
शुभ
लाभ
Lord Ganesha
PRIMEWALLPAPERS.COM

MCNEIL & ARGUS PHARMACEUTICALS LTD.

Organisational Profile.

The factory was awarded **WHO GMP Certificate** in **the year 1998**. The factory is carrying out manufacturing of Life Saving Drugs and Pharmaceuticals as per conditions laid down by W.H.O.

Recently as per Schedule 'M', the infrastructural requirements of Pharmaceutical Industries have increased many folds. **Mcneil & Argus Pharmaceuticals Limited** keeping into view the changing international scenario is one of the coveted manufacturing units to jump and erect the infrastructure as per laid down norms of WHO & Schedule 'M'.

The factory is situated in Ambala Cantt Town Area in an area which is more than 5 Acres of scenicaly landscaped land. The covered area is approximately 60,000 Sq. Feet.

The Factory Mcneil & Argus Pharmaceuticals Limited is divided into three different sections for manufacturing as per **Standards laid down in Schedule 'M'/ WHO GMP**.

Plant-I

It is constructed as per schedule M and WHO GMP requirements. The section is fully equipped for the manufacturing of Anti Retroviral Drugs such as **Didanosine, Lamivudine, Nevirapine, Stavudine, Zidovudine, Efavirenz, Indinavir, Nelfinavir & Cytotoxic drugs** in Tablet & Capsule forms. The Air in the Tablet & Capsule section is processed by separate Air Handling Unit's, so that even the air of Tablet & Capsule section cannot intermix with each other. The air is re-circulated through high performance separate Air Handling units equipped with on line humidity control system and Air Conditioned in thermostatically controlled atmosphere. This is as per best international standards. The purity and filtration of Air is maintained by latest Hepa Filters.

Plant – II

This section is fully equipped to manufacture Beta Lactum range of drugs ie Ampicillin and other penicillin derivatives. The Beta Lactum section is separate and independent. The Air Handling system is also equipped with Hepa Filters. This section is compeletely separate and isolated Air Handling Units with on line and thermostatically controlled Humidity and Atmospheric temperature are installed here. As per latest requirements of Schedule 'M' Beta Lactum section should be in a separate factory.

Plant – III

The air of this plant is also controlled through Air Handling system with filtration, on line humidity controlled Air Handling Units and with Air Conditioned Manufacturing & Storage areas. This section is equipped to manufacture Tablet, Capsules of Non Betalactum Group Liquids and Dry Syrup both Biologial and Non-biological.

I feel immense pride and honor to welcome you in the family of

MCNEIL & ARGUS PHARMACEUTICALS LIMITED

A trusted name for unwavering Devotion, Dedication, Achievements and Service to mankind in the hour of need or natural calamities. The company has crossed many milestones during its long sojourn of 30 years in manufacturing, marketing and quality assurance in the field of Pharmaceuticals. The Company is a leading and Trusted Supplier of Medicines to Central Government Health Scheme, Directorate General of Health Services, Ministry of Health & Family Welfare and many other Ministries & Autonomous Bodies of Government of India.

The company achieved glory of paramount importance when it was awarded license to manufacture and market Antiretroviral drugs for the treatment of HIV+ve & AIDS cases in the tear 2002 The company believes that it owes a great deal to the society. The comparative low cost treatment of its Antiretroviral drugs will cover more number of ailing people and will help them to get rid of this dreaded disease. The company has successfully executed the ART supply orders of various Government of India AIDS control Programs such as, Maharashtra AIDS Control Society. An extension of National AIDS control Organization (NACO). Registered with Ministry of Railways where we have successfully executed ART supply orders of Efavirenz 200mg and 600mg, Ritonavir Tablets 100mg, Lamivudine, Nevirapine and Indinavir etc. Leading HIV Specialists in India are using our ART molecules and have found them to be very effective in controlling HIV and AIDS cases.

The company has successfully exported Antiretroviral Drugs to Developed countries like Malaysia where Fast Forward status has been granted to its molecules for Registration of products. Also we are exporting our Antiretroviral Drugs, Anti T.B. Drugs to many countries including Myanmar, DPR Korea, Angola, Fiji, Mauritius etc. The registration and marketing of our ART is in progress in many other countries. The efficacy and Quality of its ART is assured because we are using API of ART exclusively from a USFDA approved company. In the years to come the company is all set to grow globally with your dedicated participation.

With profound Greetings & best wishes

BHAI G.D. CHHIBBER
Chairman

MCNEIL & ARGUS PHARMACEUTICALS LTD.

100 - Rampur Sarsehri Road , Ambala Cantt 133001
(A WHO GMP & ISO Certified Unit)
Ph. 91-171- 2699126, 2650396, 9416025364, 9315107399, 9354705345
E-Mail : info@mcneilargusindia.com, mcneilargusindia@sify.com
Visit us at: www.mcneilargusindia.com

List of Antiretroviral Drugs

D SINE Tablets
Didanosine 25,50,100, 200,250,400 mg

ARGAVIR Tablets
Ritonavir 100mg

ARGA L Tablets
Lopinavir 200mg
Ritonavir 50mg

ARGA LR Tablets
Lopinavir 133.3mg
Ritonavir 33.3mg

E.F. Capsules
Efavirenz 200,600 mg

INDA-400 Capsules
Indinavir 400 mg

LAMI-Tablets
Lamivudine 100,150,300 mg

LAMI-Plus Tablets
Lamivudine 150mg
Zidovudine 300mg
Nevirapine 200mg

NEV - 200 Tablets
Nevirapine 200 mg

NEV Suspension
Nevirapine 50mg/5ml

NEL - 250 Tablets
Nelfinavir 250mg

STV Capsules
Stavudine 30,40mg

STV PLUS Tablets
Stavudine 30,40 mg
Lamivudine 150 mg

STV COMP. Tablets
Stavudine 30,40 mg
Lamivudine 150mg
Nevirapine 200mg

ZVD Tablets
Zidovudine 100,300mg

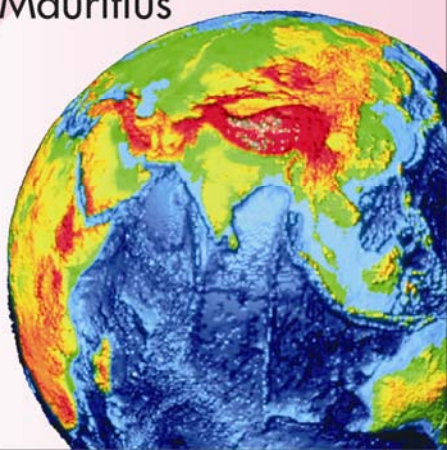
ZVD PLUS Tablets
Zidovudine 300mg
Lamivudine 150 mg

MCABAVIR Tablets
Abacavir 300mg

ARCYCLO Tablets
Aciclovir 400,800mg

WHO GMP Certified in 1998 & ISO 9001:2000 Certified Unit.

Registered Suppliers of Antiretroviral Drugs to Ministry of Railways, Maharashtra State Aids Control Society & Exporters of ART to Malaysia, Fiji Myanmar, Mauritius and many other parts of the world.



Mcneil & Argus Pharmceuticals Ltd

ANTIBIOTICS

CPF - 250 Tablets
Ciprofloxacin 250mg
CPF - 500 Tablets
Ciprofloxacin 500mg
CREX Tablets
Ciprofloxacin 500mg
CPF TZ Tablets
Ciprofloxacin 500mg
Tinidazole 600mg
SCIP 250 Tablets
Ciprofloxacin 250mg
SCIP 500 Tablets
Ciprofloxacin 500mg
SCIP TZ Tablets
Ciprofloxacin 500mg
Tinidazole 500mg
OFAX 200 Tablets
Ofloxacin 200mg
MCFLOX 400 Tablets
Ofloxacin 400mg
SUREFLOX Tablets
Ofloxacin 200mg
OFZ 200 Tablets
Ofloxacin 200mg
SUREFLOX OZ Tablets
Ofloxacin 200mg
Ornidazole 480mg
MCFLOX OZ Tablets
Ofloxacin 200mg
Ornidazole 500mg
MCFLOX Suspension
Ofloxacin 50mg/5ml
CEFMAC Capsules
Cefadroxil 500mg

ANTI ULCER

LANSOMAC 30 Capsules
Lansoprazole 30mg
LANSVIN Capsules
Lansoprazole 30mg
OMMAC 20 Capsules
Omeprazole 20mg
OMMAC Plus Capsules
Omeprazole 20mg
Domperidone 10mg
SZOLE D Capsules
Omeprazole 20mg
Domperidone 10mg
HYPA Capsules
Omeprazole 20mg
HYPA PLUS Capsules
Omeprazole 20mg
Domperidone 10mg

APPETITE STIMULANTS

BIO CYP Syrup
Cyproheptadine 2mg
Tricholine Citrate 55mg
M CYP Syrup
Cyproheptadine 2mg
Tricholine Citrate 275mg

PENICILLINS

D MOX 250 Capsules
Amoxycillin 250mg
D MOX 500 Capsules
Amoxycillin 500mg
D MOX BR Capsules
Amoxycillin 250mg
Bromhexine HCL 8mg
D MOX Dry Syrup
Amoxycillin 125mg/5ml
MERIMOX Dry Syrup
Amoxycillin 125mg/5ml
MOTIBETA Capsules
Amoxycillin 250mg
Cloxacillin 250mg
Lactic acid bacillus 60 mill.
MOTIMOX 250 Capsules
Amoxycillin 250mg
MOTIMOX 500 Capsules
Amoxycillin 500mg
MOXICILLIN Capsules
Amoxycillin 250mg
Cloxacillin Sodium 250mg
MACROLIDES
ROXIMAC 150 Tablets
Roxithromycin 150mg
MOTIROX 150 Tablets
Roxithromycin 150mg

CEPHALOSPORINS

PHELEX 250 Capsules
Cephalexin 250mg
PHELEX 500 Capsules
Cephalexin 500mg
MOTICEF 500 Capsules
Cephalexin 500mg
PROPHELEX Capsules
Cephalexin 250mg
Probencid 250mg
VERIN Capsules
Cephalexin 250mg
Lactic Acid Bacillus 60m Spor
PHELEX Dry Syrup
Cephalexin 125mg/5ml
C-LEX Dry Syrup/5ml
Cephalexin 125mg

ERECTILE DYSFUNCTION

MCGRA 25 Tablets
Sildenafil Citrate 25mg
MCGRA 50 Tablets
Sildenafil Citrate 50mg
MCGRA 100 Tablets
Sildenafil Citrate 100mg

CORTICOSTERIODS

CORT 5 Tablets
Prednisolone 5mg
CORT 10 Tablets
Prednisolone 10mg
ENCLOR 250 Capsules
Chloramphenicol 250mg
ENCLOR 500 Capsules
Chloramphenicol 500mg

ANALGESTICS & ANTIPYRETICS

ARNIM P Tablets
Nimesulide 100mg
Paracetamol 500mg
ARNIM P Suspension
Nimesulide 50mg
Paracetamol 125mg
ARNIM Suspension
Nimesulide 50mg
ACETOFEN PET Tablets
Diclofenac Sodium 50mg
Paracetamol 500mg
DOLEN PLUS Tablets
Nimesulide 100mg
Paracetamol 500mg
DOLEN PLUS Suspension
Nimesulide 50mg
Paracetamol 125mg

COUGH EXPECTORANTS

VECILEX Expectorant
Diphenhydramine HCL 14.08mg
Ammonium Chloride 80mg
Sodium Citrate IP 35mg
Menthol 1mg
CILEX Expectorant
Diphenhydramine HCL 14.08mg
Ammonium Chloride 80mg
Sodium Citrate IP 35mg
Menthol 1mg
KUFCARE Expectorant
Diphenhydramine HCL 14.08mg
Ammonium Chloride 80mg
Sodium Citrate IP 35mg
Menthol 1mg
VECILEX GT Expectorant
Bromhexine HCL 8mg
Phenylepherine HCL 5mg
Turbutaline Sulphate 2.5mg
Guaiphenesin 100mg
Menthol 1mg

ANTI ALLERGICS

CIZ-L Tablets
Levocetirizine Di HCL 5mg
LR-10 Tablets
Loratidine 10mg
DECOLD PLUS Tablets
Phenylepherine HCL 5mg
Paracetamol 400mg
Chlorpheniramine Maleate 2mg
Caffeine 15mg
DECOLD CP Syrup
Phenylpropanolamine HCL 12.5mg
Chlorpheniramine Maleate 2mg

ANTHELMINTICS

ALBAMAC Tablets
Albendazole 400mg
BANDA Tablets
Albendazole 400mg

Mcneil & Argus Pharmceuticals Ltd

ANTI DEPRESSANTS

BENZOLAM 0.25 Tablets
Alprazolam 0.25mg
BENZOLAM 0.5 Tablets
Alprazolam 0.5mg

ANTI DIARRHOEALS

FTZ Tablets
Ofloxacin 200mg
Tinidazole 600mg
NTZ 400 Tablets
Norfloxacin 400mg
Tinidazole 600mg
DIACURE-N Tablets
Norfloxacin 400mg
Tinidazole 600mg
NORMAC Tablets
Norfloxacin 400mg
FURAMAC Tablets
Furazolidone 100mg

ANTI SPASMODICS

P SPA Tablets
Dicyclomine HCL 20mg
Paracetamol 500mg
DOLEN-AS Tablets
Nimesulide 100mg
Dicyclomine HCL 10mg

ANTI EMETICS

VEGO Tablets
Prochlorperazine Maleate 5mg
Paracetamol 500mg

CALCIUMS

VECAL Suspension
Calcium Carbonate 250mg
Vitamin D 3 200IU
L Lysine Mono HCL 25mg
MILKAL Tablets
Alfacalcidol with Milk Calcium
MILKAL-G Tablets
Milk Calcium Tablets

FOOD SUPPLEMENTS

SPIRAMIN Z Capsules
Antioxidant & Spirulina 300mg
POWERMIN Capsules
Antioxidant & Spirulina 300mg
M REFRESH Capsules
Antioxidant & Spirulina 300mg

SULPHONAMIDES

COMEX P Tablets
Trimethoprim 80mg
Sulphamethoxazole 400mg
COMEX DS Tablets
Trimethoprim 160mg
Sulphamethoxazole 800mg
COMEX Suspension
Trimethoprim 40mg
Sulphamethoxazole 200mg

ANTIDIABETIC

MCFORMIN Tablets
Metformin HCL 500mg
MET G Tablets
Metformin HCL 500mg
Glipizide 5mg

ANTIHYPERTENSIVES

MACPRIL 25 Capsules
Captopril 25mg
ARPRIL - 5 Capsules
Ramipril 5mg
ARPRIL - 2 Capsules
Ramipril 2.5mg

HAEMATINICS

CALPHOS Capsules
Ferrous Fumarate 300mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
CALPHOS Syrup
Ferric Ammonium Citrate 350mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
Vitamin B 6 2mg
Niacinamide 25mg
CALCEFOL Capsules
Ferrous Fumarate 300mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
L Lysine Mono HCL 50mg
VINFER Syrup Ferric
Ammonium Citrate 350mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
Vitamin B 6 2mg
Niacinamide 45mg
VINFER Capsules
Ferrous Fumarate 300mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
L Lysine Mono HCL 50mg
MCMIN Capsules
Mecobalamin 1.5mg
FETONE Capsules
Ferrous Fumarate 300mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
L Lysine Mono HCL 50mg
FETONE Syrup
Ferric Ammonium Citrate 350mg
Folic Acid 1.5mg
Vitamin B 12 15mcg
Vitamin B 6 2mg
Niacinamide 25mg

ANTIFUNGALS

FEZ 150 Tablets
Fluconazole 150mg
VICON Tablets
Fluconazole 150mg

ANTI TUBERCULOSIS

P Z 750 Tablets
Pyrazinamide 750mg
P Z 500 Tablets
Pyrazinamide 500mg
Rifampicin 150mg Capsules
Rifampicin 150mg
R-300 Capsules
Rifampicin 300mg
R-450 Capsules
Rifampicin 450mg
R K D Tablets
Rifampicin 100mg
Isoniazid 100mg
R P Z Capsules
Rifampicin 150mg
Pyrazinamide 350mg
Isoniazid 100mg
KIN Tablets
Isoniazid 300mg
Thiacetazone 150mg
Ethambutol Tablets
Ethambutol 400mg
R F I Tablets
Rifampicin 150mg
Isoniazid 100mg
Pyridoxine HCL Tablets
Vitamin B 6 5mg
E B 400 Tablets
Ethambutol 400mg
I Z Forte Tablets
Isoniazid 100mg
R NEX S Capsules
Rifampicin 150mg
Isoniazid 100mg
R NEX D Capsules
Rifampicin 300mg
Isoniazid 200mg
P Z S Capsules
Rifampicin 150mg
Pyrazinamide 333mg
Isoniazid 100mg
P Z Comp Tablets
Rifampicin 150mg
Pyrazinamide 400mg
Isoniazid 100mg

TETRACYCLINES

DOXYCAP Capsules
Doxycycline 100mg
DOXTASE Capsules
Doxycycline 100mg
Serratiopeptidase 10mg

