years: 100 mg children: 1 month-12 years: 2-4 mg/kg
Lorazepam (4 mg/ml)	Very agitated or violent patients with psychiatric illness and convulsion	adults: 1-2 mg IM or 4 mg by slow intravenous injection into a large vein
Lidocaine 2% Injection	for the treatment of ventricular tachycardia in haemodynamically stable patients, and ventricular fibrillation and pulseless ventricular tachycardia in cardiac arrest refractory to defibrillation.	in patients without gross circulatory impairment, 100 mg as a bolus over a few minutes (50mg in lighter patients or those whose circulation is severely impaired), followed immediately - by infusion of 4 mg/minute for 30 minutes, 2 mg/minute for 2 hours, then 1 mg/minute;
Metoclopramide (5 mg/ml)	Nausea and vomiting, can be given with diamorphine in patients with myocardial infection	adults: 10 mg IM or intravenously over 1-2 min
Midazolam 5mg/5ml and 15mg/5ml Injection	status epilepticus; febrile convulsions	Given by continuous subcutaneous infusion, it is given initially in a dose of 20-40 mg/24 hrs.
Morphine (100 mg/ml)	Severe pain	Adults: 10 mg (15 mg for heavier well-muscled patients) subcutaneously (but not if patient is edematous) or IM, or 2.5-7.5 mg by slow (2 mg/min) intravenous injection Children, subcutaneously or intramuscularly: 12-18 years: 10 mg 5-12 years: 5-10 mg 1-5 years: 2.5-5 mg 1-12 months: 200 microgram/kg children, intravenously (over at least 5 min): 12-18 years: 2.5-10 mg 1 month-12 years: 100-200 microgram/kg
Naloxone (400 microgram/ml)	Opioid overdose	Give intravenously (subcutaneously or IM and if intravenous route not feasible): Adults and children 12-18 years: 0.4-2 mg

		Dose can be repeated every 2-3 min up to a maximum of 10 mg Children 1 month- 12 years: 1 microgram/kg with a subsequent dose of 100 microgram/kg if there is no response
Phenobarbitone Sodium (200mg/ml Injection)	status epilepticus	Dilute injection 10 mg/kg at a rate of not more than 100 mg/minute; max. 1 g
Phenytoin (50mg/ml Injection)	acute symptomatic seizures associated with head trauma or neurosurgery, status epilepticus	By slow intravenous injection or infusion (with blood pressure and ECG monitoring), ADULT: 20 mg/kg (max. 2 g) at a rate not exceeding 1 mg/kg/minute (max. 50mg per minute), CHILD: 1 month–12 years, 20 mg/kg at a rate not exceeding 1 mg/kg/minute (max. 50mg per minute) as a loading dose; maintenance dose of 5–10 mg/kg daily (max. 300 mg daily) in 2 divided doses; NEONATE 20 mg/kg at a rate not exceeding 1 mg/kg/minute, as a loading dose; maintenance dose of 5–10 mg/kg daily in 2 divided doses
Potassium Chloride 15% Injection	Severe hypokalaemia	Ready-mixed infusion solutions should be used containing 1.5 g (K^+ 20 mmol) in 10 mL, is thoroughly mixed with 500mL of sodium chloride 0.9% intravenous infusion and given slowly over 2 to 3 hours
Pralidoxime chloride (2-PAM) 25mg/ml Injection	In Organophosphorus poisoning as cholinesterase inhibitor	By intravenous infusion, ADULT and CHILD initially 30 mg/kg over 20 minutes, followed by 8 mg/kg/hour; usual max. 12 g in 24 hours.
Prochlorperazine (12.5 mg/ml)	Nausea and vomiting	Give by deep IM injection: Adults and children 12-18 years: 12.5 mg 5-12 years: 5-6.25 mg 2-5 years: 1.25-2.5 mg
Procyclidine (5 mg/ml)	Oculogyric crisis or acute dystonia	Give IM or intravenously: adults and children 10-18 years: 5-10 mg (occasionally more than 10 mg is needed) 2-10 years: 2-5 mg under 2 years: 0.5-2 mg
Salbutamol sulphate Inhalation	severe or life-threatening acute asthma	High-flow oxygen plus salbutamol 5mg via oxygen-driven nebuliser for ADULT; CHILD under 5 years 2.5 mg, 5–12 years 2.5–5 with prednisolone and inhaled ipratropium bromide.
Sodium bicarbonate 8.4% Injection	Severe metabolic acidosis (pH<7.1)	sodium bicarbonate (1.26%) should be infused over 3–4 hours with plasma-pH and electrolyte monitoring
Streptokinase Injection	acute myocardial infarction	MI (initiated within 12 hours of symptom onset), by intravenous infusion, 1.5 million units over 60 minutes

Table of ideal weight for age (kg)

newborn	1month	3months	6months	1 years	3 years	5 years	7 years	12 years	adult female	adult male
3.5	4.2	5.6	7,7	10	15	18	23	39	56	68

Compiled from: British National Formulary (BNF) and BNF for Children

DENTAL PRACTITIONERS' FORMULARY

Dentistry as a profession continues to undergo changes including improvements in clinical treatment. Although the major part of the dentist's work is still of a restorative nature, the increasing improvements in prevention, diagnosis, and treatment of oral diseases and the oral manifestation of many systemic disease is becoming well recognized internationally. Recent views reflect the systemic implicationsof oral diseases is of great concern. Periodontal disease is being considered as a risk factor for developing ischemic heart disease, myocardial infarction, stroke, kidney disease,, pre matured child birth, malformed babies etc. So, oral rehabilitations including dental implants surgery has become a part of general dentistry.

The dentist's role has therefore been broadened to include the management of patients with soft tissue diseases such as oral cancer, and AIDS, facial pain, Tempero Mandibular Joint (TMJ) disorders and salivary dysfunction etc. In addition, dental caries and its sequel and periodontal disease still prevalent in Bangladesh.
The profession seems to feel that dentistry is currently in something of a state of transition. Dental caries once the main area of dental work has declined strikingly in the most developed nations, as the profession has come under the eagle eye of the Health and safety Executive. But the theme virtually does not reflect the present situation of dentistry in Bangladesh, due to lack of knowledge, integration, cooperation between the dental professionals and health executives. It can be regrettably said that unfortunately, oral health is still neglected in Bangladesh and not included in the primary health care system of the Government. Should oral health be the ninth component of primary health care system of Bangladesh! As without oral health we cannot think of a sound human being. Mouth is the gateway of health containing more than 740 species of microorganisms!

In this way dental and oral health is increasingly being seen as part of general health. In such circumstances the need for the dentists to have more of an oral physician's approach and to be more concerned with the patients' previous history, drug history and life style is obvious. Dentists must know much more about medical conditions that can affect the management of their patients.

Medically compromised patients who are attending for dental treatment require special needs. Other requires only routine dentistry, but their medical conditions may require it to be modified to varying degrees.

Therefore, it is essential that general dental practitioners keep up to date and this dental practitioners formulary is primarily intended to help them to do so in their daily clinical practice.

COMMON DENTAL DISEASES IN BANGLADESH

1. Dental caries
2. Gingivitis
3. Periodontitis
4. Pericoronitis
5. Pulpitis
6. Osteomyelitis of the jaw
7. Alveolar ostitis (Dry Socket)
8. Cervico facial cellulitis
9. Cancrum oris

10. Actinomycosis
11. Infective endocarditis
12. Cavernous sinus thrombosis
13. Cysts of the jaw
14. Odontogenic tumors of the jaw
15. Non-odontogenic tumors of the jaw
16. Rickets
17. Scurvy
18. Tempero mandibular joint disorders
19. Primary herpetic stomatitis
20. Oral ulceration
21. Oral candidiasis
22. Recurrent aphthae (Aphthous stomatitis)
23. Lichen plannus
24. Mucous membrane pemphigoid
25. Pemphigus vulgaris
26. Ulceration of the tongue
27. White oral mucosal lesions
28. Oral pre-malignant lesions
29. Oral cancer
30. Diseases of the salivary glands, salivary gland tumours.
31. Pyogenic granuloma and pregnancy epulis
32. Medically compromised patients
33. Oral Manifestations of many systemic diseases
34. Trigeminal neuralgia
35. Glossopharyngeal neuralgia
36. Bell's palsy
37. Emergencies in dental practice such as Faints, strokes, sudden loss of consciousness etc.

LIST OF DRUGS USED IN DENTISTRY

1. Acetylsalicylic Acid (Aspirin)
2. Acyclovir
3. Adrenaline
4. Aluminum Hydroxide Magnesium Hydroxide + Simethicone
5. Ampicillin
6. Amoxicllin
7. Azithromycin
8. Erythromycin
9. Clindamycin
10. Betacarotine + Vitamin C + Vitamin E
11. Betamethasone + Neomycin
12. Bupivacaine
13. Calcium gluconate
14. Carbamazepine
15. Cefazoline
16. Ceftriaxone
17. Celecoxib
18. Cephradine
19. Chlorhexidine
20. Ciprofloxacin
21. Clarithromycin
22. Clobazam

23. Cloxacillin
24. Co- trimoxazole
25. Dexamethasone
26. Diazepam
27. Diclofenac
28. Diclofenac + Lignocaine
29. Dicloxacilline
30. Doxycycline
31. Ferrous Sulphate + Folic Acid + Zinc sulfate
32. Fluconazole
33. Folic Acid + Zinc Sulfate
34. Griseofulvin
35. Hydrocortisone
36. Ibuprofen
37. Indomethacin
38. Ketoconazole
39. Ketoprofen
40. Lignocaine
41. Lignocaine + Adrenaline
42. Mefenamic Acid
43. Metronidazole
44. Miconazole + Hydrocortisone
45. Multivitamine + Minerals
46. Naproxen
47. Neomycin + Bacitracin + Polymyxin-B
48. Nimesulide
49. Nystatin
50. Omeprazole
51. Oxytetracycline
52. Paracetamol
53. Phenoxymethyl penicillin
54. Phenytoin
55. Piroxicam
56. Povidone Iodine
57. Prednisolone
58. Ranitidine
59. Rofecoxib
60. Sodium Chloride Solution
61. Tetracycline
62. Tetanus Antitoxin (10,000 IU)
63. Tetanus Toxoid
64. Tinidazole
65. Tramadol
66. Tranexamic Acid
67. Triamicinolone
68. Vitamin B-Complex

LIST OF DENTAL PHARMACOLOGICAL AGENTS AND THERAPEUTICS

1. Antiplaque Agents- Chlorohexidine gluconate-
   a) 0.2% mouth ringe
   b) 0.2% mouth irrigator
   c) 1% gels
   d) 4% antiseptic in surgical scrub.

2. Anticaries Agents: Fluoride
   a) Community water fluoridation
   b) Fluoride supplements
      - Tablets
      - Drops
        dentifriges
      - Lozens
      - Table salt
      - Milk
      - Mixed with vitamins
   c) Topical fluoridation-
      - Mouth washes
      - gels
      - Dentrifriges

3. Mouth washes
   a) 0.2% chlorohexidine gluconate
   b) Sodium chloride and sodibicarbonate
   c) Milk of magnesia
   d) Potassium permenganate.
   e) 1% Povidone iodine solution
   f) Mixed solution of menthol, Thymol, eucalyptol etc.

4. Obtundents-
   a) Essential oils- Eugenol, clove oil
   b) Chlorobutanol- (Dentanol)
   c) Zinc chlorite-
   d) Zinc nitrate- as desensitizing agents

5. Haemostatic agents:
   a) Local haemostatic agents-
      - Oxidized cellulose
      - Gel foam
      - Fibrin foam
      - Tannic acid
      - Salts of zinc
      - Salts of iron, potassium
      - Tranexamic acid
      - Bone wax
      - Salts of nitrate
      - Calcium alginate
   b) Systemic haemostatic agents-
      - Fresh frozen plasma
      - Anti haemophilic globulin
      - Vitamin-K

- Amino caproic acid
- Adrenaline
- Nor-adrenaline

6. Local Anaesthetics:
   a) Natural- Cocaine
   b) Synthetic- Nitrogenous- Lidocaine
      Non-nitrogenous- ethylalcohol
   c) Short acting- procain, pyrrocaine
   d) Medium acting- Lidocain, prilocaine
   e) Long acting- Tetracaine, Mepivacaine
   f) Surface anaesthetic- Lignocaine, Lidocaine
   g) Infiltration Anaesthetic- Lignocaine 5%, 10%, 15% etc.
   h) Block anaesthetic- 2%, Lignocaine, 2% mepivacaine

7. Mummifying agents
   a) Formal dehyde
   b) Para formal dehyde
   c) Iodoform
   d) Phenol
   e) Para-chlonophenol
   f) Cresol
   g) Cresote
   h) Formocresol
   i) Resorsinol
   j) Camphorated Mono-chloro-phenol (CMCP)
   k) Pulp devitalizing agents (costinerve forte)

8. Root canal medicaments
   a) 5% sodium hypochlorite
   b) Eugenol, Cresol
   c) 15% EDTA (Etheline di-amine Tetra acetic acid)
   d) 0.9% Nacl
   e) Phenol, parachlorophenol
   f) 30% urea solution
   g) 6% Hydrogen peroxide
   h) 50% citric acid
   i) 0.25% Metronidazole solution
   j) 0.25% Tinidazole solution
   k) Calcium hydroxide solution
   l) MTA (Mineral trioxide aggregate)/MTD
   m) 3 Drug mix (Ciprofloxacin + metronidazole + Minocycline + Polyethylene glycol)
   n) Gutta percha, chloropercha points
   o) Silver points, titanium points
   p) Resorbable paste- iodoform, KRI-1 paste
   q) BMP (Bone Morphogenetic Protein)
   r) Frizzed dries hydroxypeptide crystals

9. Agents affecting salivary secretion

   a) Sialogogue (↑ Salivary secretion)
      - Prilocarpine
      - Volatile oils
      - Alcohol
      - Nicotine
      - Carbacol

   b) Anti-sialogogue (↓ Salivary secretion)
      - Astringents
      - Hyocine
      - Beladona
      - Atropine
      - Opium
      - Morphine
      - Hexamithonium

10. Acidulated Caffeine phosphoprotein (ACPP) - Anti caries agents

    - Mixed with baby food Products

DRUGS USED FOR PERIODONTITIS AND PERICORONITIS

1. Doxycycline
2. Tetracycline
3. Metronidazole
4. Tinidazole
5. Cephalaxin
6. Cephradine
7. Amoxycillin
8. Phenoxymethyl penicillin
9. Erythromycin
10. Ibuprofen
11. Diclofenac Sodium
12. Ketoprofen
13. Povidone Iodine
14. Aspirin
15. Zinc-oxide engenol
16. Resorcinol

ANTIMICROBIALS USED FOR PERIODONTITIS AND PERICORONITIS

DOXYCYCLINE

This drug has a broad range of anti-microbial activity like tetracycline and administered orally and better absorbed in the gut. They are bacteriostatic.
Indications: Chronic periodontitis with deep periodontal pockets,
Lyme disease of the T.M joint; *see also section 1.1.6*
Cautions: This drug should not be used with antacids and iron preparations as they reduce absorption.

Contraindications: Children below 12 years, pregnant and lactating mothers.
Interactions: S*ee Appendix-2*
Side-effects: Gastrointestinal disturbances, staining of developing teeth.
Dose: By oral route, in adult, 100 to 200 mg once daily

TETRACYCLINE

It is the drug having broadest spectrum of activity of all microbial drugs. It is bacteriostatic.
Indications: Chronic periodontitis with deep periodontal pockets; topical applications in mouth rinse for the treatment of apthous ulcer*; see also section 1.1.6*
Cautions & Contraindications: *Same as for doxycycline*.
Side-effects: Gastrointestinal disturbances like nausea, vomiting, diarrhoea, super infection, renal and metabolic complications, staining of developing teeth.
Dose: Orally, 250-500 mg capsules 6 hourly for 5-7 days.

METRONIDAZOLE & TINIDAZOLE: *See section 1.1.9*

CEPHALEXIN and CEPHRADINE

The pharmacology of the cephalosporins in terms of absorption, action and excretion is similar to that of penicillin. They are acid stable and can be given orally. They are bactericidal drugs.
Indications: Mixed infections of oral cavity due to alveolar abscess, fascial cellulitis, septicemia, maxillofacial injury with soft tissue trauma*; see section 1.1.2.1*
Cautions: Should not be used in case of penicillin sensitivity, as the drug will produce 10% hypersensitivity reactions in penicillin sensitive patients.
Contraindications: In case of known hypersensitivity to penicillin.
Side-effects: *See section 1.1.2.1*
Dose: Adult dose, by oral route, 250-500 mg capsules 8 hourly for 5-7 days.

ERYTHROMYCIN

Erythromycin has a generally similar spectrum of action to penicillin and can be used as an alternative in patients allergic to penicillin. It is bacteriostatic.
Indications: As an alternative to patients allergic to penicillin; *see also section 1.1.5*
Cautions, Contraindications & Side-effects: *See section 1.1.5*
Dose: Adult dose, by oral route, 250 mg 6 hourly for 5-7 days.

IBUPROFEN: *See section 9.1.1*

This drug is a propionic acid derivative of NSAIDs, usually the drug of choice and are likely to be the most effective in most dental pain. It is well absorbed after an oral dose and is inactivated by metabolism.
Indications: Most painful condition of teeth, gingiva, oral mucosa and alveolar bone, inflammatory condition of pulp and periodontium like pulpits, gingivitis, periodontitis, alveolitis, abscess etc., injury due to maxillofacial trauma.
Cautions: Should be used under coverage of gastric irritation with antacids or H_2 receptor blockers (e.g. Ranitidine).
Contraindications: Known peptic ulcer patients.
Side-effects: Epigastric discomfort, activation of peptic ulcer, bleeding, headache, dizziness, rashes etc.
Dose: Adult dose is 400-600 mg 3 times daily.

ANALGESICS USED FOR PERIODONTITIS AND PERICORONITIS

KETOPROFEN

This drug is similar in action to Ibuprofen and mostly used in painful conditions like rheumatoid disease, musculoskeletal disorders, toothache, and TMJ disorders.
Indications: *Like Ibuprofen*.
Caution, Contraindications & Side-effects: *Like Ibuprofen.*
Dose: Orally, 50-100 mg 3 times daily.
NOTE : Ibuprofen, Ketoprofen, Fenoprofen and Naproxen have almost same anti-inflammatory action but are to be used in different doses.

DICLOEENAC: *See 9.1.1*

Among the NSAIDs, this drug is one of the potent anti inflammatory and analgesic drug that is widely used in acute painful situation in dentistry.
Indications: Acute pulpitis, acute periopical periodontitis, acute painful conditions in the oral cavity including tooth ache .
Caution: *Like other NSAIDs.*
Contraindications: In case of known peptic ulcer diseases.
Side-effects: *Like other NSAIDs.*
Dose: Adult 25-100 mg 3 times daily.

DRUG USED FOR DENTAL CARIES

FLUORIDES have a caries-prevention action. They are as yet the only effective drugs for the purpose. The optimum effect is achieved when drinking water containing about 1 part per million (PPM) of fluoride ingested through out the period of dental development.
Indications: For prevention of dental caries, to prevent bacterial metabolism in dental plaque, for remineralization of tooth substance.
Cautions: Should be used cautiously by measuring the level of fluoride in community water.
Contraindications: Known hypersensitivity, tetany.
Side-effects: Dental fluorosis mottled enamel, skeletal fluorosis, osteoclerosis, acute fluoride poisoning.
Route of administration: Ingestion by oral route

(a) In drinking water, other fluids or foods.
(b) Fluoride tablets.

Local application :

(a) Tooth pastes containing fluoride.
(b) Fluoride Mouth rinse.
(c) Topical application.

Dose: If flouride-content less than 0.3 ppm in water :
Up to 6 months – None.
6 months to 2 years - 0.5 mg NaF/day.
2-4 years - 1.1 mg NaF/day.
Over 4 years - 2.2 mg NaF/day.
If flouride-content is 0.3 to 0.7 ppm in water :
Up to 2 years – None.
2-4 years - 0.5 mg NaF/day.

DRUGS USED FOR GINGIVITIS

1. Ampicillin; *see section 1.1.1.2.1*
2. Amoxicillin; *see section 1.1.1.2.1*
3. Tinidazole; *see section 1.1.9*
4. Metronidazole; *see section 1.1.9*
5. Acetamenophen (Paracetamol); *see section 7.5.2.1 & 9.1.1*
6. Chlorhexidine;

AMPICILLIN: *See section 1.1.1.2.1*

It is a broad-spectrum bactericidal drug that inhibit the cell wall synthesis of susceptible bacteria. It is acid stable and is moderately well absorbed when swallowed. It is highly effective in the infections caused by Gram-positive and Gram-negative organisms.
Indications: Orofacial infections like abscess, periodontal infections, osteomyelitis etc.; *see also section 1.1.1.2.1*
Cautions: Not to be given to those subjects hypersensitive to penicillin; *see also section 1.1.1.2.1*
Contraindications: In case of known penicillin hypersensitivity.
Side-effects: Diarrhoea, skin rash, urticaria; *see also section 1.1.1.2.1*
Dose: The usual adult dose by all routes is 250-500 mg 6 hourly for 5-7 days.

CHLORHEXIDINE has proven to be a useful effective and safe antiseptic with many applications. Aqueous chlorhexidine of 0.1% or 0.2% inhibit dental bacterial plaque formation. It is commercially available as a gel (1%) and as a 0.2% mouthwash.
Indications: Acute ulcerative gingivitis, chronic gingivitis and periodontitis, for the prevention of bacterial plaque, any infection of the oral tissues that is related to bacterial dental plaque, for prevention of oral sepsis.
Cautions: Before a course of chlorhexidine is started, all dental plaque and calculus should be removed to allow the drug a fair start.
Contraindications: It is not used in case of deep periodontal pocket, as it does not penetrate into subgingival pockets or stagnation area.
Side-effects: Prolonged use of chlorhexidine mouth washes produce tooth staining both natural and artificial teeth, restoration of composite, hypersensitivity reaction to some individuals, unpleasant taste in the month due to disturbance of taste buds.
Dose: Only topical application as gel or mouth rinse, external use as surgical scrub 0.2% chlorhexidine 2 spoon full mixed with water used 3 times daily for 5-7 days. 1% gel applied on gingival area for 5 mints twice daily in case denture stomatitis 4% chlorhexidine used as a surgical scrub.

ACETAMINOPHEN (PARACETAMOL): *see also section 7.5.2.1 & 9.1.1*

This is a popular domestic analgesic and antipyretic for adults and children. It inhibits prostaglandin synthesis in the brain but hardly in the periphery. It is the analgesic recommended for children under 12 years old.
Indications: As analgesic for headache, toothache, arthralgia, amyalgia; as antipyretic in fever; *see also section 9.1.1*
Cautions: It should not be used in liver disease and kidney diseases. *See also section 9.1.1*
Contraindications: Severe liver diseases and kidney diseases.

Side-effects: Nausea, vomiting, anorexia, abdominal pain; hepatic necrosis, liver cell damage, renal tubular necrosis, hypoglycemic coma, pancytopenia, skin rash, urticaria; *see also section 9.1.1*
Dose: For adult, 500 mg 4 hourly*; see also section 9.1.1*

AMOXYCILLIN: *See also section 1.1.1.2.1*
This is semi-synthetic penicillin with a broad spectrum of antibacterial activity similar to that of ampicillin. It is better absorbed following oral administration and absorption is not influenced by food.
Indications*: See also section 1.1.1.2.1* Skin and soft tissue infections as mentioned in Ampicillin, infections caused by Gram-positive and Gram-negative cocci. For prophylaxis of bacterial endocarditis.
Cautions: *Like ampicillin.*
Contraindications: *Like ampicillin.*
Side-effects: *Like ampicillin*.
Dose: Normal adult dose, 250-500 mg 8 hourly for 5-7 days.

METRONIDAZOLE: *See also section 1.1.9 & 1.3.2*
It is active against a wide range of anaerobic bacteria and protozoa. It binds with DNA and prevents nucleic acid formation. It is bacteriostatic. It is well absorbed after oral and rectal administration.
Indications: Acute ulcerative gingivitis, dental infections like pericoronitis, osteomyelitis of the jaw, abscess; *see also section 1.1.9 & 1.3.2*
Cautions: Patients given metronidazole should be warned against taking alcohol during and for a week after completion of treatment; *see also section 1.1.9 & 1.3.2*
Contraindications: In case of known hypersensitivity to the drug, in case of chronic alcoholic patients; *see also section 1.1.9 & 1.3.2*
Side-effects: Metallic taste due to excretion of drug in saliva, nausea, vomiting, diarrhoea, headache, furred tongue, angioedema, peripheral neuropathy, flushing, sweating, palpitation due to interaction with alcohol.
Dose: In adult, ulcerative gingivitis, 200 mg 8 hourly for 3 days.

TINIDAZOLE: *see also section 1.1.9 & 1.3.2*
It is similar to metronidazole but has a longer half-life (13 hour). It is excreted mainly through urine unchanged. Due to its longer action it is considered better than metronidazole in giardiasis, trichomoniasis and acute ulcerative gingivitis.
Indications: Any inflammatory conditions and pain in orofacial structures such as gingivitis, periodontitis, pulpitis, oral ulceration etc. like metronidazole.
Cautions : *Like metronidazole.*
Contraindications : *Like metronidazole.*

POVIDONE IODINE

This drug is widely used in dentistry as an antiseptic mouthwash prior to different orodental procedures such as extraction of tooth, scaling, minor surgical procedures to prevent post-operative infections. 1% povidone iodine is used as mouthwash to prevent bacteremia and bacterial endocarditis.