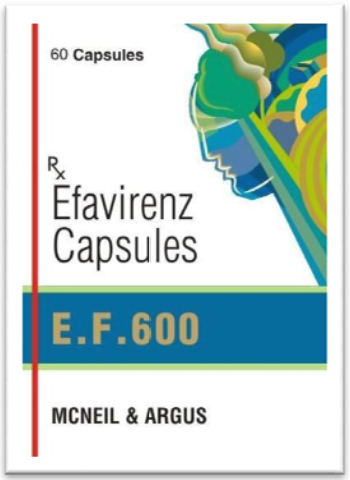

℞ Didanosine
Tablets BP
D-Sine-25


℞ Stavudine
Capsule I.P.
STV-30
MCNEIL & ARGUS


℞ Stavudine
Capsule I.P.
MCNEIL & ARGUS

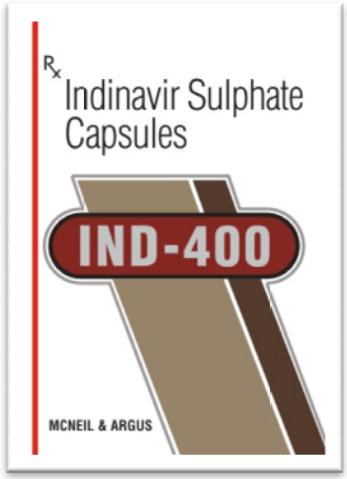

℞ Lopinavir and
Ritonavir Tablets I.P.
Arga-L
MCNEIL & ARGUS


Rx Didanosine Tablets BP
D-Sine-100
10 x 10 Tablets


60 Capsules
Rx Efavirenz Capsules
E.F.600
MCNEIL & ARGUS

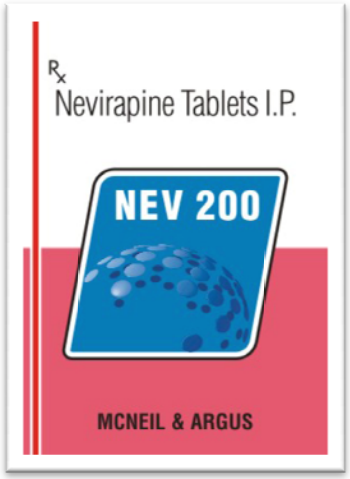

3 x 10 Capsules
Efavirenz Capsules I.P.
E.F.200
MCNEIL & ARGUS


℞ Abacavir Tablets IP
Mcabavir
MCNEIL & ARGUS


℞ Indinavir Sulphate Capsules
IND-400
MCNEIL & ARGUS


60 Tablets
℞ Lamivudine Tablets I.P.
LAMI-150
MCNEIL & ARGUS


60 Capsules
℞ Nelfinavir Mesylate Capsules
NEL 250
MCNEIL & ARGUS


℞
Nevirapine Tablets I.P.
NEV 200
MCNEIL & ARGUS

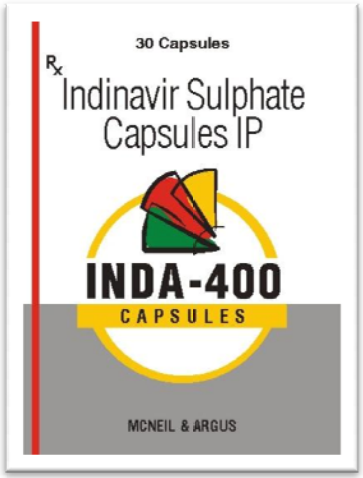

℞
Ritonavir
Tablets I.P.
Argavir
MCNEIL & ARGUS


℞
Aciclovir
Tablets IP
ARCYCLO-D
MCNEIL & ARGUS


℞
Lopinavir and
Ritonavir Tablets I.P.
Arga-LR
MCNEIL & ARGUS

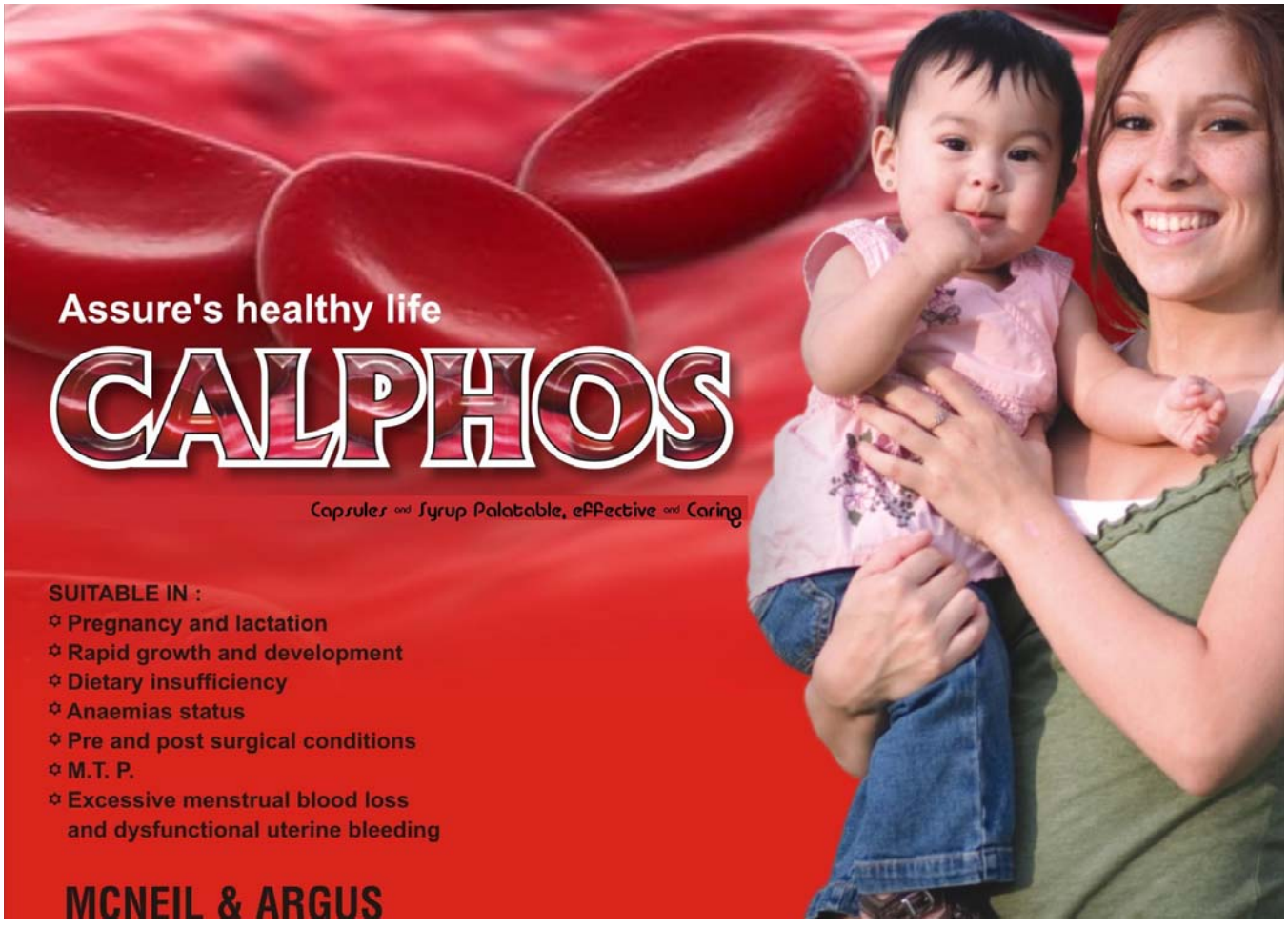

60 Tablets
℞
Lamivudine, Stavudine and Nevirapine Tablets
STV Comp 30
MCNEIL & ARGUS


℞
Aciclovir Tablets IP
ARCYCLO
MCNEIL & ARGUS


30 Capsules
℞
Indinavir Sulphate Capsules IP
INDA-400
CAPSULES
MCNEIL & ARGUS


℞
Zidovudine and Lamivudine Tablets I.P.
ZVD PLUS
MCNEIL & ARGUS


MCNEIL & ARGUS
Get rid of nausea Feel fresh with....
VEGO
Prochlorperazine Maleate & Paracetamol Tablets
For Treatment and Prevention of Nausea and Vomiting


Assure's healthy life
CALPHOS
Capsules and Syrup Palatable, effective and Caring
SUITABLE IN :
Pregnancy and lactation
Rapid growth and development
Dietary insufficiency
Anaemias status
Pre and post surgical conditions
M.T. P.
Excessive menstrual blood loss and dysfunctional uterine bleeding
MCNEIL & ARGUS

Rx Vecilex

Expectorant

A Effective formula for dry and asthamatic Cough

Contents :

1. Diphenhydramine Hydrochloride

A antihistamine (H1 blocker) with anticholinergic action.

2. Ammonium Chloride

(a) A directly acting mucodialator.

(b) Reduces viscosity of the mucous by direct action.

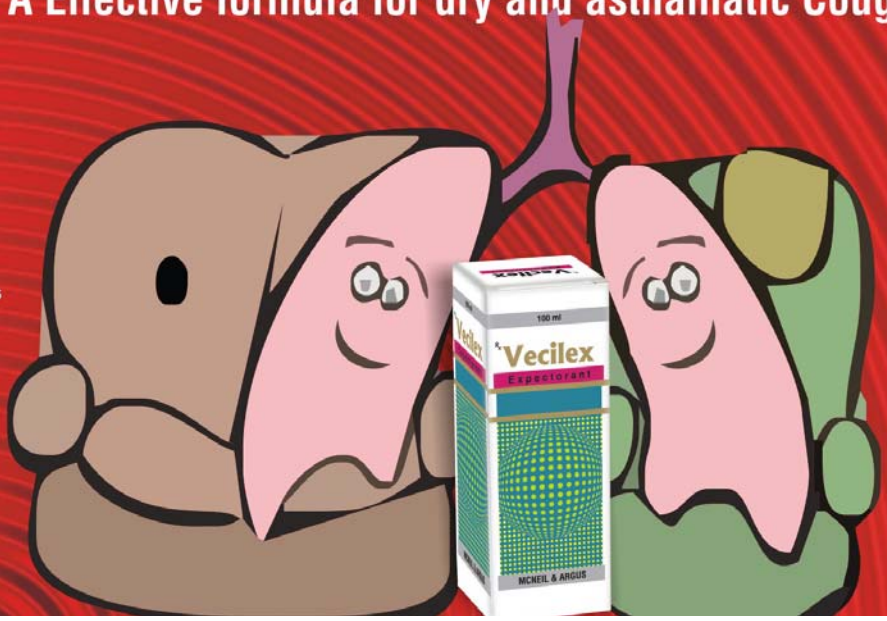
3. Sodium Citrate

(a) Helps to dilute mucus

(b) Helps in loosen cough

4. Menthol

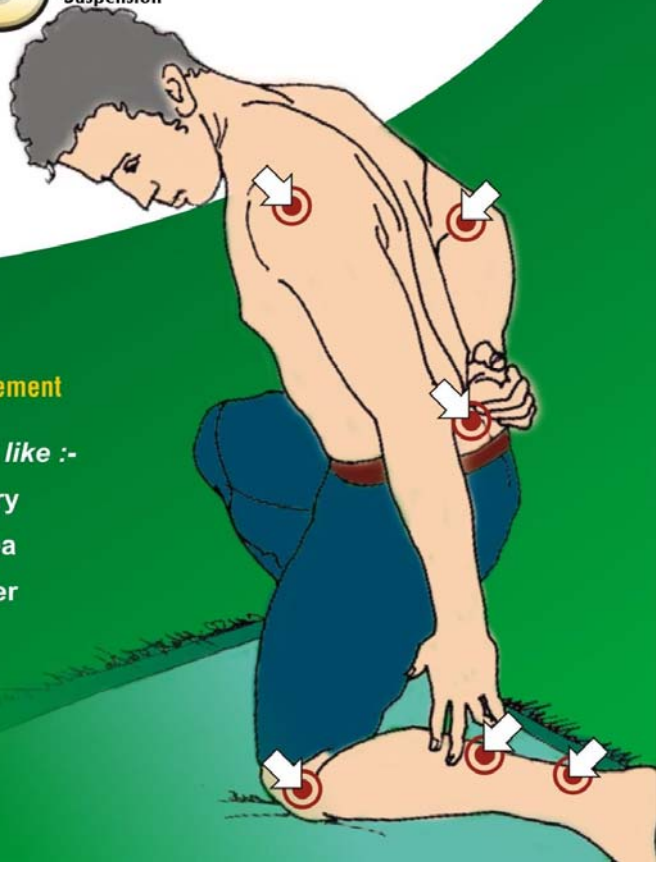
Form soothing and counter irritant action.



Arnim-P

Tablets
Suspension

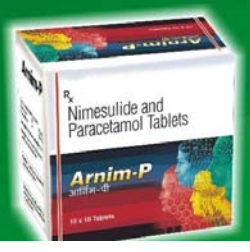
nimesulide + paracetmol cox-2 inhibitor



- Ensure faster recovery from pain and fever
- The proven remedy to sucess in pain & fever management

Fast relief in painful inflammatory conditions like :-

★ Sports Injuries ★ Sinusitis ★ Dental Surgery
★ Bursitis ★ Low backache ★ Dysmenorrhoea
★ Postoperative Pain ★ Osteoarthritis ★ Fever



MCNEIL & ARGUS

MIXED INFECTION SPECIALIST

Doxycap

Doxycycline Hydrochloride Capsules

Doxtase

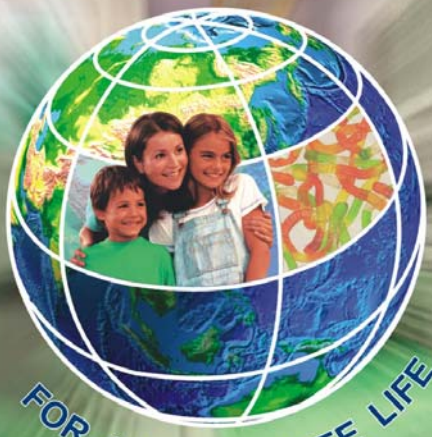
Doxycycline and Serratiopeptidase Capsule

Doxycycline - A broad spectrum antibiotic
High potency
complete absorption
Least alteration of intestinal flora

Indications :
- **Acne ◇ Syphilis**
- **Susceptible infections**
- **Sensitive gonococcal infections**
- **Relapsing fever and Loose-Borne Typhus**

MCNEIL & ARGUS

Perfect anthelmintic for single or mixed worm infestations



FOR A WORM FREE LIFE

ALBAMAC

Albendazole 400 mg Tablets

MCNEIL & ARGUS

Spirulina, Vitamin A, E, C, Selenium, Minerals Capsules

Spiramin Z

Hit the free radicals to win a healthy life

The comprehensive nutrient care for all

- Helps build body resistance to fight infections
- Hastens wound healing process
- Prevents free radical damage
- Helps to prevent diabetic complications

MCNEIL & ARGUS

Indications : Urinary tract infections, Gonorrhea, Chancroid, Bacterial gastroenteritis, Typhoid, Bone, Soft tissue, gynecological and wound infections, Respiratory infections, Tuberculosis Meningitis

MCNEIL & ARGUS

LR-10

Loratadine Tablets

More than just non-sedating

- Tackles both, early and late phase of allergy
- Fast acting
- Once daily

MCNEIL & ARGUS

For Chronic Urticaria

Hits right on target

Vicon-150

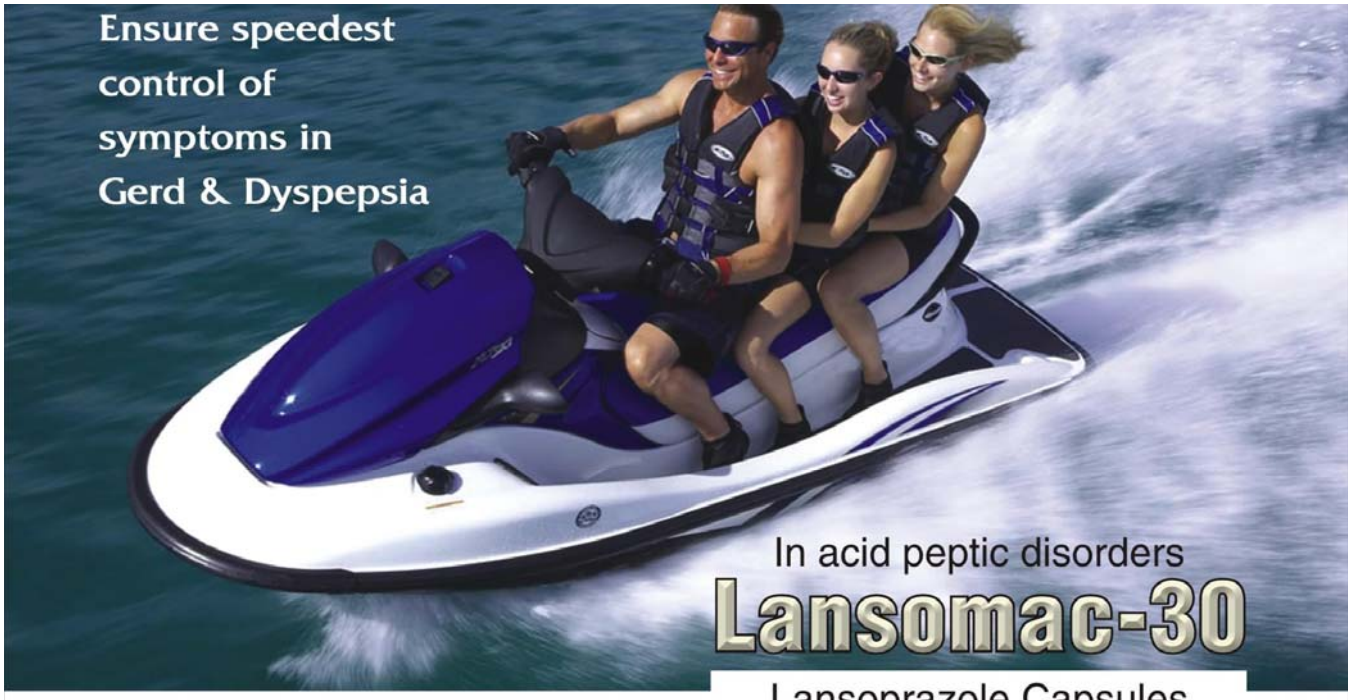
Fluconazole Tablet 150 mg

F.E.Z-150

Fluconazole Tablet 150 mg

- Vaginal Candidiasis
- Systemic Candidiasis
- Mucosal Candidiasis
- Cryptococcal Meningitis
- Achieves high concentration
- Superior to other antifungals

MCNEIL & ARGUS



- GERD
- Peptic Ulcer
- Acid related dyspepsia
- NSAID-associated ulceration

MCNEIL & ARGUS

Get rid of cough and congestion with...

KUFCARE

Diphenhydramine HCl, Ammonium Chloride,
Sodium Citrate and Menthol Expectorant

MCNEIL & ARGUS

SUITABLE IN :

- Pregnancy and lactation
- Rapid growth and development
- Dietary insufficiency
- Anaemias status
- Pre and post surgical conditions
- M.T. P.

  Excessive menstrual blood loss
  and dysfunctional uterine bleeding

Bring back the colors of life

FE-TONE

An Ideal Haematinic Syrup with Vitamin B-Complex

MCNEIL & ARGUS

A winning combination..... for definite results

Mcflox-OZ

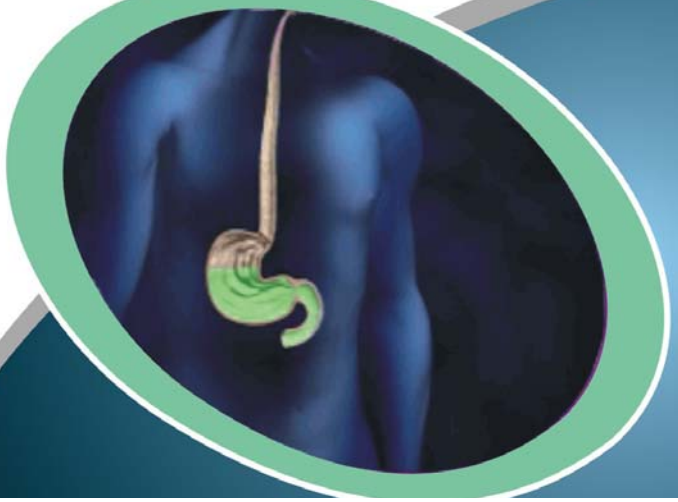
Ofloxacin and Ornidazole Tablets

Mcflox

Ofloxacin Oral Suspension

Treatment of

- Amoebiasis
- Amoebic Dysentery
- Giardiasis
- Trichomoniasis



ORNIDAZOLE :
A highly active nitroimidazole amoebicide

Broad-spectrum cidal activity against Protozoa and many Anaerobic bacteria

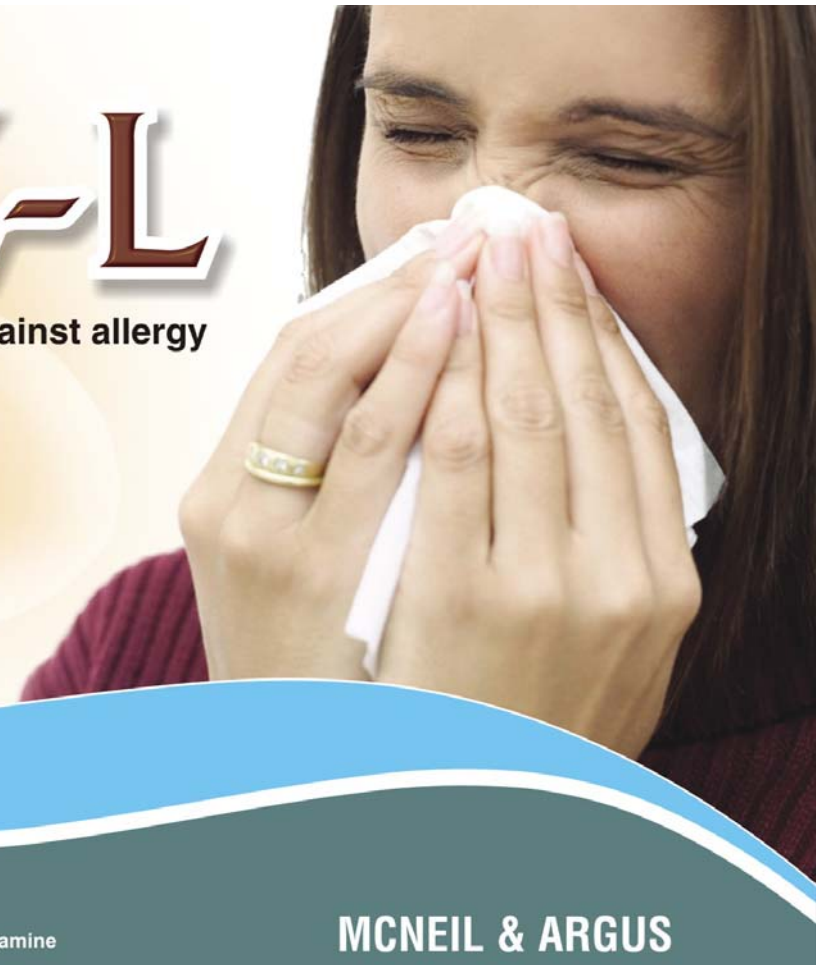
MCNEIL & ARGUS

CIZ-L

A protective shield against allergy

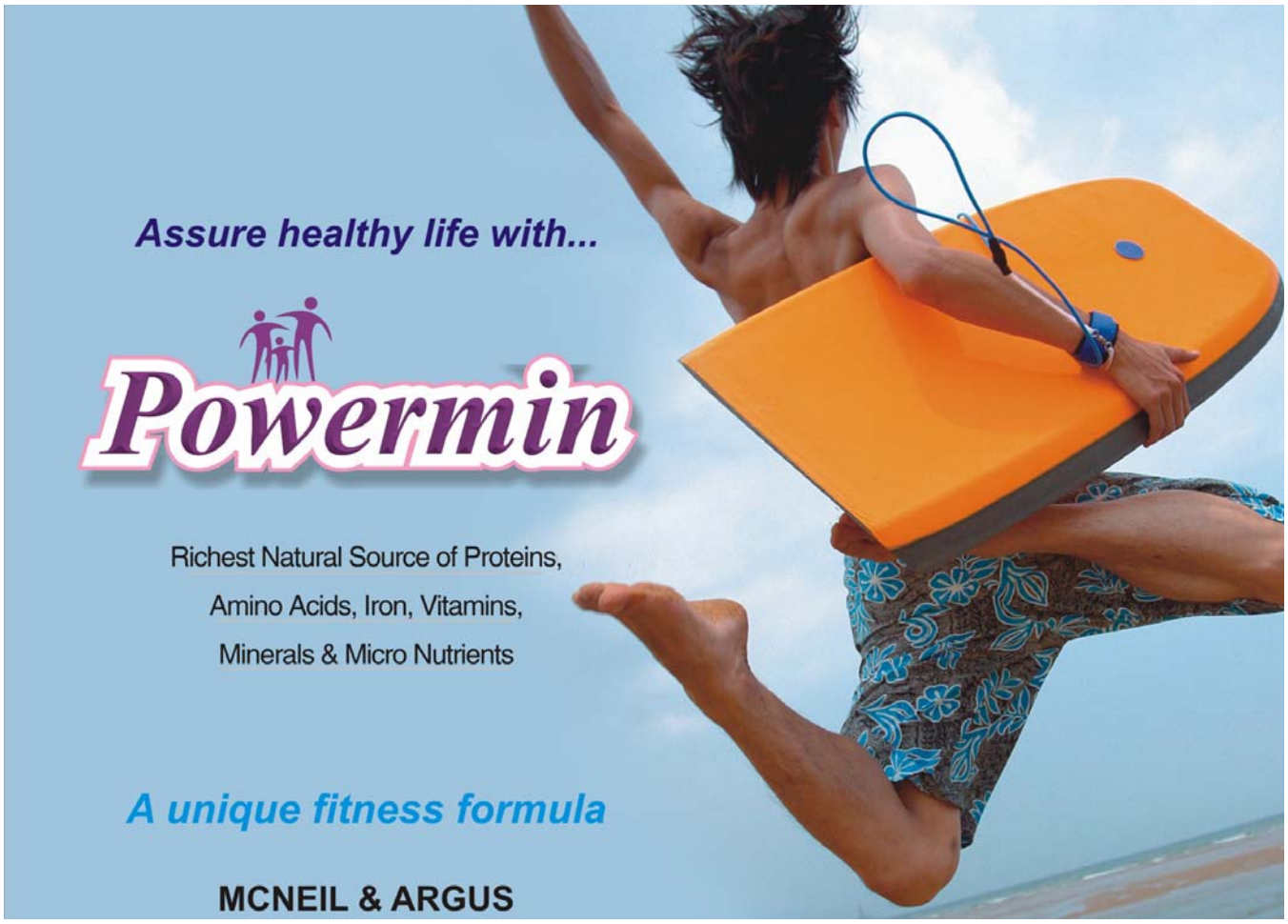
Provides protection against :

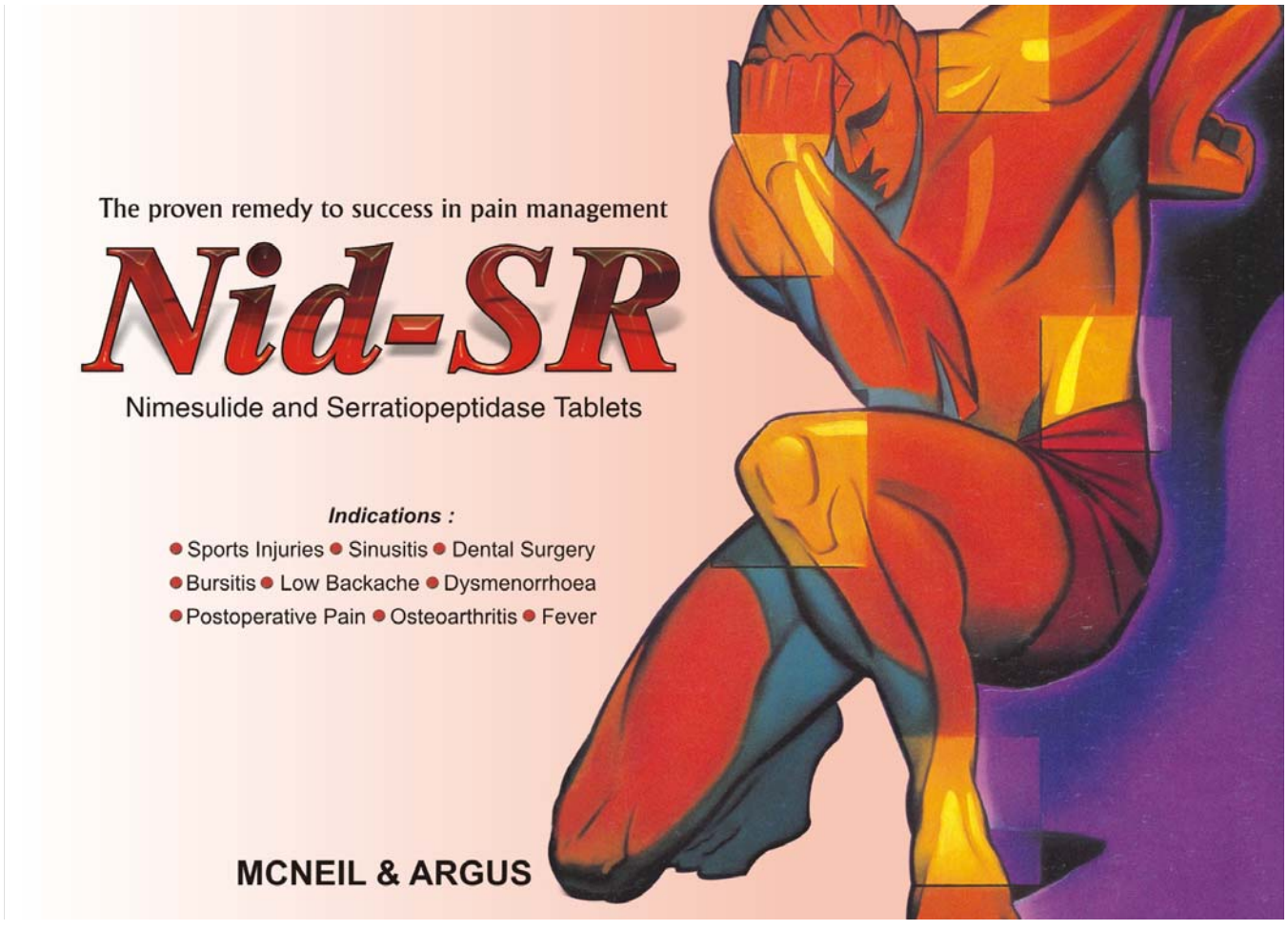
- Allergic Rhinitis
- Anaphylactic Reactions
- Iodopathic urticaria
- Skin Rash



Levocetirizine -a long acting peripheral H1 receptor antagonist antihistamine

MCNEIL & ARGUS


Assure healthy life with...
Powermin
Richest Natural Source of Proteins,
Amino Acids, Iron, Vitamins,
Minerals & Micro Nutrients
A unique fitness formula
MCNEIL & ARGUS


The proven remedy to success in pain management
Nid-SR
Nimesulide and Serratiopeptidase Tablets
Indications :
Sports Injuries Sinusitis Dental Surgery
Bursitis Low Backache Dysmenorrhoea
Postoperative Pain Osteoarthritis Fever
MCNEIL & ARGUS

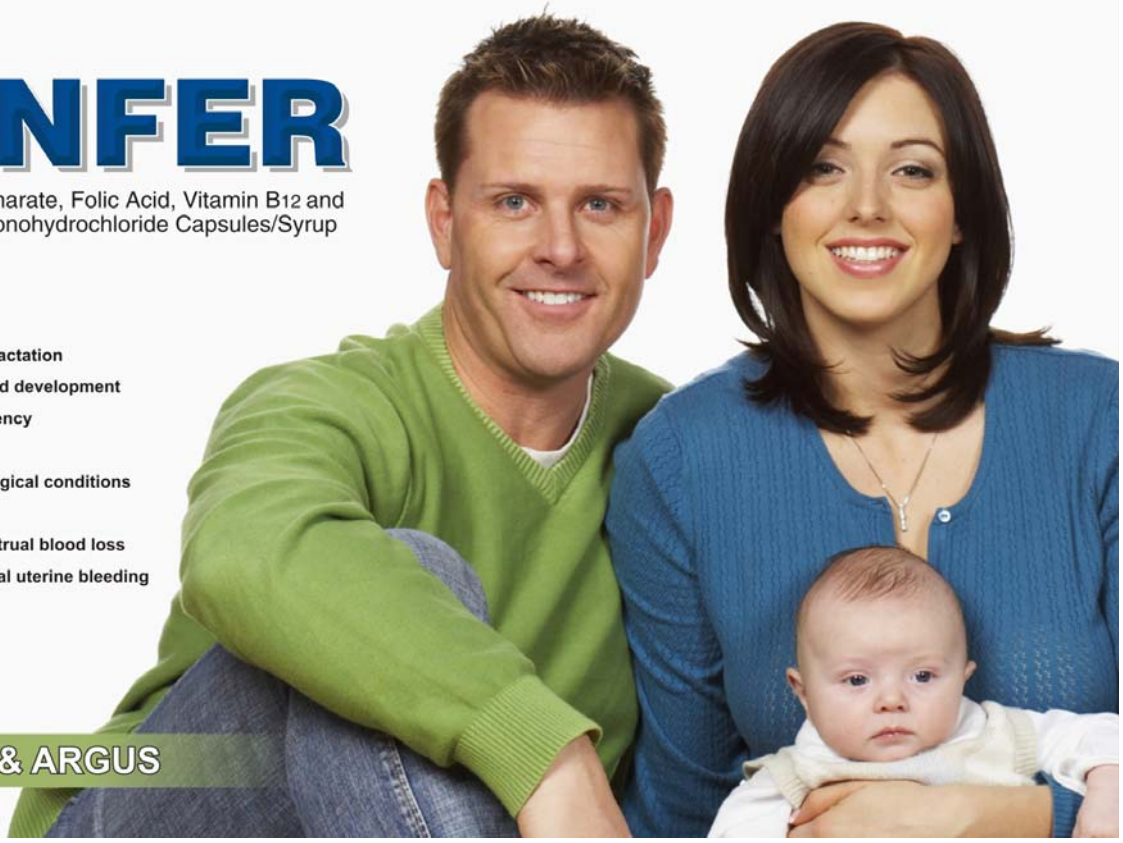
The comprehensive nutrient care for all

VINFER

Ferrous Fumarate, Folic Acid, Vitamin B12 and
L-Lysine Monohydrochloride Capsules/Syrup

SUITABLE IN :

- Pregnancy and lactation
- Rapid growth and development
- Dietary insufficiency
- Anaemias status
- Pre and post surgical conditions
- M.T. P.
- Excessive menstrual blood loss
- and dysfunctional uterine bleeding



MCNEIL & ARGUS

A real calcium regulator for all

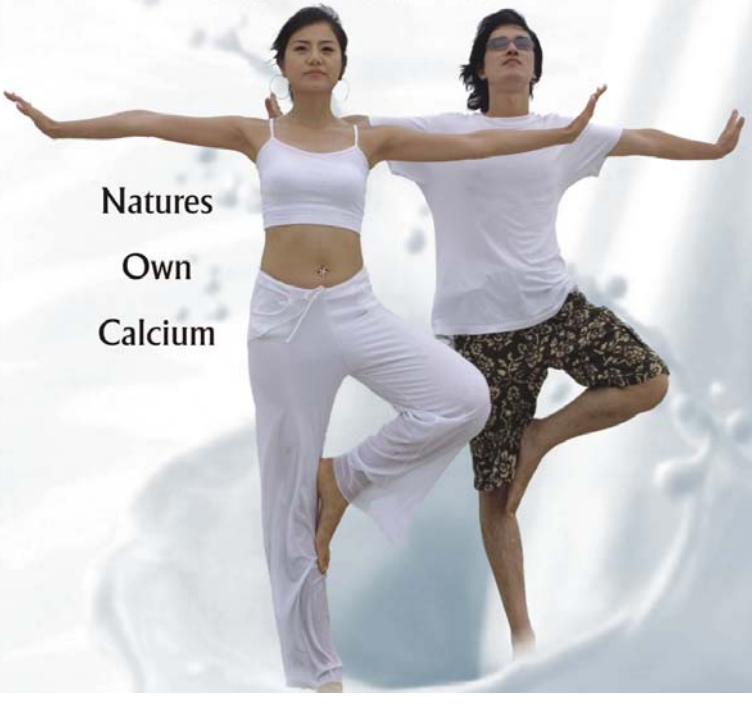
Milkal

Milk Calcium & Alfacalcidol Tablets

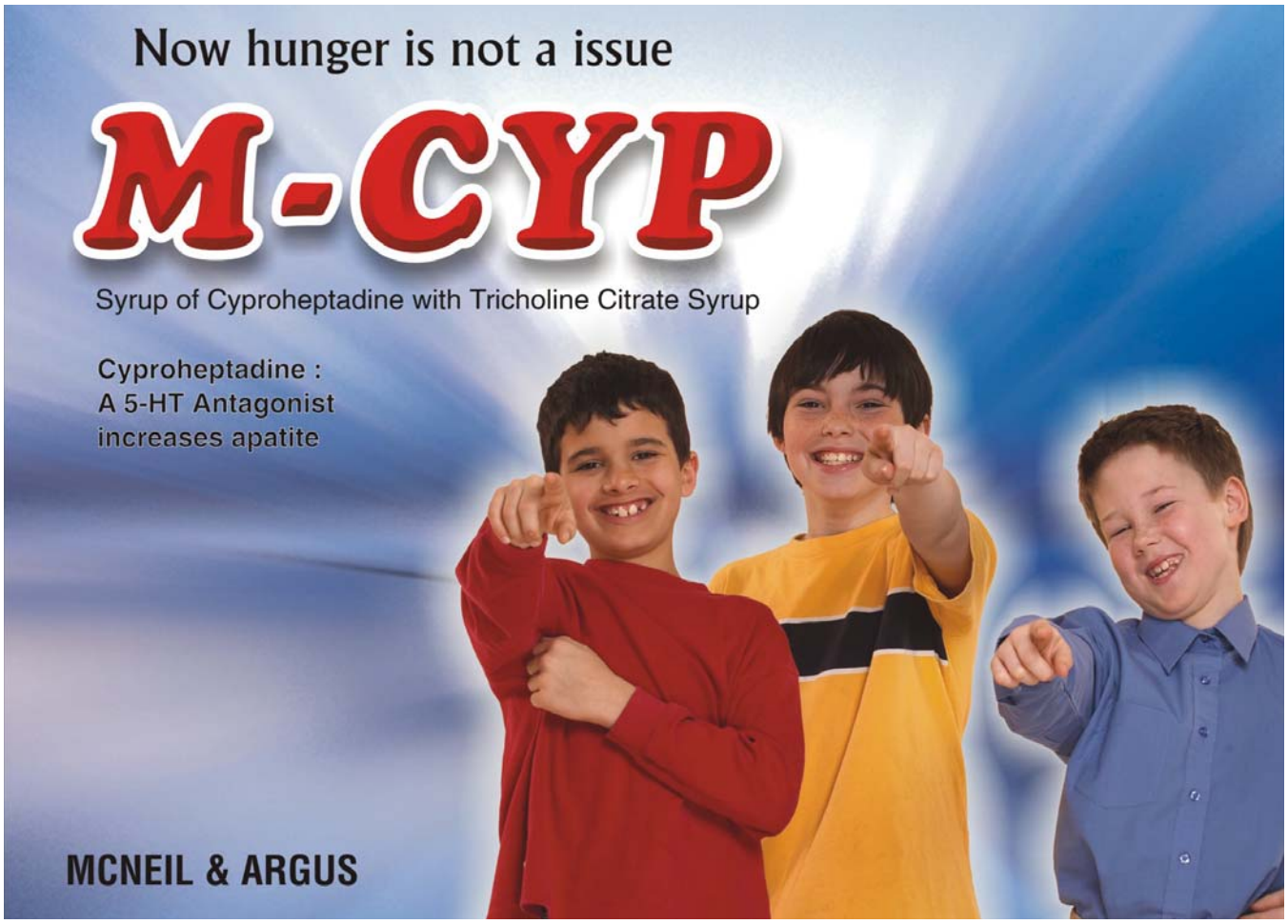
Milkal-G

Milk Calcium Tablets

Natures
Own
Calcium



MCNEIL & ARGUS


Now hunger is not a issue
M-CYP
Syrup of Cyproheptadine with Tricholine Citrate Syrup
Cyproheptadine :
A 5-HT Antagonist
increases apatite
MCNEIL & ARGUS


NEMISULIDE
VIN-100
Low Dose High Performance
In the Treatment of :
Symptomatic Relief of spasticity associated with multiple sclerosis or with spinal cord.
Sympomatic treatment of painful muscle spasm associated with musculoskeletal conditions
VIN-200
ARNIM SUSP.

Deep penetration ensures greater success

D-Mox-BR

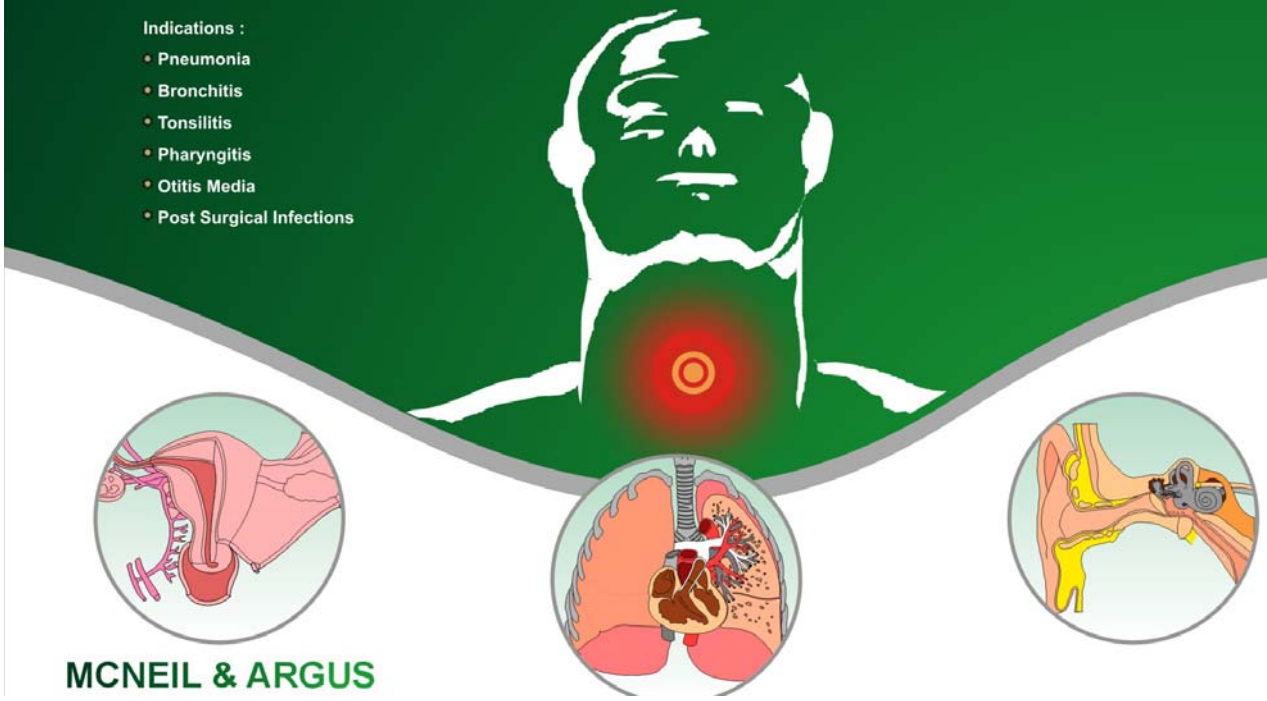
Amoxycillin and Bromhexine Hydrochloride Capsules

D-Mox-500-250

Amoxycillin Capsules

Indications :

- Pneumonia
- Bronchitis
- Tonsilitis
- Pharyngitis
- Otitis Media
- Post Surgical Infections