DRUG USED FOR PERICORONITIS

1. Ampicillin; *see section 1.1.1.2.1*
2. Amoxycillin; *see section 1.1.1.2.1*
3. Cephalexin; *see section 1.1.2.1*
4. Cephradin; *see section 1.1.2.1*

5. Metronidazole; *see section 1.1.9 & 1.3.2 and notes above*
6. Tetracycline (Topical use); *see section 1.1.6 & notes above*
7. Diclofenac and other $NSAID_S$; *see section 9.1.1 & notes above*
8. Povidone Iodine or Chlorhexidine mouthwash; *see notes above*

DRUGS USED FOR PULPITIS

1. Penicillin & its derivatives ; *see section 1.1.1.1.2.1*
2. Cephalexin; *see section 1.1.2.1*
3. Cephradine; *see section 1.1.2.1*
4. Anti-inflammatory drugs such as Diclofenac, Ibuprofen; *see section 9.1.1 & notes above*
5. Diazepam; *see section 7.1*
6. Eugenol (clove oil) as local sedative dressing into the pulp.
7. Pulp devitalizing agents
8. Intracanal medicanals
9. Root canal scolars

DRUGS USED FOR ALVEOLAR OSTITIS (DRY SOCKET)

1. Antibiotics such as Amoxycillin, Cephalexin, Cephradin; *see section 1.1.1.2 & 1.1.2.1*
2. $NSAID_S$; *see section 9.1.1*
3. Zinc oxide engal dressing

DRUGS USED FOR OSTEOMYELITIS OF THE JAW

1. Benzyl Penicillin; *see section 1.1.1.1.1*
2. Long-term Tetracycline; *see section 1.1.6*
3. Metronidazole; *see section 1.1.9 & 1.3.2*
4. Anti-inflammatory drugs; *see section 9.1.1*
5. Cloxacillin; *see section 1.1.1.1.1*
6. Co-trimoxazole; *see section 1.1.8*

DRUGS USED FOR CERVICOFACIAL CELLULITIS

1. Penicillin & its derivatives; *see section 1.1.1.1 & 1.1.1.2*
2. Cephradine & Cephalexin; *see section 1.1.2.1*
3. Metronidazole; *see section 1.1.9 & 1.3.2 and notes above*
4. Ciprofloxacin; *see section 1.1.7*
5. Azithromycin ;*see section 1.1.5*
6. Erythromycin; *see section 1.1.5*
7. Analgesics and anti-inflammatory drugs; *see section 7.5.2.1, 7.5.2.2 & 9.1.1*
8. Ceftriaxone; *see section 1.1.2.3*

DRUGS USED FOR ACTINOMYCOSIS

1. Long term antibiotics such as
   (a) Penicillin; *see section 1.1.1.1*
   (b) Tetracycline; *see section 1.1 .6 & notes above*
   (c) Erythromycin; *see section 1.1.5*

2. Analgesics and anti-inflammatory drugs*; see section 9.1.1*

DRUGS USED FOR CANCRUM ORIS

1. A combination of penicillins; *see section 1.1.1.1*
2. Metronidazole ; *see section 1.1.9 & 1.3.2 and notes above*
3. Analgesics; *see section 7.5.2.1, 7.5.2.2 & 9.1.1*
4. Povidone Iodine mouthwash; *see notes above;*
5. Multivitamins

DRUGS USED FOR CAVERNOUS SINUS THROMBOSIS

1. Anticoagulants drugs; *see section 3.8*
2. Antibiotics such as penicillin; *see section 1.1.1.1*
3. Analgesics such as aspirin; *see section 7.5.2.1*

DRUGS USED FOR PREVENTION OF BACTERIAL ENDOCARDITIS

1. Ampicillin; *see section 1.1.1.2.1*
2. Amoxycillin; *see section 1.1.1.2.1*
3. Cephalexin; *see section 1.1.2.1*
4. Cephradin; *see section 1.1.2.1*
5. Azithromycin; *see section 1.1.5*
6. Clindamycin; *see section 1.1.12*
7. Cefazoloin; *see section 1.1.2*
8. Povidone Iodine mouthwash reduce 50% chance of bacteremia; *see notes above*

DRUGS USED FOR RICKET

1. Vitamin D; *see section 16.2.3.4*

DRUGS USED FOR SCURVY

1. Vitamin C*; see section 16.2.3.3*

DRUGS USED FOR T.M. JOINT DISORDERS

1. Analgesics such as Mefenamic acids; *see section 9.1.1*
2. Anti-inflammatory drugs; *see section 7.5.2.1, 7.5.2.2 & 9.1.1*
3. Muscle relaxants such as diazepam; *see section 7.1*

DRUGS USED FOR PRIMARY HERPETIC STOMATITIS

1. Antiviral drugs such as acyclovir; *see section 1.4.1*
2. Antibiotics to prevent secondary infection; *see section 1.1*
3. Analgesics; *see section 7.5.2.1, 7.5.2.2 & 9.1.1*
4. Chlorhexidine mouthwash; *see notes above;*

DRUGS USED FOR ORAL CANDIDIASIS

1. Nystatin HCl tablet or suspension; *see section 1.2.3*
2. Amphotericin lozenges
3. Chlorhexidine mouth wash; *see notes above;*

DRUGS USED FOR APHTOHUS ULCER

1. Topical salicylate preparations (e.g. lotio pyral vex)
2. Vitamin $B_{12;}$ *see section 16.2.3.1*
3. Folic Acid & Iron preparations; *see section 15.1.1.2*
4. Tetracycline mouthwash ; *see section 11.3.2*
5. Hydrocortisone lozenges.
6. Analgesics and Anti-inflammatory drugs; *see section 7.5.2.1, 7.5.2.2 & 9.1.1*

DRUGS USED FOR ORAL ULCERATIONS

1. Antibiotics; *see section 11.3.1 & 11.3.2*
2. Analgesics; *see section 9.1.1*
3. Povidone Iodine mouthwash; see *notes above;*
4. Topical steroids.
5. Triamicnalone Acetonide; *see section 5.3.2*
6. Vitamin $B\text{-}_{12}$; *see section 16.2.3.2*
7. Vitamin B_2; *see section 16.2.3.2*
8. Zinc Supplements; *see section 16.2.2.7*
9. Tetracycline mouthwash.

DRUGS USED FOR TRIGEMINAL NURALGIA

1. Carbamazepine; *see section 7.5.3*
2. Phenytoin; *see section 7.6.1*

DRUGS USED FOR BELL'S PALSY

1. Prednisolone tablet 20 mg 4 times a day is given for 5 days and the tailed off over the following 4 days; *see section 5.3.2*.

MEDICAL EMERGENCIES IN DENTAL PRACTICE

This section provides guidelines on the management of the more common medical emergencies which may arise in dental practice. Dental surgeons and their staffs should be familiar with standard resuscitation procedures, but in all circumstances it is advisable to summon medical assistance as soon as possible.

SYNCOPE

Insufficient blood supply to the brain results in loss of consciousness. The commonest cause in a vasovagal attack or simple faint (syncope) due to emotional stress.

Treatment

Lay the patient flat and raise the legs to improve cerebral circulation. loosen any tight clothing around the neck. Once consciousness is regained, give sugar in water or a cup of sweet tea.

The drugs referred to in this section are:
Adrenaline injection, adrenaline I in 1000, (adrenaline 1gm/ml as acid tartrate), 1-ml amps.

Chlorpheniramine Injection, chlorpheniramine maleate 10mg/ml. 1-ml amps.
Diazepam Injection, diazepam 5mg/ml. 2-ml amps
Glucagon Injection, glucagon (as hydrochloride), 1-unit and 10-unit vials (with solvent)
Glucose-50g for one drink
Glucose injection, glucose 50% (500gm/mL), 50-mL amps
Hydrocortisone Injection, hydrocortisone 100mg (preferable as sodium succinate vials with 2-mL solvent)
Oxygen
Salbutamol Injection, salbutamol (as sulphate) 500 micrograms/mL, 1-mL amps

ANAPHYLAXIS

A severe allergic reaction may follow oral or parenteral administration of a drug. Allergic reaction in dentistry most commonly follow injections of penicillin but other drug may be implicated, including local anaesthetics. In general, the more rapid the onset of the reaction the more profound it tends of the reaction the more profound it tends to be. Symptoms may develop within minutes and rapid treatment is essential.

Treatment

First-line treatment includes restoration of blood pressure, laying patient flat, raising feet, and administration of **adrenaline**[1] injection. This is usually given intramuscularly in a dose of 0.50-1mg (0.5-1mL adrenaline injection 1 in 1000), repeated every 10 minutes, according to blood pressure and pulse, until improvement occurs.
Antihistamines given by slow intravenous injection are a useful adjunctive treatment (e.g. chlorpheniramine 10 to 20 mg diluted in syringe with 5 to 10 mL of blood and given over 1 minute).

Intravenous corticosteroids are of secondary value in anaphylactic shock as their onset of action is delayed for several hours but they should be used to prevent further deterioration in several affected patients. Usually hydrocortisone (preferable as sodium succinate) is given by intravenous injection in a dose of 100 to 300 mg.

CARDIAC EMERGENCIES

ANGINA, If there is a history of angina the patient will probably carry glycery[1] trinitrate tables or spray (or isosorbide dinitrate tables) and should be allowed to use them.
MYOCARDIAL INFARCTION. The pain of myocardial infarction is similar to that of angina but generally more severe and more prolonged.

Treatment

Call for medical assistance or an ambulance immediately. Allow patient to rest in the position that feels most comfortable; in presence of breathlessness this is likely to be

sitting position, whereas syncopal patient will want to lie flat; often an intermediate position (dictated by patient) will be most appropriate.

Intramuscular injection of drugs does not provide useful relief of pain because absorption is too slow (particularly when cardiac output is reduced) but a mixture of nitrous oxide 50% and oxygen 50% can be effective if given continuously; it is safe in this situation.

Reassure patient as much as possible to relieve further anxiety. If patient collapses and loses consciousness attempt standard resuscitation measures. For an algorithm of the procedure for cardiopulmonary resuscitation, see section p. 3.

Hypoglycaemia

Diabetic patients occasionally administer their standard dose of insulin before dental treatment but omit the usual meal (although they should not). This can lead to the blood glucose falling to an abnormally low level (hypoglycaemia). Patients can often recognise the symptoms themselves and this state responds to sugar in water or a few lumps of sugar. Children may not have such prominent changes by may appear unduly lethargic.

Treatment

In early stages, 4-6 teaspoons of sugar in water. If patient unconscious, up to 50 mL of 50% glucose intravenous injection, or glucagon 1 mg (1 unit) injected by any route (subcutaneous, intramuscular, or intravenous) (useful when intravenous injection of glucose difficult or impossible to administer).

EPILEPTIC SEIZURE

Patients with epilepsy must continue with their normal dosage of anticonvulsant drugs when attending for dental treatment. It is not uncommon for epileptic patients not to volunteer the information but there should be little difficulty in recognizing a tonic-clonic (grand mal) seizure.
Symptoms and signs

Treatment

During a convulsion try to ensure that patient is not at risk from form injury but make on attempt to put anything in month or between teeth (in mistaken belief that this will protect tongue).

Do not attempt to restrain convulsive movements. After convulsive movements have subsided place patient in coma position and check airway.

After convulsion patient may be confused (postictal confusion) and may need reassurance and sympathy. Patient should not be sent home until fully recovered but it is not necessary to seek medical attention or transfer to hospital unless convulsion was atypical, prolonged (or repeated), or in injury occurred.

Medication should only be given if convulsive seizures are prolonged (convulsive movements lasing 15 minutes or longer) or repeated rapidly. intravenous administration of diazepam 10 to 20 mg is often effective but should be used with caution because of risk of respiratory depression.

Partial seizures similarly need very little active management (in an automatism only minimum amount of restraint should be applied to prevent injury). Again patient should be observed until post-ictal confusion has completely resolved.

CARDIOVASCULAR DISEASE

Arrhythmias

Patients, especially those who have suffered a myocardial infarction, may have unstable cardiac rhythm or a degree of heart failure. Current medication should be carefully checked. Premedication (e.g. with temazepam) may be useful in some instances for very anxious patients.
See below for reference to vasoconstrictors and unstable cardiac rhythm.

Hypertension

Patients with hypertension may be under treatment with antihypertensive drugs. Their blood pressure may fall to dangerously low levels when they are given general anaesthesia and should only be administered in hospital when appropriate precautions can be taken.
See also under Vasoconstrictors (below).

Thrombo-embolic disease

Patients receiving heparin or oral anticoagulants such as warfarin, nicoumalone, or phenindione may be liable to excessive bleeding after extraction of teeth. Often dental surgery can be delayed until the anticoagulant therapy is discontinued.