MCNEIL & ARGUS

Assured pain reliver

Dolen Plus

Nimesulide and Paracetamol Tablets / Suspension

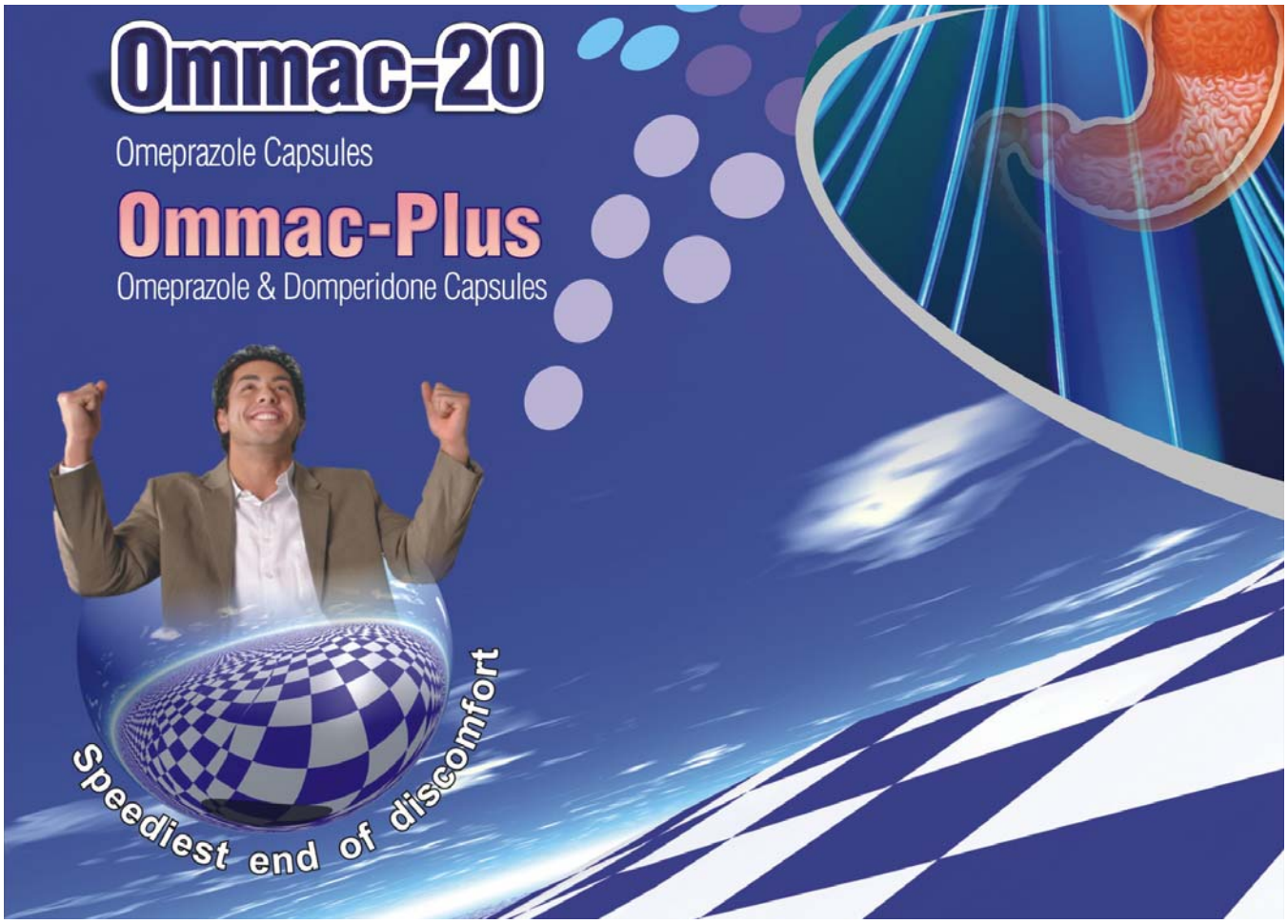
Indications :

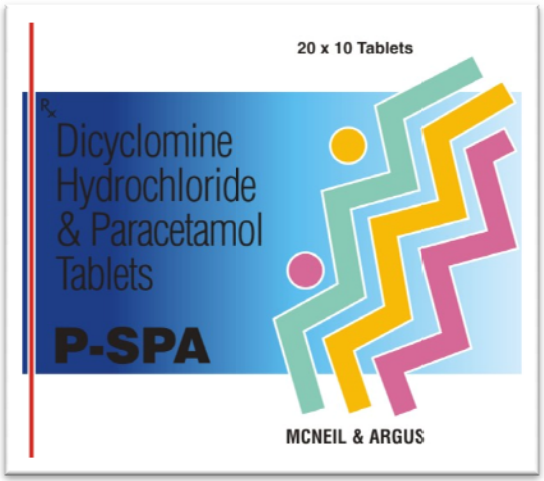
- Sports Injuries
- Sinusitis
- Dental Surgery
- Bursitis
- Low Backache
- Dysmenorrhoea
- Postoperative Pain
- Osteoarthritis
- Fever

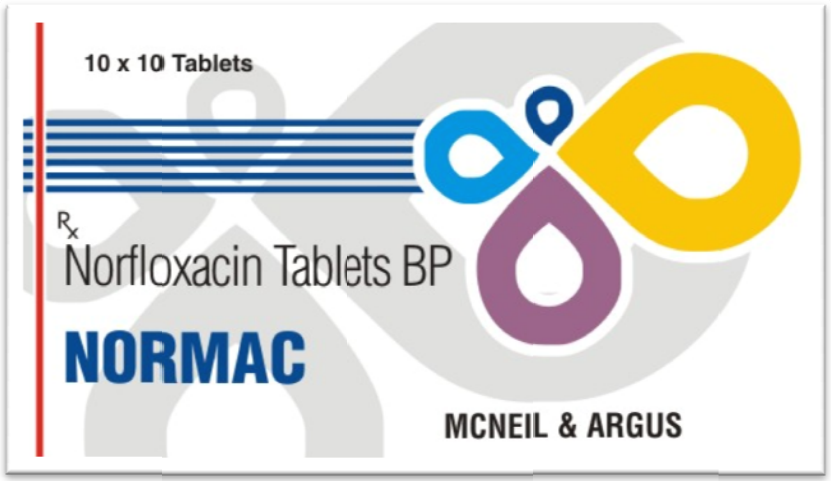
Comprehensive name in relief from

Pain & Inflamation

MCNEIL & ARGUS


Ommac-20
Omeprazole Capsules
Ommac-Plus
Omeprazole & Domperidone Capsules
Speediest end of discomfort


20 x 10 Tablets
Rx
Dicyclomine
Hydrochloride
& Paracetamol
Tablets
P-SPA
MCNEIL & ARGUS


10 x 10 Tablets
Rx
Norfloxacin Tablets BP
NORMAC
MCNEIL & ARGUS


200 Tablets
Rx
Ethambutol
Tablets IP
MCNEIL & ARGUS

℞ Diclofenac Sodium
and Paracetamol Tablets

ACETOFEN-PET

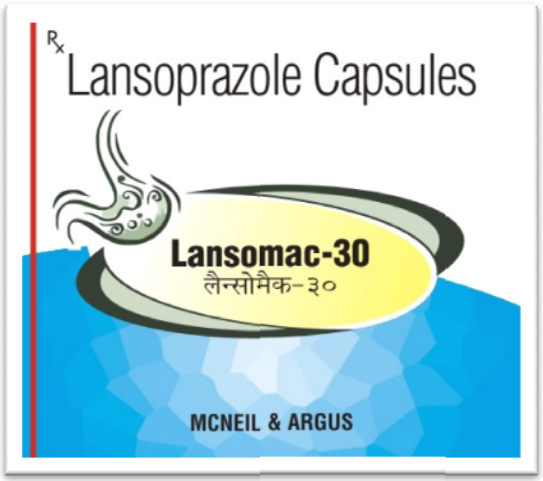
℞ Trimethoprim &
Sulfamethoxazole
Tablets B.P.

COMEX-P

10 x 10 Tablets


℞ Loratadine
Tablets USP
LR-10
10 x 10 Tablets
MCNEIL & ARGUS


℞ Metformin Tablets I.P.
MCFORMIN
10 x 10 Tablets


℞ Lansoprazole Capsules
Lansomac-30
लैन्सोमैक-३०
MCNEIL & ARGUS


Capsules of Ferrous Fumarate,
Folic Acid, Vitamin B12 with
L-Lysine Monohydrochloride
Calcefol


20 x 10 Tablets
℞ Levocetirizine Dihydrochloride Tablets
CIZ-L

℞ Trimethoprim &
Sulphamethoxazole
Tablets B.P.

Comex-P

10 x 10 Tablets

℞ Ciprofloxacin Hydrochloride
Tablets I.P.

CPF-250

MCNEIL & ARGUS 10 x 10 Tablets

℞ Ciprofloxacin Hydrochloride Tablets I.P.

CPF-500

MCNEIL & ARGUS

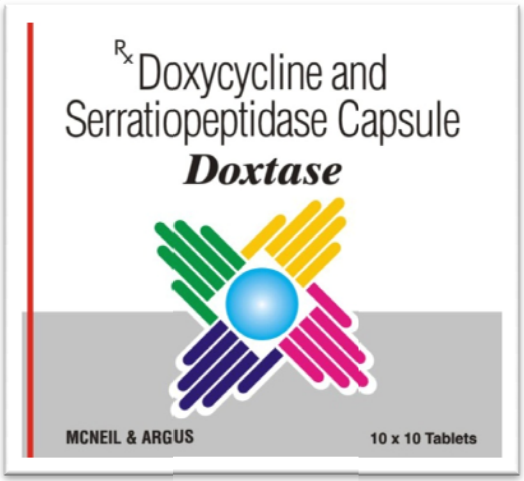
10 x 10 Tablets

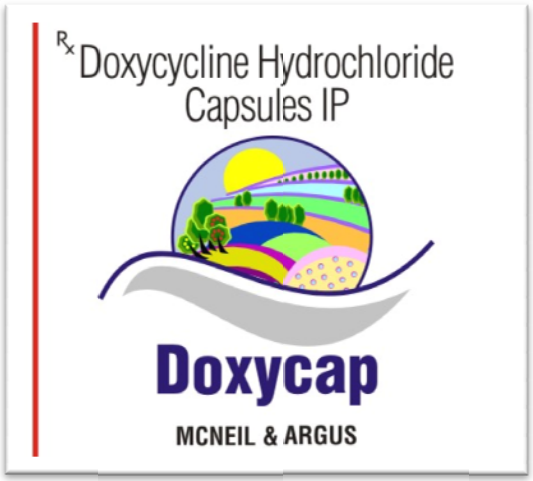
℞ Amoxycillin and Bromhexine Hydrochloride Capsules

D-MOX Br

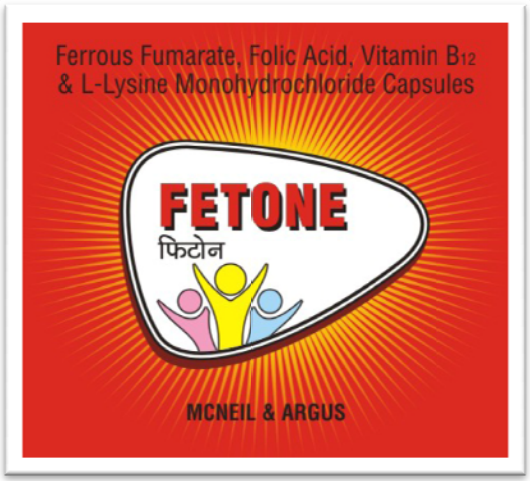
MCNEIL & ARGUS

10 x 10 Tablets


℞ Doxycycline and
Serratiopeptidase Capsule
Doxtase
MCNEIL & ARGUS
10 x 10 Tablets

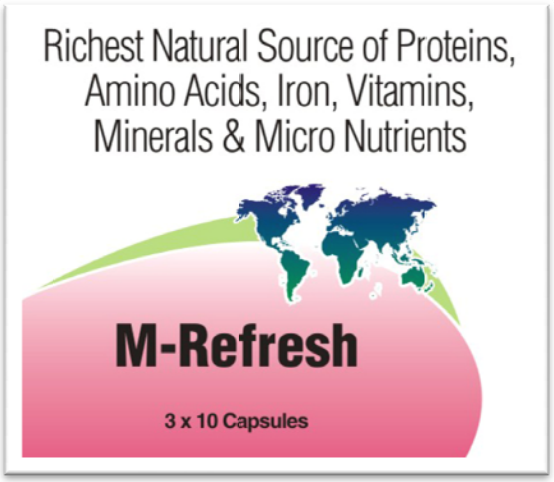

℞ Doxycycline Hydrochloride
Capsules IP
Doxycap
MCNEIL & ARGUS

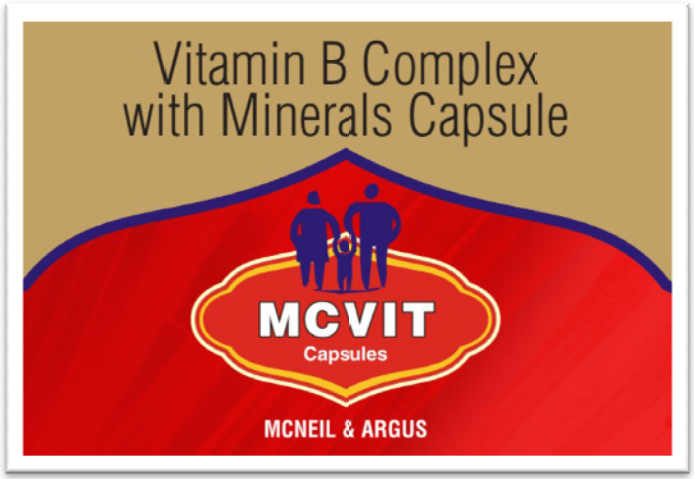

200 Tablets
℞ Isoniazid
Tablets IP
MCNEIL & ARGUS

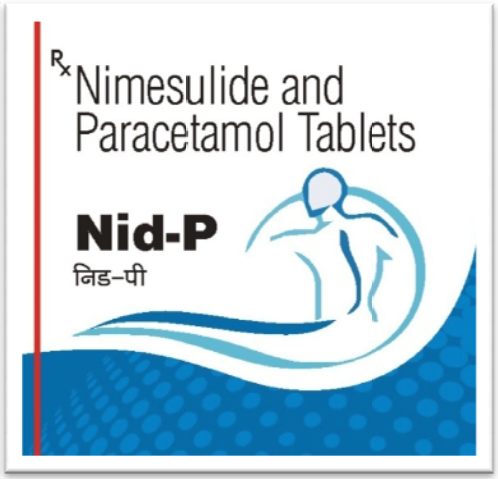

Ferrous Fumarate, Folic Acid, Vitamin B12
& L-Lysine Monohydrochloride Capsules
FETONE
फिटोन
MCNEIL & ARGUS

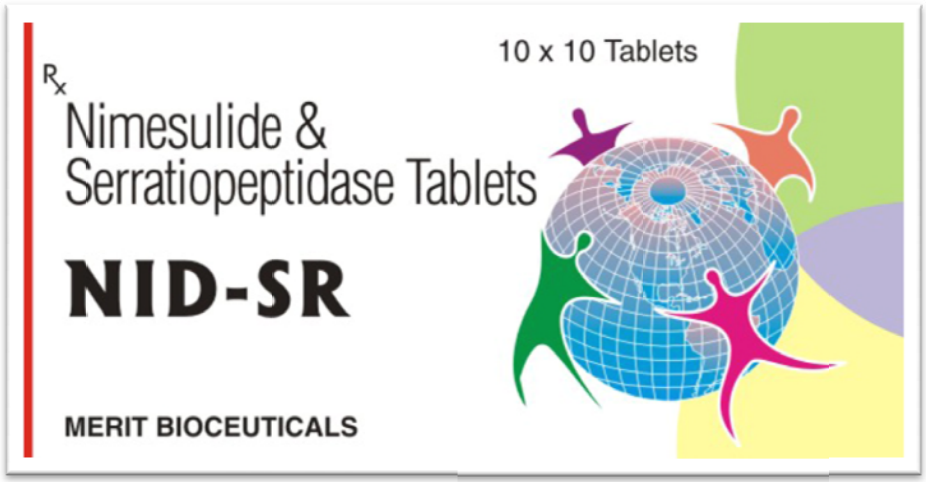

Sildenafil Citrate Tablets
Mcgra
1 x 10 tablets
MCNEIL & ARGUS


10 x 10 Tablets
℞ Ofloxacin &
Ornidazole Tablets
MCFLOX-OZ
MCNEIL & ARGUS


Richest Natural Source of Proteins,
Amino Acids, Iron, Vitamins,
Minerals & Micro Nutrients
M-Refresh
3 x 10 Capsules


Vitamin B Complex
with Minerals Capsule
MCVIT
Capsules
MCNEIL & ARGUS


℞ Nimesulide and
Paracetamol Tablets
Nid-P
निड-पी


Rx
10 x 10 Tablets
Nimesulide &
Serratiopeptidase Tablets
NID-SR
MERIT BIOCEUTICALS


Rx
Ofloxacin Tablets
Ofax-200
MCNEIL & ARGUS
10 x 10 Tablets

℞ Omeprazole and Domperidone Capsules

Ommac-Plus

MCNEIL & ARGUS

10 x 10 Capsules

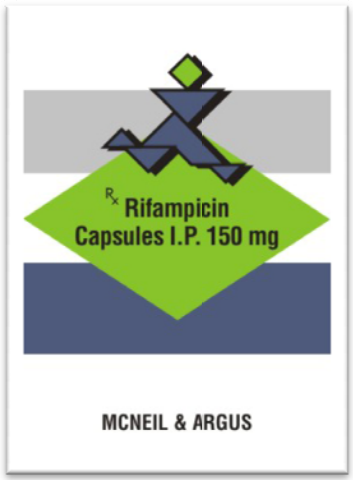
1 Tablet

℞ Fluconazole Tablets

FEZ-150

Broad Spectrum Anti-Fungal


200 Tablets
℞ Pyrazinamide
Tablets IP
MCNEIL & ARGUS

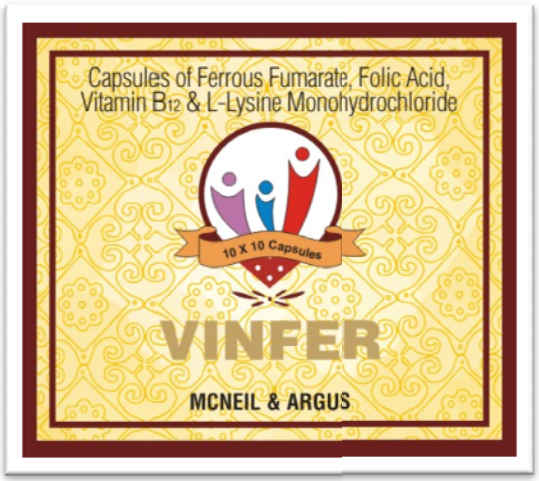

℞ Rifampicin
Capsules I.P. 150 mg
MCNEIL & ARGUS


℞ Ciprofloxacin Hydrochloride Tablets I.P.
Scip-250
10 x 10 Tablets


℞ Ciprofloxacin Hydrochloride Tablets I.P.
Scip-500
10 x 10 Tablets


10 x 10 Tablets
℞ Ofloxacin &
Ornidazole Tablets
SUREFLOX-OZ


℞ Ofloxacin Tablets
SUREFLOX
MERIT BIOCEUTICALS
10 x 10 Tablets


Capsules of Ferrous Fumarate, Folic Acid,
Vitamin B12 & L-Lysine Monohydrochloride
10 X 10 Capsules
VINFER
MCNEIL & ARGUS

100 ml

℞ Phenylpropanolamine Hydrochloride & Chlorpheniramine Maleate Syrup

Decold-CP

SYRUP

Decongestant & Antihistaminic

MCNEIL & ARGUS

60 ml

℞ Nimesulide & Paracetamol Suspension

Arnim-P

Suspension

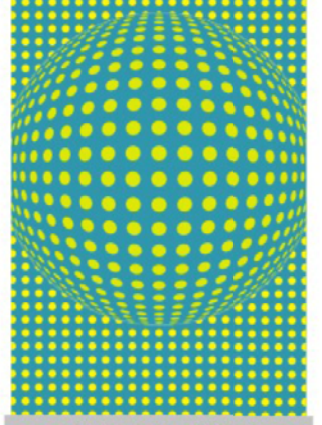
- Anti-inflammatory
- Antipyretic
- Analgesic

MCNEIL & ARGUS

100 ml

℞ **Vecilex**

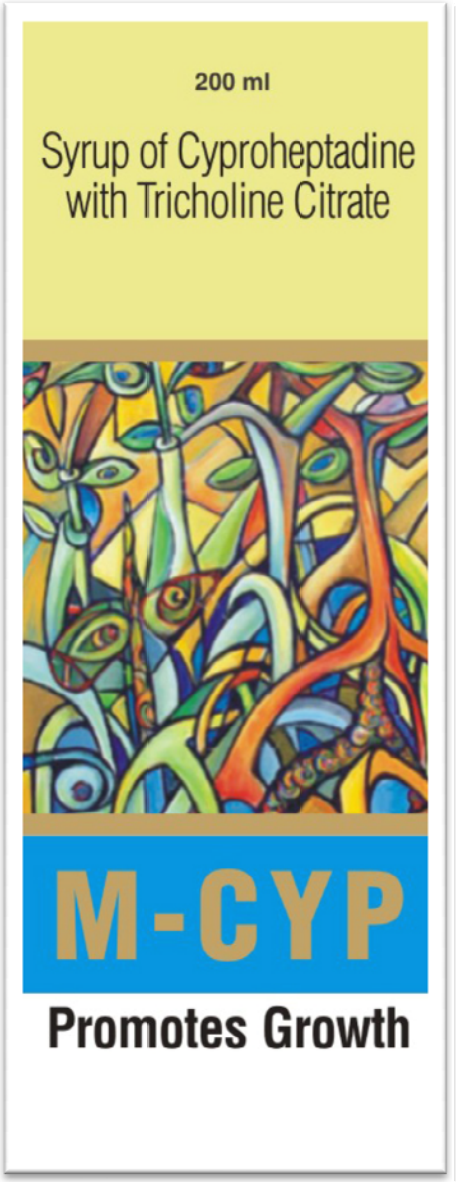
Expectorant



MCNEIL & ARGUS


180 ml
Vecal
विकैल
Calcium, Vitamin D3
& L-Lysine Suspension
MCNEIL & ARGUS


℞ Ofloxacin
Oral Suspension
Mcflox
Suspension
MCNEIL & ARGUS
30 ml


200 ml
Syrup of Cyproheptadine
with Tricholine Citrate
M-CYP
Promotes Growth


200 ml
Syrup of Cyproheptadine with Tricholine Citrate
BIOCYP
Promotes Growth
MCNEIL & ARGUS


100 ml.
Rx
KUFCARE
EXPECTORANT

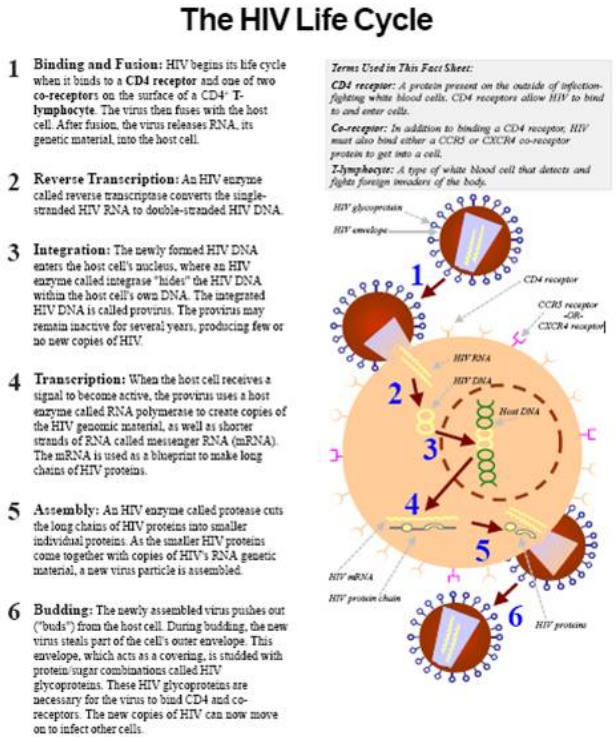

Rx
VECILEX-GT
Expectorant
60 ml

Description of HIV

H	**Human**	**because this virus can only infect human beings.**
I	**Immuno deficiency**	**because the virus creates a deficiency, within the body's immune system.**
V	**Virus**	

Description of AIDS

A	**Acquired**	**A condition one acquires or gets infected with, it is not transmitted genetically**
I	**Immune**	**It affects the body's immune system**
D	**Deficiency**	**It causes immune system deficient**
S	**Syndrome**	**Someone with AIDS may experience a wide range of different diseases and opportunistic infections**



Summary

HIV damages the immune system. Over time, the immune system becomes very weak. This stage of HIV is called AIDS. In other words, it can be said that AIDS is the late stage of infection which can take around 7-10 years to develop after patient becomes HIV positive.