Occasionally, an extraction during anticoagulant treatment may be unavoidable. The patient's physician should be consulted and the anticoagulant level adjusted (with laboratory control) so that the prothrombin time is not more then twice the control figure. If possible, a single simple extraction should be done first. If this goes well further teeth may be extracted, two or three at a time. Some dental surgeons suture the gum lightly over the socket to hold in place a haemostatic ash as oxidized cellulose.

Aspirin is contra-indicated in patients on anticoagulant therapy, and in those with any disorder of haemostasis.

Vasoconstrictors in local anaesthetic solutions

Lignocaine 2 per cent with adrenaline 1 in 80000 is probably the most used local anaesthetic agent. For the vast majority of patients, experience over many years indicates that it is a safe and effective preparation.
There is on indication for the use of noradrenaline as a vasoconstrictor for local anaesthetics since it presents on advantages. Administration of local anaesthetics containing noradrenaline 1 in 25000 has been followed by a small number of severe hypertensive episodes. These few episodes emphasise the possible danger of using local anaesthetics containing noradrenaline, especially in high concentrations.
In patients with sever hypertension or unstable cardiac rhythm, the use of adrenaline in a local anaesthetic may be hazardous if inadvertently give intravenously. For these patients prilocaine with or without felypressin can be used but there is no clinical evidence that it is any safer.

There is no clinical evidence of dangerous interactions between adrenaline containing local anaesthetics and monoamine-oxidase inhibitors (MAOLs) or tricyclic anti-depressants.

INFECTIVE ENDOCARDITIS

Patients with cardiac defects (congenital, rheumatic, etc) or who have had a prosthetic replacement of a damaged valve are at risk from infective endocarditis following dental procedures. The risk is not related to the severity of the heart defect, as the onset of endocarditis in occasionally the first overt manifestation of a defects.
Those who have had one or more episodes of infective endocarditis in the past appear to be particularly susceptible.

There is no evidence that patients with prosthetic heart valves are nay more susceptible to infective endocarditis after dental operations than those with damaged natural valves, but if it develops treatment may be more difficult.
Although almost any dental procedure is capable of causing bacteraemia, infective endocarditis is a rare and unpredictable complication even in susceptible patients. It is virtually impossible therefore to assess the relative effectiveness of different prophylactic regimens; nevertheless there is now some consensus among cardiologists and microbiologists.

Although there are theoretical advantages in giving antibiotics by injection (to ensure rapid absorption and high plasma concentrations), this present difficulties in general dental practice. It is agreed therefore that wherever possible it is more practical to give antibiotics by mouth for prophylaxis in dental out-patients.

IDENTIFICATION OF PATIENTS AT RISK. All patients must be questioned about a history of rheumatic fever or heart defects and especially whether they have previously had infective endocarditis. The value of such a history is limited in that the patient may be unaware of a vulnerable heart lesion, but this is the best that can be done. Heart murmurs in children are often of no significance but whenever there is any doubt a cardiologist should be consulted.

The peak incidence of infective endocarditis is now in the sixth and seventh decades, so that the elderly are at greater risk than young persons.

PROCEDURES THAT NEED COVER. The main source of bacteria causing dentally related infective endocarditis is the bacteria of the gingival margins and periodontal pockets. Infective endocarditis can follow virtually any dental procedure but there appears to be a significant risk only after dental extractions, scaling, periodontal surgery, or the raising of mucogingival flaps for any other purpose.

REDUCTION OF ORAL SEPSIS. A history of a dental procedure preceding an attack of infective endocarditis is obtained in only a minority of patients but oral bacteria enter the blood stream on may other occasions. The frequency and severity of bacteraemia is also related to the severity of bacteraemia is also related to the severity of the gingival sepsis. Maintenance of the highest possible standards of oral hygiene in patients at risk reduces:

need for dental extractions or other surgery;
chances of severe bacteraemia if dental surgery has to be carried out;
chance or frequency of ‘spontaneous’ bacteraemia.

Application of an antiseptic such as 0.2% chlorhexidine gluconate solution to the gingival margins before dental treatment reduces the severity of any resulting bacteraemia and may be used to supplement antibiotic prophylaxis in those at risk.

POSTOPERATIVE CARE. It is imperative to warn every patients at risk to report to the doctor or dentist if any minor illness develops after dental treatment, whether or nor antibiotics have been given, as infective endocarditis has an insidious onset and many failures of treatment develops it is likely to be within a month of dental treatment.

RECOMMENDATIONS

Under local or no anaesthesia (taken in presence of dentist or dental nurse):
Patients not allergic to penicillin and who have not received a penicillin more than once in the pervious month including those with a prosthetic heart valve (but not those who have had endocarditis)

ADULT single dose of amoxycillin[1] 3 g by mouth 1 hour before procedure
CHILD under 5 years, quarter adult dose; 5-10 years, half adult dose
Patients allergic to penicillin or who have received a penicillin more than once in the previous month ADULT erythromycin (as sterate) 1.5 g by mouth[2] 1-2 hours before procedure, then 500 mg 6 hours later
CHILD under 5 years, quarter adult dose; 5-10 years, half adult dose
or
ADULT single dose of clindamycin 600 mg by mouth 1 hour before procedure
CHILD under 10 years, 6 mg/kg as single dose by mouth 1 hour before procedure
Under general anaesthesia:
Patients not allergic to penicillin and who have not received a penicillin more than once in the previous month
ADULT amoxycillin 1 g by intramuscular injection[3] (in 2.5 mL lignocaine hydrochloride 1% injection) jest before induction then 500 mg by mouth 6 hours later
CHILD under 10 years, half adult dose[4]
or
ADULT amoxycillin 3 g by month 4 hours before procedure then a further 3 g as soon as possible after procedure
CHILD under 5 years, quarter adult dose; 5-10 years half adult dose
or
ADULT amoxycillin 3 g by mouth and probenecid 1 g by mouth 4 hours before procedure

Special risk patients who should be referred to hospital:
Patients who are to have a general anaesthetic and who are allergic to penicillin or have had a penicillin more than once in the previous month
Patients who have had a pervious attack of endocarditis
For recommendations for these patients see BNF section 5.1, table 2

1. Amoxycillin is liable to cause irritating rashes, especially in people with infectious mononucleosis (glandular fever) in whom it should be avoided.
2. Erythromycin (stearate) 1.5g may cause nausea.
3. If the interamuscular route is considered necessary it may be preferable for the procedure to be carried out in hospital.
4. Whenever possible painful intramuscular injections should be avoided in children.

Oral Side-effects of Drugs

Drug-induced disorders of the month may be due to a local action on the mouth or to a systemic effect manifested by oral changes.

Oral mucosa
Medicaments applied directly to the oral mucosa can lead to inflammation and ulceration.

Elderly patients may have difficulty swallowing tablets; if left in the mouth, ulceration may develop. They should always take their tablets or capsules with fluid, and in some cases it may be wise to prescribe capsules if available.

Aspirin tablets allowed to dissolve in the sulcus for the treatment of toothache can lead to a white patch followed by painful ulceration. **Choline salicylate** gels are also irritant and are particularly troublesome if placed under dentures.

Potassium chloride ustained-release tablets are irritant to the mucosa.

Crystal violet, another irritant, is no longer used on mucous membranes.

Flavouring agents, particularly **essential oils**, may cause contact oils, may cause contact hypersensitivity prominent.

The oral mucosa is particularly vulnerable to ulceration in patients treated with cytotoxic drugs, especially **methotrexate**.

An occasional complication of long-term **phenytoin** treatment is macrocytic anaemia, leading to oral manifestations such as sore tongue or severe aphthous stomatitis.

Systemic administration of some NSAIDs, e.g. indomethacin, may cause ulceration of the mucosa; this is not a topical effect but the precise mechanism is not clear. Other drugs capable of causing severe oral ulceration include **methyldopa, allopurinol, gold** (anuranofin and aurothiomalate), and **penicillamine. Captopril** can cause stomatosis.

Erythema multiforme may follow the use of certain drugs, especially **suphonamides**, **co-trimoxazole**, **antiepileptics**, **penicillin**, and **chlorpropamide**. The oral mucosa may be extensively ulcerated, with characteristic target lesions on the skin. Oral lesions of toxic epidermal necrolysis have been reported for a similar range of drugs.

Lichenoid eruptions can be clinically indistinguishable from lichen planus. Drugs associated with the appearance of white striae and plaques, atrophic changes and ulceration include **NSAIDs**, **methyldopa**, **chloroquine**, **oral antidiabetics**, **diuretics**, **phenothiazines**, and **gold** (auranofin and aurothiomalate).

Thrush and other types of candidiasis complicate treatment with **antibiotics** and **immunosuppressants**. Oropharyngeal thrush is an occasional side-effect of **corticosteroid** inhalers.

Teeth
Brown staining of the teeth frequently follows the use of chlorhexidine mouthwash or gel; this can readily be removed by polishing at the end of the course of treatment. Ferric salts in liquid form can stain the enamel black.

Intrinsic staining of the teeth is most commonly due to tetracyclines. The will affect the teeth if given at any time from about the fourth month in utero until the age of twelve years. All tetracyclines cause this; the colour varies from yellow to grey.

Excessive ingestion of fluoride leads to dental fluorosis with mottling of the enamel and areas of hypoplasia or pitting; fluoride tablets or drops may cause mild mottling (white patches) if the dose is too large for the child's age or for the fluoride content of the local drinking water.

Periodontium

Gingivitis and ulceration are common in patients receiving cytotoxics or mmunosuppressants.

Hyperplasia of the gingivae is a side-effect of phenytoin and sometimes of cyclosporin or nifedipine. The degree of hyperplasia varies but can reach the extent that the crowns of the teeth are virtually covered.

Thrombocytopenia may be drug related, and cause bleeding of the gingival margins, which may follow mild trauma, such as toothbrushing, or eventually be spontaneous.

Salivary glands
The main effect of drugs on the salivary glands is a reduction in flow (xerostomia). Patients with a persistently dry mouth may develop a burning or scalded sensation, and have poor oral hygiene, increased dental caries, periodontal disease, intolerance of dentures, and oral infections (particularly candidiasis).

Many drugs have been implicated in xerostomia, particularly antimuscarinics (anticholinergics) and tricyclic antidepressants. Excessive use of diuretics can also result in xerostomia.

Increased production of saliva is not a problem unless the patients has difficulty in swallowing.

Pain in the salivary glands has been reported following the use of some antihypertensives (e.g. bethanidine, clonidine, methyldopa) and the vinca alkaloids.

Seelling of the salivary glands may be idiopathic but it has been described rarely in association with iodides, antithyroid drugs, phenothiazines, and sulphonamides.

Taste

Taste acuity may be decreased or there can be an alteration in taste sensation. Drugs implicated include penicillamine, griseofulvin, captopril and enalapril, lincomycin, carbimazole, clofibrate, phenindione, lithium salts, gold (auranofin and aurothiomalate), and metronidazole.

Antiseptics and Cleansers (See Appendix-15 & also section 12)

Superficial infections of the mouth are often helped by warm mouthwashes; they have a mechanical cleansing effect and cause some local hyperaemia. However, they must be used both frequently and vigorously to have nay effect, and some can lead to irritation of the oral mucosa.

A warm saline mouthwash is ideal and can be prepared either by dissolving half a teaspoonful of salt in a tumblerful of warm water or by diluting sodium chloride compound mouthwash with an equal volume of warm water.

Mouthwashes containing an oxidising agent such as hydrogen peroxide, may be useful in the treatment of acute ulcerative gingivitis (Vincent's infection) as the organisms responsible are anaerobes. Hydrogen peroxide also has a mechanical cleansing action since it froths on contact with oral debris. Sodium perborate has a similar effect, but should not generally be used for periods longer than 7 days because of possible absorption of borate.

Chlorhexidine is an effective antiseptic which has the advantage of inhibiting plaque formation on the teeth. It does not, however, completely control plaque deposition and is not a substitute for effective toothbrushing. Moreover it does not penetrate significantly into stagnation areas and is therefore of little value in the control of dental caries or of periodontal disease once pocketing has developed.

Chlorhexidine can be used as a mouthwash for secondary infection in mucosal ulceration. The mouthwash or the gel may be used for controlling gingivitis, as an adjunct to other oral hygiene measures. The mouthwash or the gel may also be used as an alternative to toothbrushing where there is a painful periodontal condition (e.g. primary herpetic stomatitis) or if the patients has a haemorrhagic disorder, or is handicapped.

Povidone-iodine is another effective antiseptic. The mouthwash is a useful preparation in dealing plaque accumulation. Caution must be exercised in prolonged use as a significant amount of iodine is absorbed.

Neither chlorhexidine nor povidone-iodine mouthwashes have any beneficial effect in the control of acute ulcerative gingivitis.

Thymol is a weak antiseptic of negligible value for treating oral infections. Mouthwash solutiontablets are sued to rinse out the mouth to remove unpleasant tastes. Compound thymol glycerin may be used as a mechanical rinse instead of a saline mouthwash.

Zine sulphate mouthwash is a traditional astringent mouthwash and has little antibacterial activity. Some also find it useful for palliating recurrent aphthae.

CHLORHEXIDINE GLOUCONATE

Indications : oral hygiene (including endocarditis prophylaxis, p.5); plaque inhibition
side-effects : idiosyncratic mucosal irritation; reversible brown staining of teeth

Chlorhexidine Dental Gel, chlorhexidine gluconate 1%,
Brush on teeth once or twice daily
Chlorhexidine Mouthwash, chlorhexidine gluconate 0.2%. Aniseed- or mint-flavoured available; net price 300 mL = £ 1.25
Rinse mouth with 10 mL for about 1 minute twice daily.

OXIDISING AGENTS
Indications : oral hygiene

Hydrogen Peroxide Mouthwash, consists of hydrogen peroxide solution (6% = aprox, 20-volume) BP
Rinse mouth for 2-3 minutes with 15 mL in half a tumblerful of warm water 2-3 times daily

sodium Perborate Mouthwash, sodium perborate 70% (buffered).
Use 1 sachet in 30 mL of water 3 times daily; not recommended in renal impairment or for children under 5 years

POVIDONE-IODINE

Indications : oral hygiene
Cautions : pregnancy; breast-feeding
Side-effects : idiosyncratic mucosal irritation and hypersensitivity reactions

Povidone-iodine Mouthwash, povidoneiodine 1%.
Use undiluted or diluted with equal volume of warm water every 2-4 hours if necessary

SODIUM CHLORIDE

Indication : oral hygiene

Sodium Chloride Mouthwash, Compound, BP, sodium chloride 1.5%.
Use diluted with equal volume of warm water

THYMOL

Indications : oral hygiene

Compound Thymol Glycerin BP, glycerol 10%, thymol 0.05%, with colouring and flavouring
Use undiluted or diluted with 3 volumes of warm water

Mouthwash Solution-tablets, consist of tablets which may contain antimicrobial, colouring, and flavouring agents in a suitable soluble effervescent basis to make a mouthwash suitable for dental purposes.

Dissolve 1 tablet in a tumblerful of warm water

Note : Mouthwash solution-tablets may contain ingredients such as thymol.

CORTICOSTEROIDS AND OTHER DRUGS FOR ORAL ULCERATION AND INFLAMMATION

Ulceration of the oral mucosa be caused by trauma (physical or chemical), recurrent aphthae, infections, carcinoma, dermatological disorders, nutritional deficiencies, gastro-intestinal disease, haematopoietic disorders, and drug therapy. It is important to establish the diagnosis in each case as the majority of these lesions require specific management in addition to local treatment. Local treatment aims at protecting the ulcerated area, or at relieving pain or reducing inflammation.

SIMPLE MOUTHWASHES. A **saline** or **compound thymol glycerin** mouthwash may relieve the pain of traumatic ulceration. The mouthwash is made up with warm water and used at frequent intervals until the discomfort and swelling subsides.

ANTISEPTIC MOUTHWASHES. Secondary bacterial infection may be a feature of any mucosal ulceration; it can increase discomfort and delay healing. Use of a **chlorhexidine** or **povidone-iodine** mouthwash is often beneficial and may accelerate healing of recurrent aphthae.

MECHANICAL PROTECTION. **Carmellse gelatin paste** may relieve some discomfort arising from ulceration, by protecting the ulcer site. The paste adheres to the mucosa, but is difficult to apply effectively to some parts of the mouth.

ZINC SULPHATE, Zinc sulphate mouthwash is an astringent. Some patients find it beneficial in recurrent aphthae.

CORTICOSTEROIDS. Topical corticosteroid therapy may be used for different forms of oral ulceration. In the case of aphthous ulcers it is most effective if applied in the "prodromal phase".
Thrush or other types of candidiasis are recognised complications of corticosteroid treatment.

Hydrocortisone lozenges are allowed to dissolve next to an ulcer and are useful in recurrent aphthae, corsive lichen planus, discoid lupus crythematosus, and benign mucous membrane pemphigoid.

Triamcinolone dental paste is designed to keep the corticosteroid in contact with the mucosa for long enough to permit penetration of the lesion, but is difficult for patients to apply effectively to some parts of the mouth.

Hydrocortisone cream is used in treating uninfected inflammatory lesions on the lips and perioral skin. **Hydrocortisone and miconazole** cream or ointment is useful where infection by susceptible organism and inflammation co-exist, particularly for initial treatment (up to about 7 days). Organisms susceptible to miconazole include candida spp. and many Gram-positive bacteria including streptococcus and staphylococcus. Systemic corticosteriod therapy for severe conditions such as pemphigus vulgaris is best reserved for the physician because of potential side-effects.

LOCAL ANALGESICS. Local analgesics have a limited role in the management of oral ulceration. When applied topically their action is of a relatively short duration so that analgesia cannot be maintained continuously throughout the day. The main indication for a topical analgesic is to relieve the pain of otherwise intractable oral ulceration particularly when it is due to major aphthae. For this purpose **lignocaine 5% ointment** is applied to the ulcer. Care must be taken not to produce anaesthesia of the pharynx before meals as this might lead to choking.

Benzydamine mouthwash may be useful in palliating the discomfort associated with a variety of ulcerative conditions. It reduces the discomfort of post-irradiation mucositis. If the full-strength preparation causes some stinging it can be diluted with an equal volume of water. The spray may also be useful.

Choline salicylate dental gel has some analgesic action and may provide relief for recurrent aphthae, but excessive application or confinement under a denture irritates the mucosa and can itself cause ulceration. Benefit in teething may merely be due to

pressure of application (comparable with biting a teething ring); excessive use can lead to salicylate poisoning.

DRY MOUTH. This condition may be caused by irradiation of the head and neck region, damage to or disease of the salivary glands, or by the administration of drugs with antimuscarinic (anticholinergic) side-effects, for example antispasmodics, tricyclic antidepressants, and some antipsychotic drugs. It may be relieved in many patients by simple measures such as frequent sips of cool drinks, sucking pieces of ice or sugar-free fruit pastilles, or by the use of an different hospitals and are commercially available. They are usually viscous, slightly flavoured, aqueous liquids.

BENZYDAMINE HYDROCHLORIDE

Indications : painful inflammatory conditions of orpharynx
Side-effects : occasional numbness or stinging
Benzydamine Mouthwash, benzydamine hydrochloride 0.15%. Rinse or gargle, using 15 mL, diluted if necessary, every $1\frac{1}{2}$-3 hours as required, usually for not more than 7 days; not suitable for children under 12 years
Benzydamine Oral Spray, benzydamine hydrochloride 0.15%.
4-8 puffs onto affected area every $1\frac{1}{2}$-3 hours; CHILD 6-12 years 4 puffs every $1\frac{1}{2}$-3 hours

CARMELLOSE SODIUM

Indications : mechanical protection of oral and perioral lesions
Carmellose Gelatin Paste, geltain, pectin, carmellose sodium, 16.58% of each in a suitable basis.
Apply a thin layer when necessary after meals

CORTICOSTEROIDS

Indications : mechanical protection of oral and perioral lesions
Contra-indications : untreated oral infection

Hydrocortisone Lozenges BP, hydrocortisone 2.5 mg (as sodium succinate).
Dissolve 1 lozenge slowly in the mouth in close contact with the lesion initially 4 times daily; if ulcers recur rapidly treatment may be continued for a period at reduced dosage

Hydrocortisone Cream BP, hydrocortisone 1%[1].
Apply sparingly 2-4 times daily
1. The BP does not specify one particular strength but when hydrocortisone cream is prescribed by a dental practitioner on form FP14 (GP14 in Scotland) a cream containing 1% will be dispensed.
Triamcinolone Dental Paste BP, traincinolone acctonide 0.1% in an adhesive basis.
Apply a thin layer 2-4 times daily
With antifungal

Hydrocortisone and Miconazole Cream, hydrocortisone 1% and miconazole nitrate 2%,

Hydrocortisone and Miconazole Ointment, hydrocortisone 1% and miconazole nitrate 2%,

For angular cheilitis apply sparingly 2-3 times daily; do not use for longer use for longer than 7 days

LIGNOCAINE HYDROCHLORIDE

Indications : relief of pain in oral lesions
Cautions : avoid prolonged use; hypersensitivity may occur
Lignocaine 5% Ointment, lignocaine 5% in a suitable basis. Rub gently into affected areas. Max. dose for 70 kg man 200 mg lignocaine (= $\frac{1}{4}$ tube)

SALICYLATES

Indications : mild oral and perioral lesions
Cautions : frequent application, especially in children, may give rise to salicylate poisoning
Note. The recent CSM warning on aspirin and Reye's syndrome does not apply to non-aspirin salicylates or to topical preparations such as teething gels.

Choline Salicylate Dental Gel BP, choline salicylate 8.7% in a flavoured gel basis.
Apply ever 3-4 hours with gentle massage before food and at bedtime

ARTIFICIAL SALIVA

Indications : dry mouth

Artificial Saliva, consists of a suitable inert, slightly viscous, aqueous liquid; it may contain a suitable antimicrobial preservative, normal salivary constituents, small amounts of fluoride, and colouring and flavouring agents.

ZINC SULPHATE

Indications : see notes above

Zinc Sulphate Mouthwash, consists of zinc sulphate lotion BP
Dilute 1 part with 4 parts of warm water

VITAMINS

vitamin deficiency due to inadequate dietary intake is rare in Bangladesh but can develop in elderly people or alcoholics. Most other patients with develop a nutritional deficiency have malabsorption and if this is suspected the patient should be referred to a physician.

It is unjustifiable to treat stomatitis or glossitis with mixtures of vitamin preparations; this delays diagnosis and correct treatment.

Severe cases of scurvy cause gingival swelling and bleeding margins as well as petechiae on the skin. This is, however, exceedingly rare and a patient with this

appearance is more likely to have leukaemia. Investigation should not be delayed by a trial period of vitamin treatment.

ASCORBIC ACID (Vitamin C)

Indications : prevention and treatment of scurvy
Dose : prophylactic, 25-75 mg daily; therapeutic, not less than 250 mg daily in divided doses
Ascorbic Acid Tablets BP, ascorbic acid 25 mg; 50 mg, 20 = 6; 50 mg, 200 mg, 500 mg.
Vitamin B Tablets, Compound, strong, brown, f/c or s/c, nicotinamide 20 mg, pyrodoxine hydrochloride 2 mg, riboflavine 2 mg, thiamine hydrochloride 5 mg.
Dose : treatment of vitamin D deficiency, 1-2 tablets 3 times daily

FLUORIDES

Availability of adequate fluoride confers significant resistance to dental caries. It is now considered that the topical action fluoride on enamel and plaque is more important than the systemic effect.

Where the natural fluoride content of the drinking water is significantly less than 1 mg per litre (one part per million) artificial fluoridation is the most economical method of supplementing fluoride intake.

Daily administration of tablets or drops is a suitable alternative, but systemic fluoride supplements should not be prescribed without prior reference to the fluoride contents of the local water supply; they are not advisable when the water contains more than 700 micrograms per liter (0.7 parts per million). In addition, it is now recommended that infants need not receive fluoride supplements until age of 6 months.
Use of dentifrices which incorporate sodium fluoride and/or monofluorophosphate is also a convenient source of fluoride.

Individuals who are either particularly caries prone or medically compromised may be given additional protection by use of fluoride rinses or by application of fluoride gets. Rinses may be used daily or weekly; daily use of a less concentrated rinse is more effective than weekly use of a more concentrated one. Gets must be applied on a regular basis under professional supervision; extreme caution is necessary to prevent the child form swallowing any excess. Less concentrated gets have recently become available for home use. Varnishes are also available and children since they adhere to the teeth and set in the presence of moisture.

SODIUM FLUORIDE

Note. Sodium fluoride 2.2 mg provides approx. 1 mg fluoride ion
Indications : prophylaxis of dental caries-see notes above
Contra-indications : not for areas where drinking water is fluoridated
Side-effects : occasional white flecks on teeth with recommended doses; rarely yellowish-brown discoloration if recommended doses are exceeded
Dose : Child, as fluoride ion :
Water content less than 300 micrograms/litre, up to 6 months none; 6 months-2 years, 250 micrograms daily; 2-4 years, 500 micrograms daily; over 4 years, 1 mg daily
Water contend between 300 and 700 micrograms/litre, up to 2 years, none; 2-4 years, 250 micrograms daily; over 4 years, 500 micrograms daily

Fluoride preparations are listed below; they are not prescribable on form FP14 (GP14 in Scotland).
There are arrangements for health authorities to supply fluoride tablets in the course of preschool dental schemes, and they may also be supplied in school dental schemes, and they may also be supplied in school dental schemes.