No one knows for sure when a person with HIV will get AIDS. It is quiet possible that many people infected with HIV may stay healthy for years.

Origination of HIV

The most recent presentation on the origin of HIV was presented at the 6th Conference on Retroviruses and Opportunitistic Infections (Chicago, January 1999). At that conference, research was presented that suggested that HIV had "crossed over" into the human population from a particular species of chimpanzee, probably through blood contact that occurred during hunting and field dressing of the animals. The CDC states that the findings presented at this conference provide the strongest evidence to date that HIV-1 originated in non-human primates. The research findings were featured in the February 4,1999 issue of the journal, Nature.

We know that the virus has existed in the United States, Haiti and Africa since at least 1977-1978. In 1979, doctors in Los Angeles and New York were reporting rare types of pneumonia, cancer and other illnesses. The common thread was that these conditions were not usually found in persons with healthy immune systems.

In 1982 the Centers for Disease Control and Prevention (CDC) officially named the condition AIDS (Acquired Immune Deficiency Syndrome). In 1984 the virus responsible for weakening the immune system was identified as HIV (Human Immunodeficiency Virus)

Global summary of the AIDS epidemic
December 2007

Number of people living with HIV in 2007

Total	33.2 million [30.6–36.1 million]
Adults	30.8 million [28.2–33.6 million]
Women	15.4 million [13.9–16.6 million]
Children under	15 years 2.5 million [2.2–2.6 million]

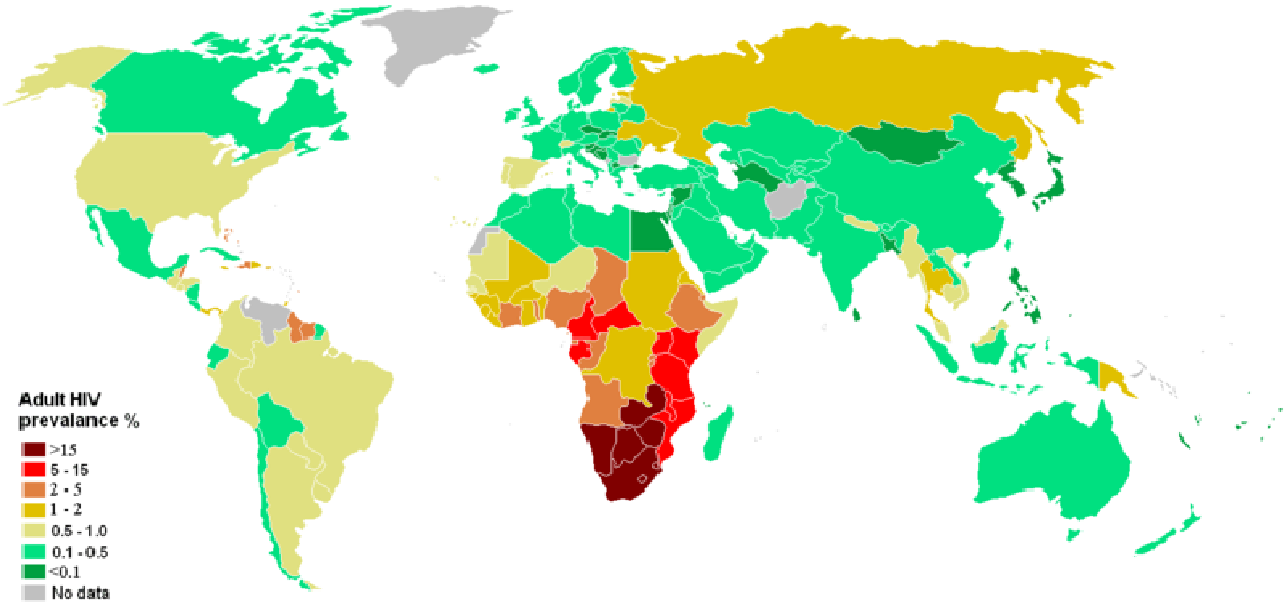
People newly infected with HIV in 2007

Total	2.5 million [1.8–4.1 million]
Adults	2.1 million [1.4–3.6 million]
Children under 15 years	420 000 [350 000–540 000]

AIDS deaths in 2007

Total	2.1 million [1.9–2.4 million]
Adults	1.7 million [1.6–2.1 million]
Children under 15 years	330 000 [310 000–380 000]

The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.



Effect of HIV on the immunity system

PATHOGENESIS

- The hallmark of HIV disease causes profound immunodeficiency resulting from a progressive deficiency of helper or inducer T-cells (CD4+ T cells). HIV recognizes a CD4 surface molecule on the membrane of the T-lymphocyte, particularly the helper T-lymphocyte. It recognizes the information that identifies this as a “helper” T-lymphocyte. Using this membrane marker to get inside the cell, it employs its reverse transcriptase enzyme to copy its piece of RNA into the cell’s genetic material. It will stay there for the life of the cell, eventually causing the death of the cell

- HIV mediates the destruction and depletion of mature CD4 T-cells. HIV invades and destroys the immune system by damaging the CD4 lymphocytes, which results in a fall in the number of CD4 lymphocytes with the result that the immune system cannot function normally. As a result the risk of infection and cancer increases. HIV also invades macrophages, which leads to further depression of the functions of the immune system

- When the number of CD4+ T cells declines below a certain level, the patient is at high risk of developing a variety of opportunistic infections and neoplasms

Spreading of HIV

Means of HIV Transmission

HIV can be transmitted from an infected person to another through:

• **Blood** (including menstrual blood)
• **Semen**
• **Vaginal secretions**
• **Breast milk**

Blood contains the highest concentration of the virus, followed by semen, followed by vaginal fluids, followed by breast milk.

HIV Transmission
• Unprotected sexual contact
• Direct blood contact, including injection drug needles, blood transfusions, accidents in health care settings or certain blood products
• Mother to baby (before or during birth, or through breast milk)

The following are few of the most common routes through which HIV spreads:

- **Sexual transmission:**

HIV is transmitted by both homosexual and heterosexual unsafe contact. Unsafe Heterosexual transmission is the most common mode of infection worldwide, particularly in developing countries. The presence of sexually transmitted diseases further increases the risk of HIV transmission

Sexual intercourse (vaginal and anal): In the genitals and the rectum, HIV may infect the mucous membranes directly or enter through cuts and sores caused during intercourse (many of which would be unnoticed). Vaginal and anal intercourse is a high-risk practice.

A woman can give HIV to a man during vaginal intercourse
Yes. If the woman is infected, HIV is present in vaginal and cervical secretions (the wetness in a woman's vagina) and can enter the penis through the urethra (the hole at the tip) or through cuts or abrasions on the skin of the penis. The presence of other STDs can increase the risk of transmission. The correct and consistent use of a latex condom or female condom can reduce the risk of transmitting HIV during vaginal intercourse.

Oral transmission:

The mouth is an inhospitable environment for HIV (in semen, vaginal fluid or blood), meaning the risk of HIV transmission through the throat, gums, and oral membranes is lower than through vaginal or anal membranes. There are however, documented cases where HIV was transmitted orally, so we can't say that getting HIV-infected semen, vaginal fluid or blood in the mouth is without risk. However, oral sex is considered a low risk practice**.**

Oral sex
there is considerable debate within the HIV/AIDS prevention community regarding the risk of transmission of HIV through oral sex. What is currently known is that there is some risk associated with performing oral sex without protection; (there have been a few documented cases of HIV transmission through oral sex). While no one knows exactly what that risk is, cumulative evidence indicates that the risk is less than that of unprotected anal or vaginal sex. The risk from receiving oral sex, for both a man and a woman, is considered to be very low.

Currently, risk reduction options when performing oral sex on a man (fellatio) include the use of latex condoms, but also include withdrawal before ejaculation without a condom (avoiding semen in the mouth) and/or refraining from this activity when cuts or sores are present in the mouth.

When performing oral sex on a woman (cunnilingus), moisture barriers such as a dam (sheet of latex), a cut-open and flattened condom, or household plastic wrap can reduce the risk of exposure to vaginal secretions and/or blood.

Effectiveness of latex condoms in preventing HIV
Several studies have demonstrated that latex condoms are highly effective in preventing HIV transmission when used correctly and consistently. These studies looked at uninfected people considered to be at very high risk of infection because they were involved in sexual relationships with HIV-infected persons. The studies found that even with repeated sexual contact, 98-100% of those people who used latex condoms consistently and correctly remained uninfected.

Transmission by blood and blood products:

HIV can be transmitted by blood and blood products, both among individuals who share contaminated paraphernalia (needles and syringes) for injection drug use and in those who receive transfusions of blood and blood products

Sharing injection needles: An injection needle can pass blood directly from one person's bloodstream to another. It is a very efficient way to transmit a blood-borne virus. Sharing needles is considered a high-risk practice.

Maternal-fetal/ infant transmission: HIV infection can be transmitted from infected mothers to infants either intrapartum, perinatally, or via breast milk

Mother to Child: It is possible for an HIV-infected mother to pass the virus directly before or during birth, or through breast milk. Breast milk contains HIV, and while small amounts of breast milk do not pose significant threat of infection to adults, it is a viable means of transmission to infants.

Occupational transmission of HIV to health care and laboratory workers: There is a risk of HIV transmission following skin puncture from a needle or a sharp object contaminated with blood from a person with documented HIV infection.

However it dose not spread by

The following "bodily fluids" are NOT infectious:
Saliva
Tears
Sweat

Feces
Urine
Mosquito bite
Any casual contact
By sneezing or coughing

HIV from kissing

Casual contact through closed-mouth or "social" kissing is not a risk for transmission of HIV. Because of the potential for contact with blood during "French" or open-mouth, wet kissing, CDC recommends against engaging in this activity with a person known to be infected. However, the risk of acquiring HIV during open-mouth kissing is believed to be very low. CDC has investigated only one case of HIV infection that may be attributed to contact with blood during open-mouth kissing. In this case both partners had extensive dental problems including gingivitis (inflammation of the gums). It is likely that there was blood present in both partners' mouths making direct blood to blood contact a possibility.

HIV from casual contact

(Shaking hands, hugging, using a toilet, drinking from the same glass, or the sneezing and coughing of an infected person)

No. HIV is not transmitted by day-to-day contact in the home, the workplace, schools, or social settings. HIV is not transmitted through shaking hands, hugging or a casual kiss. You cannot become infected from a toilet seat, a drinking fountain, a doorknob, dishes, drinking glasses, food, or pets.

HIV is a fragile virus that does not live long outside the body. HIV is not an airborne or food borne virus. HIV is present in the blood, semen or vaginal secretions of an infected person and can be transmitted through unprotected vaginal, oral or anal sex or through sharing injection drug needles.

Symptoms of AIDS

One or More of the following could be symptoms of HIV/AIDS

- **Prolonged, unexplained fatigue**
- **Fever lasting more than 10 days**
- **Chills**
- **Excessive sweating especially night sweats**
- **Mouth lesions including yeast lesions and painful, swollen gums**
- **Sore throat and cough**
- **Shortness of breath**
- **Changes in bowel habits including constipation**
- **Frequent diarrhea**
- **Symptoms of a specific opportunistic infection (such as candida, Pneumocystis, and so on)**
- **Tumor (Kaposi's sarcoma)**
- **Skin rashes or lesions of various types**
- **Unintentional weight loss**
- **General discomfort or uneasiness (malaise)**
- **Headache**

Additional symptoms that may be associated with this disease:

- **Speech impairment**
- **Muscle atrophy**
- **Memory loss**
- **Decreasing intellectual function**
- **Joint swelling**
- **Joint stiffness**
- **Joint pain**
- **Cold intolerance**
- **Bone pain or tenderness**
- **Unusual or strange behavior**
- **Slow, sluggish, lethargic movement**
- **Anxiety, stress, and tension**
- **Groin lump**
- **Generalized itching (pruritus)**
- **Genital sores (female)**
- **Genital sores (male)**
- **Blurred vision**
- **Double vision (diplopia)**
- **Light sensitivity**
- **Blind spots in the vision**
- **Decreased vision or blindness**
- **Chest pain**
- **Flank pain or pain in the sides**
- **Back pain**
- **Abdominal pain**
- **Loss of appetite, indigestion, or other gastrointestinal upset**
- **Muscle pain**
- **Bone pain or tenderness**
- **Numbness and tingling**
- **Seizures**

Testing

Antibody testing for HIV should be ordered if the person thinks that he may have been exposed to HIV.

Test should be conducted if

- A person is sexually active (three or more sexual partners in the last 12 months)
- A person has received a blood transfusion or a sexual partner received a transfusion, and later tested positive for HIV
- A person is uncertain about his sexual partner's risk behaviors
- A person is a male who has had sex with another male
- A person has used street drugs by injection, especially when sharing needles and/or other equipment
- A person has a Sexually Transmitted Disease (STD), TB or Hepatitis B & C and is practicing risky behaviors
- A person is a health care worker with direct exposure to blood on the job
- Someone is pregnant and practicing risky behaviors (There are now treatments that can greatly reduce the risk that a pregnant woman who has HIV will give the virus to her baby)

Results

- A healthy individual has no antibodies to HIV
- The tests are declared as reactive or non-reactive depending on the results
- If a person tests reactive for HIV antibodies on both the ELISA and the Western Blot tests, then he is considered to be infected with HIV

Conditions where one is HIV positive

If you test positive, the sooner you take steps to protect your health, the better. Early medical treatment, a healthy lifestyle and a positive attitude can help you stay well. Prompt medical care may delay the onset of AIDS and prevent some life-threatening conditions. It is important to know that a positive HIV test should always be confirmed; to be sure that it is a true positive. If your test result is positive, there are a number of important steps you can take immediately to protect your health:

- See a doctor, even if you don't feel sick. Try to find a doctor who has experience-treating HIV. There are now many new drugs to treat HIV infection. There are important tests; immunizations and drug treatments that can help you maintain good health. It is never too early to start thinking about treatment possibilities.
- Have a tuberculosis (TB) test done. You may be infected with TB and not know it. Undetected TB can cause serious illness. TB can be treated successfully if detected early.
- Recreational drugs, alcoholic beverages and smoking can weaken your immune system. There are programs available to help you stop.
- Consider joining a support group for people with HIV infection or finding out about other resources available in your area, such as HIV/AIDS-knowledgeable counselors for one on one therapy. There are also many newsletters available for people living with HIV and AIDS.
- There is much you can do to stay healthy. Learning as much as you can is a step in the right direction. Local and/or national resources may be available. Many HIV/AIDS organizations provide services free or on a sliding scale, based on ability to pay.

How long after a possible exposure you should be tested for HIV

The time it takes for a person who has been infected with HIV to seroconvert (test positive) for HIV antibodies is commonly called the "Window Period."

The California Office of AIDS, published in 1998, says about the window period: "When a person is infected with the HIV virus, statistics show that 95-97% (perhaps higher) of all infected individuals develop antibodies within 12 weeks (3-months)."

The National CDC has said that in some rare cases, it may take up to six months for one to seroconvert (test positive). At this point the results would be 99.9% accurate.

When do you know for sure that you are not infected with HIV

The tests commonly used to determine HIV infection actually look for antibodies produced by the body to fight HIV. According to the Centers for Disease Control and Prevention (CDC), most people will develop detectable antibodies within 3 months after infection. In rare cases, it can take up to six months. Therefore, the CDC recommends testing at 6 months after the last possible exposure. (unprotected vaginal, anal or oral sex or sharing injecting drug needles). It would be extremely rare to take longer than six months to develop detectable antibodies. It is important, during the six months between exposure and the 6-month test, to protect yourself and others from further exposures to HIV. The CDC National AIDS Hotline can provide more information and referrals to testing sites in your area

Where can you get tested for HIV infection

Many places provide testing for HIV infection. It is important to seek testing at a location that also provides counseling about HIV and AIDS. Common locations include local health departments, private physicians, hospitals, and test sites specifically set up for HIV testing.

In addition to traditional testing procedures, there are other options. For those who prefer not to have blood drawn, many sites now offer oral fluids testing, which involve testing of a sample of fluid taken from inside the mouth with a cotton swab. The OraSure Test is currently only available through a health care provider or clinic. Some clinics may also offer urine testing as an alternative to blood tests.

There is also testing which can be performed anonymously in the privacy of your own home. There are many home tests advertised through the internet, but only the Home Access Test has been approved by the FDA. The Home Access test kit can be found at most local pharmacies. The testing procedure involves pricking your finger with a special device, placing a drop of blood on a specially treated card, and then mailing the card in for testing. You are given an identification number to use when you phone in for the test results-- 3 days or 2 weeks later, depending on the test kit purchased.

The difference between an Anonymous and a Confidential Test

Anonymous and Confidential use the same testing method. The only difference is one does not have your name attached to the results.

Anonymous antibody testing is available at Anonymous Test Sites in most California counties. Anonymous testing means that absolutely no one has access to your test results since your name is never recorded at the test site.

Confidential antibody testing means that you and the health care provider know your results, which may be recorded in your medical file.

What do test results mean?

A positive result means:
- You are HIV-positive (carrying the virus that causes AIDS).
- You can infect others and should try to implement precautions to prevent doing so.

A negative result means:

- No antibodies were found in your blood at this time.

A negative result does NOT mean:

- You are not infected with HIV (if you are still in the window period).
- You are immune to AIDS.
- You have a resistance to infection.
- You will never get AIDS.

If I test positive, does that mean that I will die?

Testing positive for HIV means that you now carry the virus that causes AIDS. It does not mean that you have AIDS, nor does it mean that you will die. Although there is no cure for AIDS, many opportunistic infections that make people sick can be controlled, prevented or eliminated. This has substantially increased the longevity and quality of life for people living with AIDS.

Need for Medication

If HIV is allowed to reproduce, or "replicate," inside the body, it will cause damage to the immune system. Ultimately, the immune system becomes so weak that the body becomes vulnerable to other diseases. This is the point at which a person is usually diagnosed with full-blown AIDS, which can result in death due to other opportunistic infections like Tuberculosis, etc

Anti-HIV drugs can help HIV-infected people live longer. Treatment, therefore, is a very important option, and people living with HIV should consider starting treatment before the virus has had a chance to do serious damage to the immune system.

Sticking to therapy Ensure that the medication is taken at the right time, in the right doses and in the right way. It is an important factor in the success of anti-HIV treatments. The best response to anti-HIV drugs is seen in people who take every dose regularly. Further Fixed Dose Combinations (FDCs) have been found to increase the patient compliance as they reduce pill burden. Thus FDCs should be preferred especially for patients who have tendency to miss doses.

I'm HIV positive. Where can I go for information about treatments?

The CDC National AIDS Hotline can offer practical information on maintaining health and general information about a wide variety of treatments, including antiretroviral and prophylaxis for opportunistic infections.

ANTIRETROVIRAL AGENTS

There are currently 5 major classes of antiretroviral drugs :
- Binding and Fusion inhibitors
- Nucleoside and Nucleotide Analogue Reverse Transcriptase Inhibitors (NRTI)
- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)
- Protease Inhibitors (PI)
- Integrase Inhibitors (under research, not commercialized yet)

LAMI PLUS TABLETS
(Zidovudine, Nevirapine & Lamivudine Tablets)

Composition:

Each tablet contains:
Zidovudine BP 300mg
Lamivudine 150mg
Nevirapine 200mg

Presentation:
10x10's

Pharmacology:

It is a combination of three drugs commonly used in the management of Human Immunodeficiency Virus (HIV) infection. Both lamivudine, Nevirapine and zidovudine belong to the nucleoside analogue class of antiretroviral drugs. Both drugs act by inhibiting the reverse transcriptase enzyme of HIV, and by terminating the growth of the DNA chain. Lamivudine in combination with zidovudine & Nevirapine has been shown to have synergistic antiretroviral activity.

Pharmacokinetics:

***Lamivudine**:*

Lamivudine was rapidly absorbed after oral administration in HIV-infected patients. Absolute bioavailability in 12 adult patients was 86% ± 16% (mean ± SD) for the tablet and 87% ± 13% for the oral solution. After oral administration of 2 mg/kg twice a day to nine adults with HIV, the peak serum lamivudine concentration (Cmax) was 1.5 ± 0.5 µg/ml (mean ± SD). The area under the plasma concentration versus time curve (AUC) and Cmax increased in proportion to oral dose over the range from 0.25 to 10 mg/kg.
An investigational 25-mg dosage form of lamivudine was administered orally to 12 asymptomatic, HIV-infected patients on two occasions, once in the fasted state and once with food (1099 kcal; 75 grams fat, 34 grams protein, 72 grams carbohydrate). Absorption of lamivudine was slower in the fed state (Tmax: 3.2 ± 1.3 hours) compared with the fasted state (Tmax: 0.9 ± 0.3 hours); Cmax in the fed state was 40% ± 23% (mean ± SD) lower than in the fasted state. There was no significant difference in systemic exposure (AUC¥) in the fed and fasted states; therefore, Lamivudine may be administered with or without food.
The accumulation ratio of lamivudine in HIV-positive asymptomatic adults with normal renal function was 1.50 following 15 days of oral administration of 2mg/kg b.i.d.
The apparent volume of distribution after IV administration of lamivudine to 20 patients was 1.3 ± 0.4 L/kg, suggesting that lamivudine distributes into extravascular spaces. Volume of distribution was independent of dose and did not correlate with body weight.
Binding of lamivudine to human plasma proteins is low (<36%). In vitro studies showed that, over the concentration range of 0.1 to 100 mg/mL, the amount of lamivudine associated with erythrocytes ranged from 53% to 57% and was independent of concentration.

Metabolism of lamivudine is a minor route of elimination. In man, the only known metabolite of lamivudine is the trans-sulfoxide metabolite. Within 12 hours after a single oral dose of lamivudine in six HIV-infected adults, 5.2% ± 1.4% (mean ± SD) of the dose was excreted as the trans-sulfoxide metabolite in the urine. Serum concentrations of this metabolite have not been determined.
The majority of lamivudine is eliminated unchanged in urine. In 20 patients given a single IV dose, renal clearance was 0.22 ± 0.06 L/hr•kg (mean ± SD), representing 71% ± 16% (mean ± SD) of total clearance of lamivudine.

In most single-dose studies in HIV-infected patients with serum sampling for 24 hours after dosing, the observed mean elimination half-life (T 1/2) ranged from 5 to 7 hours. Total clearance was 0.37 ± 0.05 L/hr•kg (mean ± SD). Oral clearance and elimination half-life were independent of dose and body weight over an oral dosing range from 0.25 to 10 mg/kg.

Zidovudine:

The pharmacokinetics of zidovudine has been evaluated in 22 adult HIV-infected patients in a Phase 1 dose-escalation study. After oral dosing (capsules), zidovudine was rapidly absorbed from the gastrointestinal tract with peak serum concentrations occurring within 0.5 to 1.5 hours. Dose-independent kinetics was observed over the range of 2 mg/kg every 8 hours to 10 mg/kg every 4 hours. The mean zidovudine half-life was approximately 1 hour and ranged from 0.78 to 1.93 hours following oral dosing.
Zidovudine is rapidly metabolized to 3'-azido-3'-deoxy-5'-O- -D-glucopyra-nuronosylthymidine (GZDV) which has an apparent elimination half-life of 1 hour (range 0.61 to 1.73 hours). Following oral administration, urinary recovery of zidovudine and GZDV accounted for 14% and 74% of the dose, respectively, and the total urinary recovery averaged 90% (range 63% to 95%), indicating a high degree of absorption. However, as a result of first-pass metabolism, the average oral capsule bioavailability of zidovudine is 65% (range 52% to 75%). A second metabolite, 3-amino- 3-deoxythymidine (AMT), has been identified in the plasma following single-dose intravenous (IV) administration of zidovudine. AMT area-under-the-curve (AUC) was one fifth of the AUC of zidovudine and had a half-life of 2.7 ± 0.7 hours. In comparison, GZDV AUC was about three-fold greater than the AUC of zidovudine.
Additional pharmacokinetic data following intravenous dosing indicated dose-independent kinetics over the range of 1 to 5 mg/kg with a mean zidovudine half-life of 1.1 hours (range 0.48 to 2.86 hours). Total body clearance averaged 1900 mL/min per 70 kg and the apparent volume of distribution was 1.6 L/kg. Renal clearance is estimated to be 400 mL/min per 70 kg, indicating glomerular filtration and active tubular secretion by the kidneys.
Zidovudine plasma protein binding is 34% to 38%, indicating that drug interactions involving binding site displacement are not anticipated.
The zidovudine cerebrospinal fluid (CSF)/plasma concentration ratio was determined in 39 patients receiving chronic therapy with zidovudine. The median ratio measured in 50 paired samples drawn 1 to 8 hours after the last dose of zidovudine was 0.6.

Nevirapine

Rash, usually within first six weeks of therapy. D/C drug for severe rash or rash accompanied by other symptoms; Stevens-Johnson syndrome has occurred. Fever, headache, nausea, diarrhea, abdominal pain, thrombocytopenia, anemia, leukopenia, ulcerative stomatitis, hepatitis, peripheral neuropathy, paresthesia, or myalgia may also occur.
Grenulocytopenia has been more commonly observed in children. The safety profile of nevirapine in neonates has not been established.

Indications:

Lamivudine + Zidovudine +Nevirapine indicated for the treatment of HIV infection.

Contra-indications:

Lamivudine + Zidovudine + Nevirapine Tablets is contraindicated in patients with clinically significant hypersensitivity to the active substance or to any of the excipients.

Dosage and directions for use:

The recommended oral dose of Lamivudine + Zidovudine + Nevirapine for adults and adolescents (at least 12 years of age) is one capsule (containing 150 mg of lamivudine, 200mg of Nevirapine and 300 mg of zidovudine) twice daily with or without food.

Dose Adjustment:

Because it is a fixed dose combination, Lamivudine + Zidovudine + Nevirapine should not be prescribed for patients requiring dosage adjustment such as those with reduced renal function (creatinine clearance < 50 mL/min), those with low body weight (< 50 kg or II 0 lb), or those experiencing dose-limiting adverse events.

Warning:

Since it is a fixed-dose combination of lamivudine, Nevirapine and zidovudine, it should ordinarily not be administered concomitantly with either lamivudine or zidovudine.
The complete prescribing information for all agents being considered for use with Lamivudine + Zidovudine + Nevirapine should be consulted before combination therapy with Lamivudine + Zidovudine + Nevirapine is initiated.

Bone marrow suppression

Lamivudine + Zidovudine + Nevirapine should be used with caution in patients who have bone marrow compromise evidenced by granulocyte count <1,000 cells/ mm3 or hemoglobin < 9.5 g/dl (See Side Effects). Frequent blood counts are strongly recommended in patients with advanced HIV disease who are treated with Lamivudine + Zidovudine + Nevirapine. For HIVinfected individuals and patients with asymptomatic or early HIV disease, periodic blood counts are recommended.

Lactic acidosis/severe hepatomegaly with steatosis

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including zidovudine and lamivudine. A majority of these cases have been in women. Caution should be exercised when administering Lamivudine + Zidovudine + Nevirapine to any patient, and particularly to those with known risk factors for liver disease. Treatment with Lamivudine + Zidovudine + Nevirapine should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity.

Myopathy

Myopathy and myositis, with pathological changes similar to that produced by HIV disease, have been associated with prolonged use of zidovudine and therefore may occur with therapy with Lamivudine + Zidovudine + Nevirapine. .

Patients with hiv and hepatitis b virus coinfection

In clinical trials and postmarketing experience, some patients with HIV infection who have chronic liver disease due to hepatitis B virus infection experienced clinical or laboratory evidence of recur-rent hepatitis upon discontinuation of lamivudine. Consequences may be more severe in patients with decompensated liver disease.

Side-effects & special precautions:

The most commonly observed side effects during clinical trials were headache, malaise and fatigue, nausea, vomiting, diarrhoea, anorexia, fever/chills, neuropathy, insomnia, dizziness, nasal signs and symptoms, cough, musculoskeletal pain and neutropenia.

Special precautions:

Impaired Renal Function

Reduction of the dosages of lamivudine, Nevirapine and zidovudine is recommended for patients with impaired renal function. Patients with creatinine clearance < 50 ml/min should not receive Lamivudine + Zidovudine + Nevirapine.

Pregnancy

Category C. There are no adequate and well-controlled studies of this combination in pregnant women. Lamivudine + Zidovudine + Nevirapine should be used during pregnancy only if the potential benefits outweigh the risks.

Lactation

It is recommended that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV infection.
Zidovudine is excreted in breast milk. No data are available on this combination or lamivudine. Therefore, there is a potential for adverse effects in nursing infants. Mothers should be instructed not to breast-feed if they are receiving Lamivudine + Zidovudine + Nevirapine.

Paediatric Use

Lamivudine + Zidovudine + Nevirapine should not be administered to paediatric patients less than 12 years of age because it is a fixed-dose combination that cannot be adjusted for this patient population.

Others

Reduction of doses of lamivudine is recommended for patients with low body weight (less than 50 kg or 110 lb). Therefore patients with low body weight should not receive Lamivudine + Zidovudine + Nevirapine.

Drug Interaction:

Coadministration of ganciclovir, interferon-cc, and other bone marrow suppressive or cytotoxic agents may increase the hematologic toxicity of zidovudine.

Known symptoms of overdosage and particulars of its treatment:

There is no known antidote for Lamivudine + Zidovudine + Nevirapine.

***Lamivudine**:*

One case of an adult ingesting 6 gms of lamivudine has been reported. There were no clinical signs or symptoms noted and hematologic tests remained normal. It is not known whether lamivudine can be removed by peritoneal dialysis or hemodialysis.

***Zidovudine**:*

Acute overdoses of zidovudine have been reported in paediatric patients and adults. These involved exposures up to 50 grams. The only consistent findings were nausea and vomiting. Other reported occurrences included headache, dizziness, drowsiness, lethargy, confusion, and one report of a grand mal seizure. Hematologic changes were transient. All patients recovered. Hemodialysis and peritoneal dialysis appear to have a negligible effect on the removal of zidovudine, while elimination of its primary metabolite is enhanced.

Nevirapine

There is no known antidote for nevirapine overdosage. Cases of nevirapine overdose at doses ranging from 800 to 1800 mg per day for up to 15 days have been reported. Patients have experienced events including edema, erythema nodosum, fatigue, fever, headache, insomnia, nausea, pulmonary infiltrates, rash, vertigo, vomiting and weight decrease. All events subsided following discontinuation of nevirapine.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

STV – COMP/30 TABLETS
(Stavudine Nevirapine, & Lamivudine Tablets)

Composition:

Each tablet contains:
Stavudine 40mg/30mg
Lamivudine 150mg
Nevirapine 200 mg

Presentation:
10x10's

Pharmacology:

STV-COMP is a combination of three drugs commonly used in the management of Human Immunodeficiency Virus (HIV) infection. Stavudine, Nevirapine and lamivudine belong to the nucleoside analogue class of antiretroviral drugs. These drugs act by inhibiting the reverse transcriptase of HIV, and by terminating the growth of the DNA chain. Stavudine in combination with lamivudine & Nevirapine has been shown to have synergistic antiretroviral activity.
Each tablet of STV-COMP contains half of the commonly prescribed daily doses of stavudine, Nevirapine and lamivudine. With the availability of this combination tablet patients may be better able to adhere to complex drug treatment regimens, thereby enhancing compliance.

Pharmacokinetics:

***Lamivudine**:*

Lamivudine was rapidly absorbed after oral administration in HIV-infected patients. Absolute bioavailability in 12 adult patients was 86% ± 16% (mean ± SD) for the tablet and 87% ± 13% for the oral solution. After oral administration of 2 mg/kg twice a day to nine adults with HIV, the peak serum lamivudine concentration (Cmax) was 1.5 ± 0.5 µg/ml (mean ± SD). The area under the plasma concentration versus time curve (AUC) and Cmax increased in proportion to oral dose over the range from 0.25 to 10 mg/kg.
An investigational 25-mg dosage form of lamivudine was administered orally to 12 asymptomatic, HIV-infected patients on two occasions, once in the fasted state and once with food (1099 kcal; 75 grams fat, 34 grams protein, 72 grams carbohydrate). Absorption of lamivudine was slower in the fed state (Tmax: 3.2 ± 1.3 hours) compared with the fasted state (Tmax: 0.9 ± 0.3 hours); Cmax in the fed state was 40% ± 23% (mean ± SD) lower than in the fasted state. There was no significant difference in systemic exposure (AUC¥) in the fed and fasted states; therefore, Lamivudine may be administered with or without food.
The accumulation ratio of lamivudine in HIV-positive asymptomatic adults with normal renal function was 1.50 following 15 days of oral administration of 2mg/kg b.i.d.
The apparent volume of distribution after IV administration of lamivudine to 20 patients was 1.3 ± 0.4 L/kg, suggesting that lamivudine distributes into extravascular spaces. Volume of distribution was independent of dose and did not correlate with body weight.
Binding of lamivudine to human plasma proteins is low (<36%). In vitro studies showed that, over the concentration range of 0.1 to 100 mg/mL, the amount of lamivudine associated with erythrocytes ranged from 53% to 57% and was independent of concentration.
Metabolism of lamivudine is a minor route of elimination. In man, the only known metabolite of lamivudine is the trans-sulfoxide metabolite. Within 12 hours after a single oral dose of lamivudine in six HIV-infected adults, 5.2% ± 1.4% (mean ± SD) of the dose was excreted as the trans-sulfoxide metabolite in the urine. Serum concentrations of this metabolite have not been determined.

The majority of lamivudine is eliminated unchanged in urine. In 20 patients given a single IV dose, renal clearance was 0.22 ± 0.06 L/hr•kg (mean ± SD), representing 71% ± 16% (mean ± SD) of total clearance of lamivudine.
In most single-dose studies in HIV-infected patients with serum sampling for 24 hours after dosing, the observed mean elimination half-life (T 1/2) ranged from 5 to 7 hours. Total clearance was 0.37 ± 0.05 L/hr•kg (mean ± SD). Oral clearance and elimination half-life were independent of dose and body weight over an oral dosing range from 0.25 to 10 mg/kg.

Stavudine
:
The pharmacokinetics of stavudine have been evaluated in HIV-infected adult and pediatric patients. Peak plasma concentrations (Cmax) and area under the plasma concentration-time curve (AUC) increased in proportion to dose after both single and multiple doses ranging from 0.03 to 4 mg/kg. There was no significant accumulation of stavudine with repeated administration every 6, 8, or 12 hours.

Absorption*:*

Following oral administration, stavudine is rapidly absorbed, with peak plasma concentrations occurring within 1 hour after dosing. The systemic exposure to stavudine is the same following administration as capsules or solution.

Distribution*:*

Binding of stavudine to serum proteins was negligible over the concentration range of 0.01 to 11.4 µg/mL. Stavudine distributes equally between red blood cells and plasma.

Metabolism

*:*The metabolic fate of stavudine has not been elucidated in humans. Excretion- Renal elimination accounted for about 40% of the overall clearance regardless of the route of administration. The mean renal clearance was about twice the average endogenous creatinine clearance, indicating active tubular secretion in addition to glomerular filtration.

Pharmacokinetics:

Absorption:

Nevirapine is readily absorbed (>90%) after oral administration in healthy volunteers and in adults with HIV-1 infection. Peak plasma nevirapine concentrations of 2 ± 0.4 mc g/mL (7.5 mc M) were attained by 4 hours following a single 200 mg dose. Following multiple doses, nevirapine peak concentrations appear to increase linearly in the dose range of 200 to 400 mg/day. Steady state trough nevirapine concentrations of 4.5 ± 1.9 mc g/mL (17 ± 7 mc M), (n = 242) were attained at 400 mg/day. When Nevirapine (200 mg) was administered to 24 healthy adults (12 female, 12 male), with either a high fat breakfast (857 kcal, 50 g fat, 53% of calories from fat) or antacid (Maalox® 30 mL), the extent of nevirapine absorption (AUC) was comparable to that observed under fasting conditions. In a separate study in HIV-1-infected patients (n=6), nevirapine steady-state systemic exposure (AUCt) was not significantly altered by ddI, which is formulated with an alkaline buffering agent. Nevirapine may be administered with or without food, antacid or ddI.

Distribution:

Nevirapine is highly lipophilic and is essentially nonionized at physiologic pH. Following intravenous administration to healthy adults, the apparent volume of distribution (Vdss) of nevirapine was 1.21 ± 0.09 L/kg, suggesting that nevirapine is widely distributed in humans. Nevirapine readily crosses the placenta and is found in breast milk. Nevirapine is about 60% bound to plasma proteins in the plasma concentration range

of 1-10 mc g/mL. Nevirapine concentrations in human cerebrospinal fluid (n=6) were 45% (± 5%) of the concentrations in plasma; this ratio is approximately equal to the fraction not bound to plasma protein.

Metabolism/Elimination:

In vivo studies in humans and in vitro studies with human liver microsomes have shown that nevirapine is extensively biotransformed via cytochrome P450 (oxidative) metabolism to several hydroxylated metabolites. In vitro studies with human liver microsomes suggest that oxidative metabolism of nevirapine is mediated primarily by cytochrome P450 isozymes from the CYP3A family, although other isozymes may have a secondary role. In a mass balance/excretion study in eight healthy male volunteers dosed to steady state with nevirapine 200 mg given twice daily followed by a single 50 mg dose of 14C-nevirapine, approximately 91.4 ± 10.5% of the radiolabeled dose was recovered, with urine (81.3 ± 11.1%) representing the primary route of excretion compared to feces (10.1 ± 1.5%). Greater than 80% of the radioactivity in urine was made up of glucuronide conjugates of hydroxylated metabolites. Thus cytochrome P450 metabolism, glucuronide conjugation, and urinary excretion of glucuronidated metabolites represent the primary route of nevirapine biotransformation and elimination in humans. Only a small fraction (<5%) of the radioactivity in urine (representing <3% of the total dose) was made up of parent compound; therefore, renal excretion plays a minor role in elimination of the parent compound.
Nevirapine has been shown to be an inducer of hepatic cytochrome P450 metabolic enzymes. The pharmacokinetics of autoinduction are characterized by an approximately 1.5 to 2 fold increase in the apparent oral clearance of nevirapine as treatment continues from a single dose to two-to-four weeks of dosing with 200 - 400 mg/day. Autoinduction also results in a corresponding decrease in the terminal phase half-life of nevirapine in plasma from approximately 45 hours (single dose) to approximately 25-30 hours following multiple dosing with 200 - 400 mg/day.

Indications:

Lamivudine + Stavudine + Nevirapine is indicated for the treatment of HIV infection.

Contra-indications:

Lamivudine + Stavudine + Nevirapine Tablets is contraindicated in patients with clinically significant hypersensitivity to the active substance or to any of the excipients.

Dosage and directions for use:

1 tablet twice daily for patients weighing > 60 kg
Dose Adjustment: Because it is a fixed-dose combination, it should not be prescribed for patients requiring dosage adjustment, such as those with reduced renal function (creatinine clearance < 50 ml/min), those with low body weight (< 50 kg or 110 lbs), or those experiencing dose-limiting adverse events.

Warning:

LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS
Lactic acidosis/severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including stavudine, Nevirapine and lamivudine. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Caution should be exercised when administering stavudine to any patient, and particularly to those with known risk factors for liver disease. Cases have also been reported in patients with no known risk factors. Treatment should be discontinued in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked aminotransferase elevations).