Tablets
COUNSELLING. Tablets should be sucked or dissolved in the mouth and taken preferably in the evening.
En-De-Kay® (Sfafford-Miller)
Fluotabs 0-2 years, sodium fluoride 550 micrograms (250 micrograms F^-).
Fluotabs 2-4 years, natural orange-flavoured, scored, sodium fluoride 1.1 mg (500 micrograms F^-).
Fluor-a-days® (Dental Health)
Tablets, fuff, scored, sodium fluoride 2.2 mg (1 mg F^-).
Fluorigard® (RMT)
Tablets 0.5, purple, sodium fluoride 1.1 mg (500 micrograms F^-).
Tablets 1.0, sodium fluoride 2.2 mg (i mg F^-).
Oral-B Fluoride® (Oral-B Labs)
Tablets, sodium fluoride 1.1 mg (500 micrograms F^-).
Zymafluor® (Zyma)
Tablets, sodium fluoride 550 micrograms (250 micrograms F^-).
Tablets, yellow-grey, sodium fluoride 2.2 mg (1 mg F^-).

Oral drops
Note. Fluoride supplements no longer considered necessary below 6 months of age.

En-De-Kay® (Sfafford-Miller)
Fluodrops® (=paediatric drops), sugar-free, sodium fluoride 500 micrograms (250 micrograms F^-)/0.15 mL.

Fluorigard® (RMT)
Paediatric drops, sodium fluoride 275 micrograms (125 micrograms F^-)/drop.

Oral-B Fluoride® (Oral-B Labs)
Drops, sodium fluoride 0.15% (250 micrograms F^-/8 drops).

Mouthwashes
Rinse mouth for 1 minute and spit out COUNSELLING. Avoid eating, drinking, or rinsing mouth for 15 minutes after use

En-De-Day® (Stafford-Miller)
Fluorinse (= mouthwash), red, sodium fluoride 2%.
For daily use, dilute 5 drops to 10 mL of water; for weekly use, dilute 20 drops to 10 mL

Fluorigard ® (RMT)
Daily dental rinse (= mouthwash), blue, sodium fluoride 0.5%.

Antihistamines (See Section 4)

There is no evidence that any one of the older antihistamines is superior to another in antihistamine activity but they differ in duration of action and incidence of the main side-effects, namely antimuscarinic (anticholinergic) effects and drowsiness.

Most antihistamines are relatively short acting but some, such as **promethazine hydrochloride**, are active for up to 12 hours. All are of potential value i nasal allergy, urticaria, and allergic rashes associates with drug allergy. The majority has the serious disadvantage of causing drowsiness (some of the newer antihistamines less so, see BNF section 3.4.1).

Antihistamines are widely used as antemetics; it has been suggested that these drugs may be useful in dental surgery for patients with an over-active vomiting reflex, but diazepam is likely to be more effective.

INDEX OF PHARMACEUTICAL MANUFACTURERS IN BANGLADESH

Generic Suppliers to the Hospitals only :

1.	M/s. EDCL (Bogra)	Thonthonia, Bogra.
2.	M/s. EDCL (Dhaka)	395-397, Tajgoan I/A, Dhaka.

For National Pharma Market :

Name of the Pharmaceutical Manufacturer		Address and Licence No.
1.	M/s. Ablation Pharmaceuticals Ltd.	331, Monipur, Mirpur, Dhaka
2.	M/s. ACI Ltd.	Majeeganj Road, Godnail, Narayangonj
3.	M/s. Acme Laboratories Ltd.	Dhamrai, Dhaka
4.	M/s. Acme Specialized Pharmaceuticals Ltd.	Dhamrai, Dhaka
5.	M/s. Acmunio International Ltd.	Hemayetpur, Savar, Dhaka
6.	M/s. Active Fine Chemicals Ltd.	West Moktarpur, Munshiganj
7.	M/s. Adco Pharmaceutical & Chemicals Ltd.	Bscic I/E, Shapura Rajshahi
8.	M/s. Ad-din Pharmaceuticals Ltd.	BSCIC I/A, Jessore.
9.	M/s. Advent Pharma Ltd.	Plot No. B 50-54, BSCIC I/A, Dhamrai, Dhaka
10.	M/s. Aexim Pharmaceutical Ltd.	BSCIC I/A, Mymensingh
11.	M/s. Agrani Pharmaceuticals.	138, Tejgoan I/A, Dhaka.
12.	M/s. Albert David (BD) Ltd.	115-116 Tejgaon I/A, Dhaka
13.	M/s. Albion Laboratories Ltd.	South Rahmatnagar, Shitakunda, Chittagong
14.	M/s. Alco Pharma Ltd.	House No. 3/B, Plot No. 33, Section-7, Mirpur, Dhaka
15.	M/s. Alkad Laboratories	Alamnagar, Rangpur
16.	M/s. Alliance Chemicals Ltd.	Dhamrai, Dhaka.
17.	M/s. Allied Pharmaceuticals Ltd.	Bogair, P.O. : Ashugonj, P.S.: Ashugonj, B.Baria
18.	M/s. Al-Modina Pharmaceuticals Ltd.	1/1. Tilargati, Tongi, Gazipur
19.	M/s. Alpha Pharmaceuticals Ltd.	Tratri, Savar, Dhaka
20.	M/s. Ambee Pharmaceuticals Ltd.	184/1 Tejgaon I/A, Dhaka
21.	M/s. Amico Laboratories Ltd.	Khagan, Burilia, Savar, Dhaka
22.	M/s. Amulet Pharmaceuticals Ltd.	Singdighi, Mauna, Sreepur, Gazipur
23.	M/s. APC Pharma Ltd.	Lokhpur, Fakirhat, Bagerhat
24.	M/s. Apex Pharmaceuticals Ltd	Shafipur, Kaliakair, Gazipur
25.	M/s. Apollo Pharmaceutical Laboratories Ltd.	Plot No. 10, Sec.7, Mirpur I/A, Dhaka
26.	M/s. Aristopharma Ltd.	Plot No. 21, Road 11, Shyampur, Kadamtali I/A, Dhaka
27.	M/s. Asiatic Laboratories Ltd.	253, Tongi I/A, Gazipur
28.	M/s. Astra Biopharmaceuticals Ltd.	Gouripur, Ashulia, Savar, Dhaka.
29.	M/s. Avert Pharma Ltd.	I-22, Bank Colony, Savar, Dhaka

30.	M/s. Aztec Pharmaceuticals	Ujirpur, Damurhuda, Chuadanga
31.	M/s. B. S. Industries Ltd.	189/4, Tejgoan I/A, Dhaka.
32.	M/s. Bangladesh Antibiotic Industries Ltd.	Mouchak, Kaliakoir, Gazipur
33.	M/s. Bangladesh Immunity Co.	Amghat Road, Tangail
34.	M/s. Bangladesh Industrial Gases	BSCIC I/A, Tarotia, Tangail
35.	M/s. Bangla-German Latex Co., Ltd.	Plot No. 178 & 179, DEPZ, Savar, Dhaka
36.	M/s. Batali Pharmaceuticals Ltd.	3 Brik Field Road, Chittagong
37.	M/s. Beacon Pharmaceuticals Ltd.	Khatali, Bhaluka, Mymensingh
38.	M/s. Belsen Pharma Ltd.	Kamlapur, Faridpur
39.	M/s. Bengal Drugs & Chemical Works Pharm. Ltd.	Kandirpar, Comilla.
40.	M/s. Bengal Remedies Ltd.	A-114, BSCIC I/A, Tongi, Gazipur
41.	M/s. Bengal Techno Pharma Ltd.	Gopalganj, Dinajpur.
42.	M/s. Benham Pharmaceutical Ltd.	Plot No. 1, Aicha Nwaddah, Raja Shon Road, Savar,
43.	M/s. Beximco Pharmaceuticals Ltd.	Tongi, Gazipur.
44.	M/s. Beximco Pharmaceuticals Ltd.	Kaliakoir, Gazipur
45.	M/s. Bikalpa Pharmaceuticals Ltd.	287, Monipur, Sec-2, Mirpur, Dhaka.
46.	M/s. Bio Pharma Ltd.	A-116, Tongi, Gazipur.
47.	M/s. Biochem Pharmaceutical Ltd.	Malibag, Dhaka
48.	M/s. Bios Pharmaceutical Ltd.	Gazipur
49.	M/s. Blubell Laboratories Ltd.	Bipail, Savar, Dhaka.
50.	M/s. Bridge Pharmaceuticals Ltd.	West Tengra, Demra, Dhaka
51.	M/s. Bristol Pharma Ltd.	Konabari, Gazipur
52.	M/s. Central Pharmaceutical Ltd.	2A/1, South West Darus Salam Rd,Mirpur, Sec-1, Dhaka.
53.	M/s. Chemist Laboratories Ltd.	College Road, Barisal
54.	M/s. Cipla Ltd.	Jahangirabad, Fultola, Bogra.
55.	M/s. City Chemicals & Pharmaceuticals Works Ltd.	112, Zurain, Dhaka.
56.	M/s. City Pharmaceutices	Nasirabad, Chittagong.
57.	M/s. Comilla Laboratories Ltd.	BSCIC Industrial State, Comilla
58.	M/s. Concord Pharmaceuticals Ltd.	C-18, BSCIC I/A, Sonargaon, Narayanganj.
59.	M/s. Cosmic Chemical Industries Ltd.	Rupnagar I/A, Mirpur Dhaka-1216
60.	M/s. Cosmo Pharma Laboratories Ltd.	BSCIC Industrial Estate, Konabari, Gazipur.
61.	M/s. Cresent Pharmaceuticals Ltd.	Karamtala, Pubail, Gazipur
62.	M/s. Crystal Pharmaceuticals Ltd.	BSCIC Industrial Estate, Comilla.
63.	M/s. Decent Pharma Ltd.	Vill.- Raghpur, P.O.-Rajapur, Dist. - Comilla.
64.	M/s. Delta Pharma Ltd.	Pakundia, Kishorganj
65.	M/s. Desh Pharmaceuticals Ltd.	Rupnagar, Mirpur, Dhaka
66.	M/s. Doctor TIMS Pharmaceuticals Ltd.	Konabari, Joydapur, Gazipur
67.	M/s. Doctor's Chemicals Works Ltd.	Fulbari, Bogra
68.	M/s. Dolphin Pharmaceuticals Ltd.	82/4, North Jattrabari, Dhaka
69.	M/s. Dr. Jalil's Pharma	Sanairpar Narayangonj
70.	M/s. Drug International Ltd. Unit-2	13A & 14/A, Tongi Industrial Area,

		Squib Road, Tongi, Gazipur
71.	M/s. Drug International Ltd.	Tongi I/A, Gazipur
72.	M/s. Drugland Ltd.	Hazi Abdul Samad Madrasha Road, Mijmije, Siddirgonj, Narayanganj
73.	M/s. Eastern Drug Co. (Pvt.) Ltd.	Dakkhin Shakdi, Sanir Akhra, Demra, Dhaka.
74.	M/s. Eastern Pharmaceuticals Ltd.	Dhamrai, Dhaka
75.	M/s. Edruc Ltd.	Sitlai House, Pabna.
76.	M/s. Eon Pharmaceuticals Ltd.	217/5, Chandana, Joydebpur, Gazipur
77.	M/s. Eskayef Bangladesh Ltd.	2/C, North East, Darus Salam, Mirpur, Dhaka.
78.	M/s. Eskayef Bangladesh Ltd.	400, Tongi/ I/A. Squibb Road, Gazipur.
79.	M/s. Ethical Drug Ltd.	Godnail, Siddergonj, Narayangonj.
80.	M/s. Eureka Pharmaceuticals Ltd.	83, Shaheed Siafuddin Khaled Road, Chittagong
81.	M/s. Euro Pharma Ltd.	385, West Jurain, Shampur, Dhaka
82.	M/s. Everest Pharmaceuticals Ltd.	Plot No. 45-46, BSCIC I/A, Kanchpur, Sonargaon, Narayanganj
83.	M/s. Fn F Pharmaceuticals Ltd.	Rautoli, Nagarbathan, Jhenaidah.
84.	M/s. F.R.C Laboratories Ltd.	22, Jugginager Lane, Dhaka
85.	M/s. G.P.I Ltd.	Rupatali, Sagardi, Barisal
86.	M/s. GA Company Ltd.	Tejgoan I/A Dhaka.
87.	M/s. General Pharmaceutical Ltd.	Kaliakair, Gazipur
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89.	M/s. Gentry Pharmaceuticals Ltd.	Vangnahati, Sreepur, Gazipur
90.	M/s. Glaxo Smith kline (Bd) Ltd.	Fauzderhat I/A, Chittagong
91.	M/s. Global Capsule Ltd.	Bogra Road, Rupatali, Barisal
92.	M/s. Global Capsule Ltd. (Gelatin Division)	Bogra Road, Rupatali, Barisal
93.	M/s. Global Heavy Chemicals Ltd.	Keranigonj, Dhaka.
94.	M/s. Globe Laboratories (Pvt.) Ltd.	Mirkadim, Munshigonj.
95.	M/s. Globe Pharmaceuticals Ltd.	Begumgonj. I/A, Noakhali.
96.	M/s. Globex Pharmaceuticals Ltd.	Kamalpur (Pagla), Fatullah, Narayangonj.
97.	M/s. Gonoshasthya Antibiotics Ltd.	Nayarhat, Savar, Dhaka
98.	M/s. Gonoshasthya Chemicals Ltd.	Tongi I/A, Gazipur
99.	M/s. Gonoshasthya Pharmaceuticals Ltd.	Nayarhat, Savar, Dhaka
100.	M/s. Goodmann Pharmaceuticals Ltd.	Bhagnahati, Sreepur, Gazipur
101.	M/s. Greenland Pharmaceuticals Ltd.	BSCIC I/A, Tongi, Gazipur.
102.	M/s. Guardian Healthcare Ltd.	Amtola, Kathgora, Zirabo, Ashulia, Savar, Dhaka
103.	M/s. Hallmark Pharmaceuticals Ltd.,	B-63, BSCIC I/E, Tongi, Gazipur
104.	M/s. Health Care Pharmaceuticals Ltd.	Rajendrapur, Gazipur.
105.	M/s. Hope Pharmaceutical Ltd.	Bhairab Bazar, Kishorgong.
106.	M/s. Hudson Pharmaceutical Ltd.	Mouchak, Kaliakoir, Gazipur.