PERIPHERAL NEUROPATHY

Stavudine therapy can be associated with severe peripheral neuropathy, which is dose-related. It has occurred more frequently in patients with advanced HIV infection, a history of neuropathy, or concurrent neurotoxic drug therapy, including didanosine.
Patients should be monitored for the development of neuropathy that is usually characterized by numbness, tingling or pain in the feet or hands. Stavudine-related peripheral neuropathy may resolve if therapy is withdrawn promptly. In some cases, symptoms may worsen temporarily following discontinuation of therapy.
If symptoms resolve completely, resumption of treatment with stavudine may be considered using the following dosage schedule for adults:
20 mg twice daily for patients > 60 kg
15 mg twice daily for patients < 60 kg
IMPAIRED RENAL FUNCTION
Reduction of the dosage of stavudine, Nevirapine and lamivudine is required in patients with a creatinine clearance of 50 ml/min or less. Hence, it cannot be used in this patient population.
PATIENTS WITH HIV AND HEPATITIS B VIRUS COINFECTION
In clinical trials, some patients with HIV infection who have chronic liver disease due to hepatitis B virus infection experienced clinical or laboratory evidence of recurrent hepatitis upon discontinuation of lamivudine. Consequences may be more severe in patients with decompensated liver disease.

Side-effects & special precautions:

Lamivudine

Pancreatitis has been reported with the use of lamivudine.
Lactic acidosis and hepatic steatosis, hepatitis and liver failure have been reported with the use of antiretroviral nucleoside analogs, alone or in combination.
Other side effects associated with the use of lamivudine are diarrhea, malaise and fatigue, headache, nausea and vomiting, abdominal pain and discomfort, peripheral neuropathy, arthralgias, myalgias, skin rash, pruritus, transient neutropenia and thrombocytopenia and rarely, pancreatitis. Transiently elevated levels of hepatic enzymes and bilirubin (> 5 times the normal level) have also been observed occasionally during treatment with the drug. Resolution of transient neutropenia and raised hepatic and bilirubin levels occurred without dosage modification or discontinuation of therapy.

Stavudine

Therapy with stavudine can be associated with severe peripheral neuropathy, which is dose related and occurs more frequently in patients with advanced HIV infection or who have previously experienced peripheral neuropathy.
Lactic acidosis and hepatic steatosis, hepatitis and liver failure have been reported with the use of antiretroviral nucleoside analogues, alone or in combination.
Rash, diarrhoea, nausea/vomiting, pancreatitis, dementia and other peripheral neurologic symptoms have also been associated with the use of stavudine.
Nevirapine

Rash, usually within first six weeks of therapy. D/C drug for severe rash or rash accompanied by other symptoms; Stevens-Johnson syndrome has occurred. Fever, headache, nausea, diarrhea, abdominal pain, thrombocytopenia, anemia, leukopenia, ulcerative stomatitis, hepatitis, peripheral neuropathy, paresthesia, or myalgia may also occur.
Grenulocytopenia has been more commonly observed in children. The safety profile of nevirapine in neonates has not been established.

Special precautions:

PREGNANCY

Lamivudine, nevirapine and stavudine are classified under category C. There are no adequate and well-controlled studies in pregnant women. Lamivudine, nevirapine and Stavudine should be used during pregnancy only if the potential benefits outweigh the potential risk.

LACTATION

It is recommended that HIV-infected mothers do not breast-feed their infants to avoid risking postnatal transmission of HIV infection. It is not known whether stavudine, nevirapine or lamivudine are excreted in human milk.

PAEDIATRICS

Lamivudine, nevirapine and Stavudine is not intended for use in paediatric patients.

Drug Interaction:

Trimethoprim 160 mg/sulphamethoxazole 800 mg once daily has been shown to increase lamivudine exposure (AUC).

Known symptoms of overdosage and particulars of its treatment:

Lamivudine

There is no known antidote for lamivudine. It is not known whether lamivudine can be removed by peritoneal dialysis or hemodialysis.

Stavudine

Stavudine can be removed by hemodialysis. Experience with adults treated with 12 to 24 times the recommended daily dosage revealed no acute toxicity. Complications of chronic overdosage include peripheral neuropathy and hepatic toxicity

Nevirapine

There is no known antidote for nevirapine overdosage. Cases of nevirapine overdose at doses ranging from 800 to 1800 mg per day for up to 15 days have been reported. Patients have experienced events including edema, erythema nodosum, fatigue, fever, headache, insomnia, nausea, pulmonary infiltrates, rash, vertigo, vomiting and weight decrease. All events subsided following discontinuation of nevirapine.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

ZVD PLUS TABLETS
(Zidovudine & Lamivudine Tablets)

Composition:

Each tablet contains:
Zidovudine BP 300mg
Lamivudine 150mg

Presentation:
10x10's

Pharmacology:

It is a combination of two drugs commonly used in the management of Human Immunodeficiency Virus (HIV) infection. Both lamivudine and zidovudine belong to the nucleoside analogue class of antiretroviral drugs. Both drugs act by inhibiting the reverse transcriptase enzyme of HIV, and by terminating the growth of the DNA chain. Lamivudine in combination with zidovudine has been shown to have synergistic antiretroviral activity.

Pharmacokinetics:

Lamivudine*:*

Lamivudine was rapidly absorbed after oral administration in HIV-infected patients. Absolute bioavailability in 12 adult patients was 86% ± 16% (mean ± SD) for the tablet and 87% ± 13% for the oral solution. After oral administration of 2 mg/kg twice a day to nine adults with HIV, the peak serum lamivudine concentration (Cmax) was 1.5 ± 0.5 µg/ml (mean ± SD). The area under the plasma concentration versus time curve (AUC) and Cmax increased in proportion to oral dose over the range from 0.25 to 10 mg/kg.
An investigational 25-mg dosage form of lamivudine was administered orally to 12 asymptomatic, HIV-infected patients on two occasions, once in the fasted state and once with food (1099 kcal; 75 grams fat, 34 grams protein, 72 grams carbohydrate). Absorption of lamivudine was slower in the fed state (Tmax: 3.2 ± 1.3 hours) compared with the fasted state (Tmax: 0.9 ± 0.3 hours); Cmax in the fed state was 40% ± 23% (mean ± SD) lower than in the fasted state. There was no significant difference in systemic exposure (AUC¥) in the fed and fasted states; therefore, Lamivudine may be administered with or without food.
The accumulation ratio of lamivudine in HIV-positive asymptomatic adults with normal renal function was 1.50 following 15 days of oral administration of 2mg/kg b.i.d.
The apparent volume of distribution after IV administration of lamivudine to 20 patients was 1.3 ± 0.4 L/kg, suggesting that lamivudine distributes into extravascular spaces. Volume of distribution was independent of dose and did not correlate with body weight.
Binding of lamivudine to human plasma proteins is low (<36%). In vitro studies showed that, over the concentration range of 0.1 to 100 mg/mL, the amount of lamivudine associated with erythrocytes ranged from 53% to 57% and was independent of concentration.

Metabolism of lamivudine is a minor route of elimination. In man, the only known metabolite of lamivudine is the trans-sulfoxide metabolite. Within 12 hours after a single oral dose of lamivudine in six HIV-infected adults, 5.2% ± 1.4% (mean ± SD) of the dose was excreted as the trans-sulfoxide metabolite in the urine. Serum concentrations of this metabolite have not been determined.
The majority of lamivudine is eliminated unchanged in urine. In 20 patients given a single IV dose, renal clearance was 0.22 ± 0.06 L/hr•kg (mean ± SD), representing 71% ± 16% (mean ± SD) of total clearance of lamivudine.

In most single-dose studies in HIV-infected patients with serum sampling for 24 hours after dosing, the observed mean elimination half-life (T 1/2) ranged from 5 to 7 hours. Total clearance was 0.37 ± 0.05 L/hr•kg (mean ± SD). Oral clearance and elimination half-life were independent of dose and body weight over an oral dosing range from 0.25 to 10 mg/kg.

Zidovudine*:*

The pharmacokinetics of zidovudine has been evaluated in 22 adult HIV-infected patients in a Phase 1 dose-escalation study. After oral dosing (capsules), zidovudine was rapidly absorbed from the gastrointestinal tract with peak serum concentrations occurring within 0.5 to 1.5 hours. Dose-independent kinetics was observed over the range of 2 mg/kg every 8 hours to 10 mg/kg every 4 hours. The mean zidovudine half-life was approximately 1 hour and ranged from 0.78 to 1.93 hours following oral dosing.
Zidovudine is rapidly metabolized to 3'-azido-3'-deoxy-5'-O- -D-glucopyra-nuronosylthymidine (GZDV) which has an apparent elimination half-life of 1 hour (range 0.61 to 1.73 hours). Following oral administration, urinary recovery of zidovudine and GZDV accounted for 14% and 74% of the dose, respectively, and the total urinary recovery averaged 90% (range 63% to 95%), indicating a high degree of absorption. However, as a result of first-pass metabolism, the average oral capsule bioavailability of zidovudine is 65% (range 52% to 75%). A second metabolite, 3-amino- 3-deoxythymidine (AMT), has been identified in the plasma following single-dose intravenous (IV) administration of zidovudine. AMT area-under-the-curve (AUC) was one fifth of the AUC of zidovudine and had a half-life of 2.7 ± 0.7 hours. In comparison, GZDV AUC was about three-fold greater than the AUC of zidovudine.
Additional pharmacokinetic data following intravenous dosing indicated dose-independent kinetics over the range of 1 to 5 mg/kg with a mean zidovudine half-life of 1.1 hours (range 0.48 to 2.86 hours). Total body clearance averaged 1900 mL/min per 70 kg and the apparent volume of distribution was 1.6 L/kg. Renal clearance is estimated to be 400 mL/min per 70 kg, indicating glomerular filtration and active tubular secretion by the kidneys.
Zidovudine plasma protein binding is 34% to 38%, indicating that drug interactions involving binding site displacement are not anticipated.
The zidovudine cerebrospinal fluid (CSF)/plasma concentration ratio was determined in 39 patients receiving chronic therapy with zidovudine. The median ratio measured in 50 paired samples drawn 1 to 8 hours after the last dose of zidovudine was 0.6.

Indications:

Lamivudine + Zidovudine is indicated for the treatment of HIV infection.

Contra-indications:

Lamivudine + Zidovudine Tablets is contraindicated in patients with clinically significant hypersensitivity to the active substance or to any of the excipients.

Dosage and directions for use:

The recommended oral dose of Lamivudine + Zidovudine for adults and adolescents (at least 12 years of age) is one capsule (containing 150 mg of lamivudine and 300 mg of zidovudine) twice daily with or without food.

Dose Adjustment:

Because it is a fixed dose combination, Lamivudine + Zidovudine should not be prescribed for patients requiring dosage adjustment such as those with reduced renal function (creatinine clearance < 50 mL/min), those with low body weight (< 50 kg or II 0 lb), or those experiencing dose-limiting adverse events.

Warning:

Since it is a fixed-dose combination of lamivudine and zidovudine, it should ordinarily not be administered concomitantly with either lamivudine or zidovudine.
The complete prescribing information for all agents being considered for use with Lamivudine + Zidovudine should be consulted before combination therapy with Lamivudine + Zidovudine is initiated.

Bone marrow suppression

Lamivudine + Zidovudine should be used with caution in patients who have bone marrow compromise evidenced by granulocyte count <1,000 cells/ mm3 or hemoglobin < 9.5 g/dl (See Side Effects).
Frequent blood counts are strongly recommended in patients with advanced HIV disease who are treated with Lamivudine + Zidovudine. For HIVinfected individuals and patients with asymptomatic or early HIV disease, periodic blood counts are recommended.

Lactic acidosis/severe hepatomegaly with steatosis

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including zidovudine and lamivudine. A majority of these cases have been in women. Caution should be exercised when administering Lamivudine + Zidovudine to any patient, and particularly to those with known risk factors for liver disease. Treatment with Lamivudine + Zidovudine should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity.

Myopathy

Myopathy and myositis, with pathological changes similar to that produced by HIV disease, have been associated with prolonged use of zidovudine and therefore may occur with therapy with Lamivudine + Zidovudine .

Patients with hiv and hepatitis b virus coinfection

In clinical trials and postmarketing experience, some patients with HIV infection who have chronic liver disease due to hepatitis B virus infection experienced clinical or laboratory evidence of recur-rent hepatitis upon discontinuation of lamivudine. Consequences may be more severe in patients with decompensated liver disease.

Side-effects & special precautions:

The most commonly observed side effects during clinical trials were headache, malaise and fatigue, nausea, vomiting, diarrhoea, anorexia, fever/chills, neuropathy, insomnia, dizziness, nasal signs and symptoms, cough, musculoskeletal pain and neutropenia.

Special precautions:

Impaired Renal Function

Reduction of the dosages of lamivudine and zidovudine is recommended for patients with impaired renal function. Patients with creatinine clearance < 50 ml/min should not receive Lamivudine + Zidovudine.

Pregnancy

Category C. There are no adequate and well-controlled studies of this combination in pregnant women. Lamivudine + Zidovudine should be used during pregnancy only if the potential benefits outweigh the risks.

Lactation

It is recommended that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV infection.
Zidovudine is excreted in breast milk. No data are available on this combination or lamivudine. Therefore, there is a potential for adverse effects in nursing infants. Mothers should be instructed not to breast-feed if they are receiving Lamivudine + Zidovudine.

Paediatric Use

Lamivudine + Zidovudine should not be administered to paediatric patients less than 12 years of age because it is a fixed-dose combination that cannot be adjusted for this patient population.

Others

Reduction of doses of lamivudine is recommended for patients with low body weight (less than 50 kg or 110 lb). Therefore patients with low body weight should not receive Lamivudine + Zidovudine.

Drug Interaction:

Coadministration of ganciclovir, interferon-cc, and other bone marrow suppressive or cytotoxic agents may increase the hematologic toxicity of zidovudine.

Known symptoms of overdosage and particulars of its treatment:

There is no known antidote for Lamivudine + Zidovudine.

Lamivudine*:*

One case of an adult ingesting 6 gms of lamivudine has been reported. There were no clinical signs or symptoms noted and hematologic tests remained normal. It is not known whether lamivudine can be removed by peritoneal dialysis or hemodialysis.

Zidovudine*:*

Acute overdoses of zidovudine have been reported in paediatric patients and adults. These involved exposures up to 50 grams. The only consistent findings were nausea and vomiting. Other reported occurrences included headache, dizziness, drowsiness, lethargy, confusion, and one report of a grand mal seizure. Hematologic changes were transient. All patients recovered. Hemodialysis and peritoneal dialysis appear to have a negligible effect on the removal of zidovudine, while elimination of its primary metabolite is enhanced.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

STV PLUS/30 TABLETS
(Stavudine & Lamivudine Tablets)

Composition:

Each tablet contains:
Stavudine 40mg/30mg
Lamivudine 150mg

Presentation:
10x10's

Pharmacology:

STV PLUS is a combination of two drugs commonly used in the management of Human Immunodeficiency Virus (HIV) infection. Both stavudine and lamivudine belong to the nucleoside analogue class of antiretroviral drugs. Both drugs act by inhibiting the reverse transcriptase of HIV, and by terminating the growth of the DNA chain. Stavudine in combination with lamivudine has been shown to have synergistic antiretroviral activity.
Each tablet of STV PLUS contains half of the commonly prescribed daily doses of both stavudine and lamivudine. With the availability of this combination tablet patients may be better able to adhere to complex drug treatment regimens, thereby enhancing compliance.

Pharmacokinetics:

Lamivudine*:*

Lamivudine was rapidly absorbed after oral administration in HIV-infected patients. Absolute bioavailability in 12 adult patients was 86% ± 16% (mean ± SD) for the tablet and 87% ± 13% for the oral solution. After oral administration of 2 mg/kg twice a day to nine adults with HIV, the peak serum lamivudine concentration (Cmax) was 1.5 ± 0.5 µg/ml (mean ± SD). The area under the plasma concentration versus time curve (AUC) and Cmax increased in proportion to oral dose over the range from 0.25 to 10 mg/kg.
An investigational 25-mg dosage form of lamivudine was administered orally to 12 asymptomatic, HIV-infected patients on two occasions, once in the fasted state and once with food (1099 kcal; 75 grams fat, 34 grams protein, 72 grams carbohydrate). Absorption of lamivudine was slower in the fed state (Tmax: 3.2 ± 1.3 hours) compared with the fasted state (Tmax: 0.9 ± 0.3 hours); Cmax in the fed state was 40% ± 23% (mean ± SD) lower than in the fasted state. There was no significant difference in systemic exposure (AUC¥) in the fed and fasted states; therefore, Lamivudine may be administered with or without food.
The accumulation ratio of lamivudine in HIV-positive asymptomatic adults with normal renal function was 1.50 following 15 days of oral administration of 2mg/kg b.i.d.
The apparent volume of distribution after IV administration of lamivudine to 20 patients was 1.3 ± 0.4 L/kg, suggesting that lamivudine distributes into extravascular spaces. Volume of distribution was independent of dose and did not correlate with body weight.
Binding of lamivudine to human plasma proteins is low (<36%). In vitro studies showed that, over the concentration range of 0.1 to 100 mg/mL, the amount of lamivudine associated with erythrocytes ranged from 53% to 57% and was independent of concentration.
Metabolism of lamivudine is a minor route of elimination. In man, the only known metabolite of lamivudine is the trans-sulfoxide metabolite. Within 12 hours after a single oral dose of lamivudine in six HIV-infected adults, 5.2% ± 1.4% (mean ± SD) of the dose was excreted as the trans-sulfoxide metabolite in the urine. Serum concentrations of this metabolite have not been determined.
The majority of lamivudine is eliminated unchanged in urine. In 20 patients given a single IV dose, renal clearance was 0.22 ± 0.06 L/hr•kg (mean ± SD), representing 71% ± 16% (mean ± SD) of total clearance of lamivudine.

In most single-dose studies in HIV-infected patients with serum sampling for 24 hours after dosing, the observed mean elimination half-life (T 1/2) ranged from 5 to 7 hours. Total clearance was 0.37 ± 0.05 L/hr•kg (mean ± SD). Oral clearance and elimination half-life were independent of dose and body weight over an oral dosing range from 0.25 to 10 mg/kg.

Stavudine*:*

The pharmacokinetics of stavudine have been evaluated in HIV-infected adult and pediatric patients. Peak plasma concentrations (Cmax) and area under the plasma concentration-time curve (AUC) increased in proportion to dose after both single and multiple doses ranging from 0.03 to 4 mg/kg. There was no significant accumulation of stavudine with repeated administration every 6, 8, or 12 hours.
Absorption: Following oral administration, stavudine is rapidly absorbed, with peak plasma concentrations occurring within 1 hour after dosing. The systemic exposure to stavudine is the same following administration as capsules or solution.
Distribution: Binding of stavudine to serum proteins was negligible over the concentration range of 0.01 to 11.4 µg/mL. Stavudine distributes equally between red blood cells and plasma.
*Metabolism:*The metabolic fate of stavudine has not been elucidated in humans. Excretion- Renal elimination accounted for about 40% of the overall clearance regardless of the route of administration. The mean renal clearance was about twice the average endogenous creatinine clearance, indicating active tubular secretion in addition to glomerular filtration.

Indications:

Lamivudine + Stavudine is indicated for the treatment of HIV infection.

Contra-indications:

Lamivudine + Stavudine Tablets is contraindicated in patients with clinically significant hypersensitivity to the active substance or to any of the excipients.

Dosage and directions for use:

1 tablet twice daily for patients weighing > 60 kg
Dose Adjustment: Because it is a fixed-dose combination, it should not be prescribed for patients requiring dosage adjustment, such as those with reduced renal function (creatinine clearance < 50 ml/min), those with low body weight (< 50 kg or 110 lbs), or those experiencing dose-limiting adverse events.

Warning:

LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS

Lactic acidosis/severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including stavudine and lamivudine. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Caution should be exercised when administering stavudine to any patient, and particularly to those with known risk factors for liver disease. Cases have also been reported in patients with no known risk factors. Treatment should be discontinued in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked aminotransferase elevations).

PERIPHERAL NEUROPATHY

Stavudine therapy can be associated with severe peripheral neuropathy, which is dose-related. It has occurred more frequently in patients with advanced HIV infection, a history of neuropathy, or concurrent neurotoxic drug therapy, including didanosine.
Patients should be monitored for the development of neuropathy that is usually characterized by numbness, tingling or pain in the feet or hands. Stavudine-related peripheral neuropathy may resolve if therapy is withdrawn promptly. In some cases, symptoms may worsen temporarily following discontinuation of therapy.
If symptoms resolve completely, resumption of treatment with stavudine may be considered using the following dosage schedule for adults:
20 mg twice daily for patients > 60 kg
15 mg twice daily for patients < 60 kg

IMPAIRED RENAL FUNCTION

Reduction of the dosage of both stavudine and lamivudine is required in patients with a creatinine clearance of 50 ml/min or less. Hence, it cannot be used in this patient population.