107.	M/s. Huqsons Laboratories Ltd.	BSCIC I/E, Comilla.
108.	M/s. Hydroxide Ltd.	Mouchak, Kaliakoir, Gazipur
109.	M/s. Ibn Sina Pharmaceutical Ind. Ltd.	Kaliakoir, Gazipur
110.	M/s. Incepta Pharmaceuticals Ltd.	Jirabo, Saver, Dhaka
111.	M/s. Incepta Pharmaceuticals Ltd. (Dhamrai Unit)	Krishnapura, Sahabelishor, Dhamrai, Dhaka
112.	M/s. Incepta Vaccine Ltd.	Bara Rangamatia, Zirabo, Ashulia, Savar, Dhaka
113.	M/s. Indobangla Pharmaceutical Works Bangladesh	College Road, Barisal.
114.	M/s. Inova Pharmaceutical Ltd.	Plot No. I/8, & 9, Road No. 5, Section-7, Mirpur I/A, Pallabi, Dhaka
115.	M/s. Institute of Public Health	Mohakhali, Dhaka
116.	M/s. Institute of Public Health	46 Tejkunipara, Dhaka
117.	M/s. Islam Oxygen (Pvt) Ltd.	Tarabo, Rupganj, Narayanganj
118.	M/s. Islami Pharmaceuticals Ltd.	B-61, 62, 63, BSCIC I/E, Shiromoni, Khulna
119.	M/s. J & J Medical Bangladesh Ltd.	Plot No. 150, DEPZ, Ganakbari, Savar Dhaka
120.	M/s. J.C.I Bangladesh Ltd.	Proposed : Plot No. B-19, BSCIC I/A, Tongi, Gazipur
121.	M/s. Jalalabad Pharmaceuticals Ltd.	Kanchpur, Sonargaon, Narayangonj
122.	M/s. Jalpha Laboratories	Gotatikar, Sylhet.
123.	M/s. Jams Pharmaceuticals Ltd.	Section –7, Mirpur, Dhaka
124.	M/s. Janasheba Pharmaceuticals Ltd.	House No. 10, Road No 4, Block-A, Sec-10,Mirpur, Dhaka.
125.	M/s. Jayson Pharmaceuticals Ltd.	231,Tejgoan I/A, Dhaka.
126.	M/s. JMI Hospital Requisite Manufacturing Ltd.	Vitikandi, Gozaria, Munshiganj
127.	M/s. JMI Syringes & Medical Devices Ltd.	Rajandrapur, Chaowddhagiam, Comilla
128.	M/s. K.D.H Laboratories Ltd.	184, Shatmasjid Road, Zafrabad, Dhaka.
129.	M/s. Kafma Pharmaceuticals. Ltd.	Begumgonj, Noakhali.
130.	M/s. Kemiko Pharmaceuticals Ltd.	Ticapara, Ghoramara, Rajshahi.
131.	M/s. Khulna Essential Latex Plant	Gilatola, Fultala, Khulna
132.	M/s. Kumudini Pharma Ltd.	72, Sirajuddowla Road, Narayangonj
133.	M/s. Labaid Pharmaceuticals Ltd.	15, Genda, Savar, Dhaka
134.	M/s. Leon Pharmaceuticals Ltd.	Satkhamair, Sreepur, Gazipur
135.	M/s. Libra Pharmaceuticals Ltd.	1/7, Section-2, Mirpur, Dhaka.
136.	M/s. Linde Bangladesh Ltd.	185, Tejgoan I/A, Dhaka.
137.	M/s. Mafnaz Pharmaceuticals Ltd.	Block D-4 & 5, FIDC Road, BSIC I/A, Kalurghat, Chittagong
138.	M/s. Maks Drugs Ltd.	Konabari, Gazipur
139.	M/s. Mannaco Laboratories Ltd.	Darga Gate, Sylhet
140.	M/s. Marker Pharmaceuticals Ltd. (Shamsul Alamin)	Kalampur, Gazipur
141.	M/s. Marksman Pharmaceuticals Ltd.	Genda, Savar, Dhaka

142.	M/s. Maxborn Pharmaceuticals Ltd.	Moghbazar, Dhaka
143.	M/s. Medico Pharmaceuticals Ltd.	R.K. Road, Darshana, Rangpur
144.	M/s. Medicon Pharmaceuticals Ltd.	Plot No. 17/A/1, Avenue-1, Block-D, Section-10, Mirpur, Dhaka
145.	M/s. Medimet Pharmaceuticals Ltd.	Rupatali, Barisal
146.	M/s. MedRx Life Science Ltd.	Plot No. A-88 & A-89, BSCIC I/A, Nandanpur, B. Baria.
147.	M/s. Microbe Laboratories Ltd.	Shibati, Bogra
148.	M/s. Mig Pharmaceuticals Ltd.	Jel Garde Road, Bogra.
149.	M/s. Millat Pharmaceuticals Ltd.	65-66, Postogol I/A, Dhaka
150.	M/s. Modern Pharmaceuticals Ltd.	Jhenaidah
151.	M/s. Momtaz Pharmaceuticals Ltd.	Plot No. 551(P), Bara Deora, Tongi, Gazipur
152.	M/s. Monico Pharma Ltd.	South Dhanua, Sreepur, Gazipur
153.	M/s. Monomedi Bangladesh Ltd.	Nagbari, Post. : K. Nagbari, Ghatail, Tangail
154.	M/s. MST Pharma and Healthcare Ltd.	Bishua Kuribari, Gazipur Sadar, Gazipur
155.	M/s. Mundipharma Bangladesh (Pvt) Ltd.	Mirzapur, Sadar, Gazipur
156.	M/s. Mystic Pharmaceuticals Ltd.	16, Bhagdi Sylhet Road, Narsingdi.
157.	M/s. Naafco Pharma Ltd.	Bandai, Bhaluka, Mymensingh
158.	M/s. National Drug Company	Bangal Para, Dhamrai, Dhaka.
159.	M/s. National Laboratories Ltd.	North Azibpur, Siddirganj, Narayanganj
160.	M/s. Navana Health Care Ltd.	Rupshi, Rupgonj, Narayanganj
161.	M/s. Navana Pharmaceuticals Ltd.	Rupshi, Rupganj, Narayanganj.
162.	M/s. Newtec Pharmaceutials Ltd.	Boro Dhormopur, Comilla
163.	M/s. Nip Chemical and Pharmaceuticals Ltd.	Shahid Nagar, Daspara, Daudkandi, Comilla
164.	M/s. Nipa Pharmaceuticals Ltd.	1/5, Rupnagar, Mirpur, Dhaka.
165.	M/s. NIPRO JMI Company Ltd.	Vitikandi, Gozaria, Munshigonj
166.	M/s. NIPRO JMI Pharma Ltd.	Rajandrapur, Chauddagram, Comilla
167.	M/s. North Bengal Pharmaceuticals Ltd.	Chawk Muktar, Nawgaon.
168.	M/s. Novartis (Bangladesh) Ltd.	Squibb Road, Tongi, Gazipur.
169.	M/s. Novelta Bestway Pharmaceuticals Ltd.	Singair Road, Hemayetpur, Savar, Dhaka
170.	M/s. Novo Healthcare and Pharma Ltd.	Plot # 2, Road # 11, Block # C, Section # 6, Mirpur, Pallabi, Dhaka, 1
171.	M/s. Novo Healthcare and Pharma Ltd. (Unit-2)	East Norshingha Pur, Savar, Dhaka
172.	M/s. Novus Pharmaceuticals Ltd.	Tatul Jhara, Raj Fulbaria, Savar, Dhaka
173.	M/s. Nuvista Animal Health and Cropcare Ltd.	B/82, Bscic I/E, Tongi, Gazipur
174.	M/s. Nuvista Pharma Ltd.	97-98, Tongi I/A, Gazipur.
175.	M/s. Oasis Laboratories	Afzal Khan Road Sirajgonj.
176.	M/s. Opso Saline Ltd.	Bogra Road, Barisal

177.	M/s. Opsonin Chemical Industries Ltd. (Chemical Division)	Rupatali, Barisal.
178.	M/s. Opsonin Pharma Ltd.	Bogra Road, Barisal.
179.	M/s. Orbit Pharmaceuticals Ltd.	Shah Mirpur, P.S.:Karnaphufy, Chittagong
180.	M/s. Organic Health Care Ltd.	Gilar Chala, Sreepur, Gazipur
181.	M/s. Orion Infusion Ltd.	Maikali Rupgonj, Narayangonj
182.	M/s. Orion Pharma Ltd.	154, Tejgaon I/A Dhaka.
183.	M/s. Oyster Pharmaceuticals Ltd.	Borhan Uddin Road, Sylhet
184.	M/s. Pacific Pharmaceuticals Ltd.	BSCIC, Kanchpur, Narayangonj.
185.	M/s. Paradise Chemical Industries.	Hospital Road, Barisal.
186.	M/s. Peoples Pharma Ltd.	105-106,Tongi I/A, Gazipur
187.	M/s. Pharmacil Ltd.	B-34, BSCIC Industrial Area, Tangi, Gazipur.
188.	M/s. Pharmaco Internatioal Ltd.	Chandra, Gazipur.
189.	M/s. Pharmadesh Laboratories Ltd.	239, Tejgoan I/A, Dhaka.
190.	M/s. Pharmasia Ltd.	Gazariapara, Bhawal, Mirzapur, Gazipur
191.	M/s. Pharmatek Chemicals Ltd.	Aushpara, Beximco Complex, Tongi, Gazipur.
192.	M/s. Pharmik Laboratories Ltd.	4/5, Zakir Hossain Road, Khulshi, Chittagong.
193.	M/s. Phoenix Chemical Laboratory (BD) Ltd.	16/1, Vagdi, Narshingdi
194.	M/s. Pioneer Pharmaceuticals Ltd.	BSCIC I/E, Tongi, Gazipur.
195.	M/s. PIP Limited	Jubli Tank Road, Pabna.
196.	M/s. Popular Infusions Ltd.	164, Tongi I/A, Gazipu
197.	M/s. Popular Pharmaceuticals Ltd.	164, Tongi I/A, Gazipur
198.	M/s. Premier Pharmaceuticals Ltd.	Anantapur, Begumgonj, Noakhali
199.	M/s. Prime Pharmaceuticals Ltd.	Tapirbari, Shishu Polli Road, Sreepur, Gazipur
200.	M/s. Pure Drugs & Chemicals Ltd.	Fatehabad, Chittagong
201.	M/s. Quality Pharmaceuticals (Pvt.) Ltd.	9, Bhujango Bhusan Lane, Kushtia
202.	M/s. Radiant Pharmaceuticals Ltd.	Tongi I/A, Gazipur
203.	M/S. RAK Pharmaceuticals Ltd.	Faridpur, Sreepur, Gazipur
204.	M/s. Rampart Power (BD) Ltd.	Porabari, Gazipur.
205.	M/s. Rangs Pharmaceuticals Ltd.	226 Tejgoan I/A, Dhaka.
206.	M/s. Rasa Pharmaceuticals Ltd.	New Bogra Road, Sirajganj.
207.	M/s. Reckitt & Benckiser Bangladesh Ltd.	58-59, Nasirabad I/A, Chittagong.
208.	M/s. Reliable Drugs & Chemicals	Punchdona Bazar, Norsingdi.
209.	M/s. Reliance Laboratories Ltd.	C-98, Burshato Jahangir Sarani, Rajshahi
210.	M/s. Reliance Pharmaceuticals Ltd.	Elixir Town Area, Utttar Khan, Uttara, Dhaka
211.	M/s. Reman Drug Laboratories Ltd.	Plot No. 62-B, Block-C, Tongi, Gazipur.
212.	M/s. Remex Pharmaceuticals	Chawkpra, Mawna, Sreepur, Gazipur.
213.	M/s. Remo Chemicals Ltd.	235 Tejgaon I/A, Dhaka.
214.	M/s. Renata Ltd.	Sec-11, Mirpur, Dhaka.

215.	M/s. Renata Ltd., Gazipur	Rajendrapur, Gazipur
216.	M/s. Renata Oncology Limited	Noyapara, Dogri, Rajendrapur, Gazipur
217.	M/s. Rephco Pharmaceuticals Ltd.	Mathuranath Public School Road, Nutan Bazar, Barisal.
218.	M/s. Rid Pharma Ltd.	BSCIC Shilpa Nagory, Nondonpur, B.Baria
219.	M/s. RN Pharmaceuticals	Eidgah Compound, Kanchijuli, Mymensingh
220.	M/s. Roche Bangladesh Pharmaceuticals Ltd.	Rajendrapur, Gazipur.
221.	M/s. Royal Pharmaceuticals Ltd.	110, Chattashewary Road, Dampara, Chittagong
222.	M/s. S. N. Pharmaceuticals Ltd.	Plot No. B-35, BSCIC I/E, Kanchpur, Narayanganj
223.	M/s. Salton Pharmaceuticals Ltd.	Rajfulbaria, Savar, Dhaka
224.	M/s. Sanofi Aventis Ltd.	Tongi I/A, Gazipur.
225.	M/s. Sarma Chemical Works Ltd.	Kandirpar, Comilla
226.	M/s. Save Pharmaceuticals Ltd.	14, Cathalic Mission School Road, Mymensingh.
227.	M/s. Seema Pharmaceuticals Ltd.	Shahid Cort, Fulbari, Savar, Dhaka
228.	M/s. Seftchem Ltd.	Konabari, Gazipur
229.	M/s. Sharif Pharmaceuticals Ltd.	Barabo, Tarabo, Rupganj, Narayanganj
230.	M/s. Sheba Chemical Industries Ltd.	102, Sukrabad, Mirpur, Dhaka
231.	M/s. Sheba Laboratories Ltd.	Bhadra, Kazla, Rajshahi
232.	M/s. Silco Pharmaceuticals Ltd.	BSCIC I/E, Khadim Nagar, Sylhet
233.	M/s. Silva Pharmaceuticals Ltd.	Plot No 137, Joykrishnarampur, Maijdi Court, Noakhali
234.	M/s. Skylab Pharmaceuticals Ltd.	BSCIC I/A, Comilla
235.	M/s. Social Marketing Company	Zamiradia, Bhaluka, Mymensingh
236.	M/s. Sodical Chemical Ltd.	D-203, BSCIC I/A, Tongi, Gazipur
237.	M/s. Somatec Pharmaceutical Ltd.	Dailla, P.O. Sharulia Bazar, Demra, Dhaka
238.	M/s. Sonear Laboratories Ltd.	11/2, Toyenbi Circular Road, Dhaka
239.	M/s. Sony Pharmaceuticals	35, Gopibag 3rd Lane, Dhaka
240.	M/s. Spark Pharmaceuticals	Charpara, Mymensingh
241.	M/s. Spectra Oxygen Limited	64, Esail, P.O. : Uthaly, P.S. Shibalaya, Manikganj
242.	M/s. Square Cephalosporins Ltd.	Kaliakoir, Gazipur
243.	M/s. Square Formulations Ltd.	Momin Nagar, Gorai, Mirzapur, Tangail
244.	M/s. Square Pharmaceutical Ltd.	Salgaria, Pabna
245.	M/s. Square Pharmaceuticals Ltd.	Kaliakoir, Gazipur (Dhaka Unit)
246.	M/s. Square Pharmaceuticals Ltd., (Chemical Division)	Salgaria, Pabna
247.	M/s. Standard Laboratories Ltd.	85, Batali Hill, Flora Pass Road, Ambagan, Chittagong
248.	M/s. Stars Pharmaceuticals Ltd.	Plot No. A-20, BSCIC I/A, Barisal
249.	M/s. Sun Pharmaceutical (Bangladesh) Ltd.	Chandana, Joydevpur, Gazipur, Dhaka

250.	M/s. Sunypun Organics Ltd.	North Daulatdia, Goalando, Rajbari
251.	M/s. Sunypun Pharmaceuticals Ltd.	6 No. Anandapur, Ganda, Savar, Dhaka
252.	M/s. Super Power Pharmaceuticals Ltd.	Belabo, Narsingdi
253.	M/s. Supreme Pharmaceuticals Ltd.	Palashbari, Ashulia, Dhaka
254.	M/s. Techno Drugs Ltd.	Satipara, Narsingdi
255.	M/s. Techno Drugs Ltd., Unit-2	BSCIC I/A, Kararchar, Narshingdi
256.	M/s. Theraputics (BD) Ltd.	Kalurghat, BSCIC I/A, Chittagong
257.	M/s. Today Pharma Ltd.	Plot No. 28, Block-C, Rod-1, BSCIC I/E, Comilla
258.	M/s. Tropical Pharmaceuticals Ltd.	House No. 283, Road-1, Baitul Aman, Shyamoli, Dhaka.
259.	M/s. Ultra Pharma Ltd.,	Dulivita, Dhamrai, Dhaka
260.	M/s. Unimed & Unihealth Manufacturers Ltd.	BK Bari, Gazipur Sadar, Gazipur
261.	M/s. Union Pharmaceutical Ltd.	Karnapara I/A. Savar, Dhaka.
262.	M/s. Unique Pharmaceutical Ltd.	Barisur, Keraniganj, Dhaka.
263.	M/s. United Chemical & Pharmaceuticals Ltd.	33/E, FIDC Road, Kalur Ghat, Chittagong.
264.	M/s. United Chemist	Kha-213/4, D.I.T. Road, Middle, Gulshan, Dhaka
265.	M/s. United laboratories	Askarabad, Chittagong
266.	M/s. Universal Pharmaceutical Ltd.	Dilalpur, Pabna.
267.	M/s. Veritas Pharmaceuticals Ltd.	Vannara, Mouchak, Kaliakoir, Gazipur
268.	M/s. Virgo Pharmaceuticals Ltd.	Kaultia, Gazipura, Gazipur
269.	M/s. Weinberg Pharmaceuticals Ltd.	Chandra, Gazipur.
270.	M/s. Wellcome Chemical Industries Ltd.	Rupatali, Sagardi, Barisal.
271.	M/s. White Horse Pharma	Rajfulbaria, Savar, Dhaka
272.	M/s. Zaman Pharmaceuticals Co. Ltd.	122, Tejgaon I/A, Dhaka.
273.	M/s. Zenith Pharmaceuticals Ltd.	Trunk Road, Feni.
274.	M/s. Ziska Pharmaceuticals Ltd.	Karolsurichala, Shafipur, Kaliakoir, Gazipur

SOME OF THE ABBREVIATIONS & SYMBOLS USED IN THE FORMULARY

ASCO
American Society of Clinical Oncology

ACE
Angiotensin Converting Enzyme

ARI
Acute Respiratory Tract Infection

BBB
Blood Brain Barrier

BIRDEM
Bangladesh Institute for Research & Rehabilitation in Diabetes, Endocrine and Metabolic Disorders

BMC
Bangladesh Medical College

BSMMU
Bangladesh Sheikh Mujib Medical University

BPS
Bangladesh Pharmaceutical Society

(CD)
Controlled Drugs

CVS
Cardiovascular System

CNS
Central Nervous System

CSF
Cerebrospinal Fluid

CTC
Central Addiction Treatment Center

DGDA
Directorate General of Drugs Administration

DGHS
Director General of Health Services

DM
Diabetes Mellitus

DU
Dhaka University

DMC
Dhaka Medical College

DMARD
Disease Modifying Anti-Rheumatic Drugs

(ED)
Essential Drugs

ECG
Electrocardiogram

FAO
Food and Agricultural Organization

GIT
Gastrointestinal Tract

gm
Gram

HIV
Human Immuno-deficiency Virus

(I)
Imported Drugs

IEH
Islamia Eye Hospital

i.e.
that means

IM
Intramuscular

IV
Intravenous

Ig
Immunoglobulin
HDL
High Density Lipoprotein

JU
Jahangirnagar University

Kg
Kilogram

LDL
Low Density Lipoprotein

MMC
Mymensingh Medical College

NHF
National Heart Foundation

NICVD
National Institute of Cardiovascular Diseases

NITOR
National Institute of Trauma, Orthopaedics & Rehabilitation

NIPSOM
National Institute of Preventive & Social Medicine

NSAIDs
Non-Steroidal Inflammatory Drugs

O/W
Oil-in-Water

PGA
Pharmacy Graduates' Association

®
Registered Drug, Proprietary Name

RU
Rajshahi University

RTI
Respiratory Tract Infection

SC
Subcutaneous

SR
Sustained Release

SSMC
Sir Salimullah Medical College

STD
Sexually Transmitted Diseases

USTC
University of Science & Technology, Chittagong

UTI
Urinary Tract Infection

VD
Venereal Diseases

Viz.
For example

VLDL
Very Low Density Lipoprotein

WHO
World Health Organization

Wt.
Weight

W/V
Weight by Volume

W/W
Weight by Weight

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

W

X

Y

Z

Suspected Adverse Event Reporting Form

Identities of reporter, patient, institution, and product trade name(s) will remain confidential

স্বাস্থ্য ও পরিবার কল্যাণ মন্ত্রণালয়

ADR report number_____ (For office use only)
Date received_____

A. PATIENT AND HOSPITAL INFORMATION

Name of health facility (if applicable) _____

Patient name_____ **Registration #**_____

Patient address

_____

_____

Contact number_____

Age_____ **Weight (kg)**_____ **Height (cm)**_____ **Gender** ◯Male ◯Female

Pregnant ◯Yes ◯No ◯Unknown ◯Not applicable

B. SUSPECTED ADVERSE EVENT INFORMATION

Type of event	**Suspected product**
◯Adverse drug reaction	Brand name_____ Generic name_____
◯Product quality problem	Indication_____
◯Medication error	Start Date _____ End Date _____
	Dose [strength, unit]_____ Dosage Form_____
	Frequency _____
	Batch/Lot number_____ Manufacturer_____

Describe event including relevant tests and laboratory results:

Date the event started	**Date the event was reported**	**Date the event stopped**
_____	_____	_____

Was the adverse event treated? ◯Yes ◯No
If yes, please specify

Action taken after the reaction	**Did reaction subside after stopping/reducing the dose of the suspected product?**
◯Dose stopped ◯Dose reduced ◯No action taken	◯Yes ◯No ◯Not applicable **Did reaction appear after reintroducing the suspected product?** ◯Yes ◯No ◯Not applicable

Seriousness of the adverse event:	**Outcomes attributed to the adverse event:**
☐ Not serious ☐ Hospitalization or prolongation of hospitalization ☐ Disability or permanent damage ☐ Congenital anomaly/birth defect ☐ Life threatening ☐ Other serious ☐ Death	☐ Recovered ☐ Recovered/resolved with sequela ☐ Not recovered ☐ Unknown ☐ Fatal (date of death: _____)
Other relevant history (including pre-existing medical conditions, allergies, pregnancy, smoking, alcohol use, liver or kidney problems, hypersensitivity, history of ADRs, etc.):	

C. OTHER CONCOMITANT PRODUCT INFORMATION

	Product 1	Product 2	Product 3	Product 4
Brand name				
Generic name				
Indication				
Dosage form				
Route				
Dose				
Frequency				
Date started				
Date stopped				

D. REPORTER INFORMATION

Name_____ **Designation**_____

Address

_____

_____

Email address_____

Mobile phone_____ **Land phone**_____

Signature_____ **Date of submission**_____

General instructions for completing the form

- Detailed information about each field can be found in the instructions.
- Fill in as much information as possible. Do not leave anything blank. If unknown, write "unknown" or "n/a" if not applicable.

- What to report:
  - Serious adverse drug reactions
  - Unknown or unexpected ADRs
  - All suspected reactions to new drugs
  - Unexpected therapeutic effects
  - All suspected drug interactions
  - Product quality problems
  - Treatment failures
  - Medication errors

Send all completed forms to:

Directorate General of Drug Administration
105-106, Motijheel Commercial Area, Dhaka-1000, Bangladesh
Tel: 8802 9556126; Fax: 8802 9568166; Email: drugs@citech.net