PATIENTS WITH HIV AND HEPATITIS B VIRUS COINFECTION

In clinical trials, some patients with HIV infection who have chronic liver disease due to hepatitis B virus infection experienced clinical or laboratory evidence of recurrent hepatitis upon discontinuation of lamivudine. Consequences may be more severe in patients with decompensated liver disease.

Side-effects & special precautions:

Lamivudine

Pancreatitis has been reported with the use of lamivudine.
Lactic acidosis and hepatic steatosis, hepatitis and liver failure have been reported with the use of antiretroviral nucleoside analogs, alone or in combination.
Other side effects associated with the use of lamivudine are diarrhea, malaise and fatigue, headache, nausea and vomiting, abdominal pain and discomfort, peripheral neuropathy, arthralgias, myalgias, skin rash, pruritus, transient neutropenia and thrombocytopenia and rarely, pancreatitis. Transiently elevated levels of hepatic enzymes and bilirubin (> 5 times the normal level) have also been observed occasionally during treatment with the drug. Resolution of transient neutropenia and raised hepatic and bilirubin levels occurred without dosage modification or discontinuation of therapy.

Stavudine

Therapy with stavudine can be associated with severe peripheral neuropathy, which is dose related and occurs more frequently in patients with advanced HIV infection or who have previously experienced peripheral neuropathy.
Lactic acidosis and hepatic steatosis, hepatitis and liver failure have been reported with the use of antiretroviral nucleoside analogues, alone or in combination.
Rash, diarrhoea, nausea/vomiting, pancreatitis, dementia and other peripheral neurologic symptoms have also been associated with the use of stavudine.

Special precautions:

PREGNANCY

Both lamivudine and stavudine are classified under category C. There are no adequate and well-controlled studies in pregnant women. Lamivudine and Stavudine should be used during pregnancy only if the potential benefits outweigh the potential risk.

LACTATION

It is recommended that HIV-infected mothers do not breast-feed their infants to avoid risking postnatal transmission of HIV infection. It is not known whether stavudine or lamivudine are excreted in human milk.

PAEDIATRICS

Lamivudine and Stavudine is not intended for use in paediatric patients.

Drug Interaction:
Trimethoprim 160 mg/sulphamethoxazole 800 mg once daily has been shown to increase lamivudine exposure (AUC).

Known symptoms of overdosage and particulars of its treatment:

Lamivudine

There is no known antidote for lamivudine. It is not known whether lamivudine can be removed by peritoneal dialysis or hemodialysis.

Stavudine

Stavudine can be removed by hemodialysis. Experience with adults treated with 12 to 24 times the recommended daily dosage revealed no acute toxicity. Complications of chronic overdosage include peripheral neuropathy and hepatic toxicity

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

NEV 200 TABLETS
(Nevirapine Tablets 200mg)

Composition:

Each uncoated tablet contains:
Nevirapine 200mg

Presentation:
10x10's

Pharmacology:

Nevirapine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) of HIV-1. Nevirapine binds directly to reverse transcriptase (RT) and blocks the RNA-dependent and DNA-dependent DNA polymerase activities by causing a disruption of the enzyme's catalytic site. The activity of nevirapine does not compete with template or nucleoside triphosphates. HIV-2 RT and eukaryotic DNA polymerases (such as human DNA polymerases a , ß, g , or d) are not inhibited by nevirapine.

Pharmacokinetics:

Absorption:

Nevirapine is readily absorbed (>90%) after oral administration in healthy volunteers and in adults with HIV-1 infection. Peak plasma nevirapine concentrations of 2 ± 0.4 mc g/mL (7.5 mc M) were attained by 4 hours following a single 200 mg dose. Following multiple doses, nevirapine peak concentrations appear to increase linearly in the dose range of 200 to 400 mg/day. Steady state trough nevirapine concentrations of 4.5 ± 1.9 mc g/mL (17 ± 7 mc M), (n = 242) were attained at 400 mg/day. When Nevirapine (200 mg) was administered to 24 healthy adults (12 female, 12 male), with either a high fat breakfast (857 kcal, 50 g fat, 53% of calories from fat) or antacid (Maalox® 30 mL), the extent of nevirapine absorption (AUC) was comparable to that observed under fasting conditions. In a separate study in HIV-1-infected patients (n=6), nevirapine steady-state systemic exposure (AUCt) was not significantly altered by ddI, which is formulated with an alkaline buffering agent. Nevirapine may be administered with or without food, antacid or ddI.

Distribution:

Nevirapine is highly lipophilic and is essentially nonionized at physiologic pH. Following intravenous administration to healthy adults, the apparent volume of distribution (Vdss) of nevirapine was 1.21 ± 0.09 L/kg, suggesting that nevirapine is widely distributed in humans. Nevirapine readily crosses the placenta and is found in breast milk. Nevirapine is about 60% bound to plasma proteins in the plasma concentration range of 1-10 mc g/mL. Nevirapine concentrations in human cerebrospinal fluid (n=6) were 45% (± 5%) of the concentrations in plasma; this ratio is approximately equal to the fraction not bound to plasma protein.

Metabolism/Elimination:

In vivo studies in humans and in vitro studies with human liver microsomes have shown that nevirapine is extensively biotransformed via cytochrome P450 (oxidative) metabolism to several hydroxylated metabolites. In vitro studies with human liver microsomes suggest that oxidative metabolism of nevirapine is mediated primarily by cytochrome P450 isozymes from the CYP3A family, although other isozymes may have a secondary role. In a mass balance/excretion study in eight healthy male volunteers dosed to steady state with nevirapine 200 mg given twice daily followed by a single 50 mg dose of 14C-nevirapine, approximately 91.4 ± 10.5% of the radiolabeled dose was recovered, with urine (81.3 ± 11.1%) representing the primary route of excretion compared to feces (10.1 ± 1.5%). Greater than 80% of the radioactivity in urine was made up of glucuronide conjugates of hydroxylated metabolites. Thus cytochrome P450 metabolism, glucuronide conjugation, and urinary excretion of glucuronidated metabolites represent the primary route of nevirapine biotransformation and elimination in humans. Only a small fraction (<5%) of the radioactivity in urine (representing <3% of the total dose) was made up of parent compound; therefore, renal excretion plays a minor role in elimination of the parent compound.
Nevirapine has been shown to be an inducer of hepatic cytochrome P450 metabolic enzymes. The pharmacokinetics of autoinduction are characterized by an approximately 1.5 to 2 fold increase in the apparent oral clearance of nevirapine as treatment continues from a single dose to two-to-four weeks of dosing with 200 - 400 mg/day. Autoinduction also results in a corresponding decrease in the terminal phase half-life of nevirapine in plasma from approximately 45 hours (single dose) to approximately 25-30 hours following multiple dosing with 200 - 400 mg/day.

Indications:

Nevirapine is indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection.
Resistant virus emerges rapidly and uniformly when nevirapine is administered as monotherapy. Therefore, nevirapine should always be administered in combination with at least one additional antiretroviral agent.

Contra-indications:

Nevirapine is contraindicated in patients with clinically significant hypersensitivity to any of the components contained in the tablet.

Dosage and directions for use:

Adults/adolescents:

The recommended dose is one 200-mg tablet once daily for the first 14 days of therapy (the "lead-in" period) followed by the standard dose of one 200-mg tablet twice daily. The lead-in period may reduce the incidence of drug-related rash.
Nevirapine may be taken with or without food.

Pediatric (2 months up to 8 years):

4 mg/kg once daily for the first 14 days followed by 7 mg/kg twice daily thereafter, not to exceed 400 mg. Because of nevirapine's long half-life, patients discontinuing antiretroviral therapy should stop taking nevirapine 1 or 2 days before stopping NRTIs to minimize the risk of acquiring NNRTI resistance during the washout period.

Warnings:

Severe, life-threatening skin reactions, including fatal cases, have occurred in patients treated with nevirapine. These have included cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, and hypersensitivity reactions characterized by rash, constitutional findings, and organ dysfunction. Patients developing signs or symptoms of severe skin reactions or hypersensitivity reactions (including, but not limited to, severe rash or rash accompanied by fever, blisters, oral lesions, conjunctivitis, facial edema, muscle or joint aches, general malaise and/or significant hepatic abnormalities) must discontinue nevirapine as soon as possible.
Nevirapine therapy must be initiated with a 14-day lead-in period of 200 mg/day (4 mg/ kg/day in paediatric patients), which has been shown to reduce the frequency of rash. If rash is observed during this lead-in period, dose escalation should not occur until the rash has resolved.
Severe or life-threatening hepatotoxicity, including fatal fulminant hepatitis (transaminase elevations, with or without hyperbilirubinemia, prolonged partial thromboplastin time, or eosinophilia), has occurred in patients treated with nevirapine. Some of these cases began in the first few weeks of therapy, and some were accompanied by rash. Nevirapine administration should be interrupted in patients experiencing moderate or severe ALT or AST abnormalities until these return to baseline values. Nevirapine should be pertpanently discontinued if liver function abnormalities recur upon readministration. Monitoring of ALT and AST is strongly recommended, especially during the first six months of nevirapine treatment.
The duration of clinical benefit from antiretroviral therapy may be limited. Patients receiving nevirapine or any other antiretroviral therapy may continue to develop opportunistic infections and other complications of HIV infection, and therefore should remain under close clinical observation by physicians experienced in the treatment of patients with associated HIV diseases.
When administering nevirapine as part of an antiretroviral regimen, the complete product information for each therapeutic component should be consulted before initiation of treatment.

Side-effects and special precautions:

Rash, usually within first six weeks of therapy. D/C drug for severe rash or rash accompanied by other symptoms; Stevens-Johnson syndrome has occurred. Fever, headache, nausea, diarrhea, abdominal pain, thrombocytopenia, anemia, leukopenia, ulcerative stomatitis, hepatitis, peripheral neuropathy, paresthesia, or myalgia may also occur.
Grenulocytopenia has been more commonly observed in children. The safety profile of nevirapine in neonates has not been established.

Precautions:

Pregnancy:

Category C. There are no adequate and well-controlled studies in pregnant women. Nevirapine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.
Lactation: Data indicate that nevirapine is found in breast milk. It is recommended that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV. Mothers should discontinue nursing if they are receiving nevirapine.
Impaired renal and hepatic function: Nevirapine is extensively metabolized by the liver and nevirapine metabolites are extensively eliminated by the kidney. However, the pharmacokinetics of nevirapine have not been evaluated in patients with either hepatic or renal dysfunction. Therefore, nevirapine should be used with caution in these patient populations.

Drug Interactions:

Oral contraceptives, beta-blockers, doxycycline, griseofulvin, methadone, metronidazole, nifedipine, quinidine, steroids, theophyllin, coumadin may have decreased plasma levels. Saquinavir and indinavir levels are decreased by 27-28%. Rifampin and rifabutin may decrease nevirapine concentrations. Nevirapine may decrease levels of protease inhibitors, and should not be used with them. Oral contraceptives or other hormonal birth control methods, and the usual protease inhibitor dosages should not be used with nevirapine due to potential decreases in their levels (indinavir dose can be increased to 1000 mg po q8h to compensate.) Macrolides and cimetidine may somewhat increase nevirapine levels.

Known symptoms of overdosage and particulars of its treatment:

There is no known antidote for nevirapine overdosage. Cases of nevirapine overdose at doses ranging from 800 to 1800 mg per day for up to 15 days have been reported. Patients have experienced events including edema, erythema nodosum, fatigue, fever, headache, insomnia, nausea, pulmonary infiltrates, rash, vertigo, vomiting and weight decrease. All events subsided following discontinuation of nevirapine.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

NEL-250 CAPSULE
(Nelfinavir Tablets 250mg)

Composition:

Each Capsule contains:
Nelfinavir Mesylate 250mg

Presentation:
10x10's

Description:

Nelfinavir meyslate is an inhibitor of the human immunodeficiency virus (HIV) protease. Nelfinavir capsules are formulated as meyslate salt and available for oral administration in strength of 250mg of Nelfinavir.

Mechanism of Action:

Nelfinavir is competitive inhibitor of HIV protease, an enzyme involved in the replication of HIV. protease inhibitor renders the virus non-infectious. Nelfinavir inhibits both HIV-1 and HIV-2 proteases.

Pharmacokinetics:

The pharmacokinetic properties of nelfinavir were evaluated in healthy volunteers and HIV-infected patients; no substantial differences were observed between the two groups.

Absorption:

After single and multiple oral doses of 500 to 750 mg (two to three 250 mg capsules) with food, peak nelfinavir plasma concentrations were typically achieved in 2 to 4 hours. After multiple dosing with 750 mg three times daily (TID) for 28 days (steady-state), peak plasma concentrations (Cmax) averaged 3-4 µg/mL and plasma concentrations prior to the morning dose (trough) were 1-3 µg/mL (trough sample collection times averaged 11 hours after the previous evening dose). A greater than dose-proportional increase in nelfinavir plasma concentrations was observed after single doses; however, this was not observed after multiple dosing.

Effect of Food on Oral Absorption:

Maximum plasma concentrations and area under the plasma concentration-time curve (AUC) were 2- to 3-fold higher under fed conditions compared to fasting. The effect of food on nelfinavir absorption was evaluated in two studies (n=14, total). The meals evaluated contained 517 to 759 Kcal, with 153 to 313 Kcal derived from fat.

Distribution:

The apparent volume of distribution following oral administration of nelfinavir was 2-7 L/kg. Nelfinavir in serum is extensively protein-bound (>98%).

Metabolism:

Unchanged nelfinavir comprised 82-86% of the total plasma radioactivity after a single oral 750 mg dose of 14C-nelfinavir. In vitro, multiple cytochrome P-450 isoforms including CYP3A are responsible for metabolism of nelfinavir. One major and several minor oxidative metabolites were found in plasma. The major oxidative metabolite has in vitro antiviral activity comparable to the parent drug.
Elimination: The terminal half-life in plasma was typically 3.5 to 5 hours. The majority (87%) of an oral 750 mg dose containing 14C-nelfinavir was recovered in the feces; fecal radioactivity consisted of numerous oxidative metabolites (78%) and unchanged nelfinavir (22%). Only 1-2% of the dose was recovered in urine, of which unchanged nelfinavir was the major component.

Indications:

Nelfinavir in combination with antiretroviral agents preferably in combination with nucleoside anologs in the treatment of HIV infection.

Contra-indications:

Nelfinavir Mesylate is contraindicated in patients with clinically significant hypersensitivity to any of the components.

Warnings:

Protease inhibitors causing high blood sugar and diabetes. Symptoms to watch out for include increased thirst and hunger, unexplained weight loss, increased urination, fatigue, and dry, itchy skin. There have been 83 cases of this problem reported so far, usually 10-11 weeks after starting the protease inhibitor, although in one case symptoms started just four days afterwards. There are also reports of protease inhibitors causing high levels of fats (called cholesterol and triglycerides) in the blood. Because this can lead to heart problems, fat levels should be closely monitored in people taking protease inhibitors.

Dosage and directions for use:

Adults / Adolescents:

Orally 1,250 mg (five 250-mg capsules or two 625-mg capsules) twice daily or 750 mg (three capsules) three times daily, with a meal or light snack.

Pediatric:

Children aged 2 to 13 years, 20 to 30 mg/kg three times daily with a meal or light snack.

Neonates:

Not determined.

Drugs requiring dose modification Rifabutin :

The coadministration of nelfinavir 750 mg every 8 hours with refibutin should be half that of the normal dose.
Nelfinavir plasma concentrations may increase in presence of Indinavir resulting in potential increases in side effects (the safety of these combinations have not been established. Caution is advised if sildenafil is prescribed in patients receiving proteases inhibitors.
Use an alternative method of contraception from birth control pills during nelfinavir therapy.

Concomitant therapy:

Nelfinavir's effectiveness may be decreased with concomitant nevirapine.

Drugs not requiring dose modification:

Nucleoside analogue antiretroviral agents. Administration of Nelfinavir (750 mg every 8 hours) with Lamivudine (150 mg every 12 hours) and Zidovudine (300 every 12 hours) not require dose modification.

Side-effects and special precautions:

The most frequent side effect associated with nelfinavir therapy is diarrhea, with moderate or severe diarrhea occurring in up to 20% of those taking the drug. Metabolic (lipid and glucose) and morphologic (fat accumulation and fat atrophy) abnormalities have been associated with protease inhibitors in general.

Precautions:

Pregnancy :

There are no adequate and well-controlled studies in pregnant women. Nelfinavir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mother :

Animal studies suggest that nelfinavir may be excreted in milk. Hence advise against breast feeding by HIV infected mothers to avoid postnatal transmission of the virus to the infant.

Drug Interactions:

Hypersensitivity to nelfinavir or product components concurrent therapy with the following drugs are contraindicated astemizole, cisapride, triazolam, midazolam, ergot derivatives or nevirapine.
Rifampin decreases nelfinavir plasma AUC BY - 82%, the two drugs should not be administered.
Concomitant administration of nelfinavir with lovastatin or simvastatin is not recommended because the risk of myopathy.
The risk of Myopathy may be increased when protease inhibitors are used in combination with Atorvastatin, cerivastatin, lovastatin, or simvastatin.
Unlike other protease inhibitors,Nelfin may be administered with dapsone, trimethoprim / sulfamethoxazole, clarithromycin, itraconazole and fluconazole.

Known symptoms of overdosage and particulars of its treatment:

No data available. However, unabsorbed drug should be removed via gastric lavage and activated charcoal: Significant symptoms beyond gastrointestinal disturbance is likely following acute overdose, hemodialysis will not be effective due to high protein binding of nelfinavir.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 capsules packed in blister strip, 10 such blisters packed in a carton.

LAMI-100/150/300 TABLETS/ TABLETS
(Lamivudine Tablets 100mg/150mg/300mg)

Composition:

Each Tablet contains:
Lamivudine 100mg/150mg/300mg

Presentation:
10x10's

Microbiology:

Antiviral Activity In Vitro:

The relationship between in vitro susceptibility of HIV to lamivudine and the inhibition of HIV replication in humans has not been established. In vitro activity of lamivudine against HIV-1 was assessed in a number of cell lines (including monocytes and fresh human peripheral blood lymphocytes) using standard susceptibility assays. IC50 values (50% inhibitory concentrations) were in the range of 2 nM to 15 mM. Lamivudine had anti—HIV-1 activity in all acute virus-cell infections tested. In HIV-1—infected MT-4 cells, lamivudine in combination with zidovudine had synergistic antiretroviral activity. Synergistic activity of lamivudine/zidovudine was also shown in a variable-ratio study.

Pharmacokinetics:

Lamivudine was rapidly absorbed after oral administration in HIV-infected patients. Absolute bioavailability in 12 adult patients was 86% ± 16% (mean ± SD) for the tablet and 87% ± 13% for the oral solution. After oral administration of 2 mg/kg twice a day to nine adults with HIV, the peak serum lamivudine concentration (Cmax) was 1.5 ± 0.5 µg/ml (mean ± SD). The area under the plasma concentration versus time curve (AUC) and Cmax increased in proportion to oral dose over the range from 0.25 to 10 mg/kg.
An investigational 25-mg dosage form of lamivudine was administered orally to 12 asymptomatic, HIV-infected patients on two occasions, once in the fasted state and once with food (1099 kcal; 75 grams fat, 34 grams protein, 72 grams carbohydrate). Absorption of lamivudine was slower in the fed state (Tmax: 3.2 ± 1.3 hours) compared with the fasted state (Tmax: 0.9 ± 0.3 hours); Cmax in the fed state was 40% ± 23% (mean ± SD) lower than in the fasted state. There was no significant difference in systemic exposure (AUC¥) in the fed and fasted states; therefore, Lamivudine may be administered with or without food.
The accumulation ratio of lamivudine in HIV-positive asymptomatic adults with normal renal function was 1.50 following 15 days of oral administration of 2mg/kg b.i.d.
The apparent volume of distribution after IV administration of lamivudine to 20 patients was 1.3 ± 0.4 L/kg, suggesting that lamivudine distributes into extravascular spaces. Volume of distribution was independent of dose and did not correlate with body weight.
Binding of lamivudine to human plasma proteins is low (<36%). In vitro studies showed that, over the concentration range of 0.1 to 100 mg/mL, the amount of lamivudine associated with erythrocytes ranged from 53% to 57% and was independent of concentration.

Metabolism of lamivudine is a minor route of elimination. In man, the only known metabolite of lamivudine is the trans-sulfoxide metabolite. Within 12 hours after a single oral dose of lamivudine in six HIV-infected adults, 5.2% ± 1.4% (mean ± SD) of the dose was excreted as the trans-sulfoxide metabolite in the urine. Serum concentrations of this metabolite have not been determined.

The majority of lamivudine is eliminated unchanged in urine. In 20 patients given a single IV dose, renal clearance was 0.22 ± 0.06 L/hr•kg (mean ± SD), representing 71% ± 16% (mean ± SD) of total clearance of lamivudine.
In most single-dose studies in HIV-infected patients with serum sampling for 24 hours after dosing, the observed mean elimination half-life (T 1/2) ranged from 5 to 7 hours. Total clearance was 0.37 ± 0.05 L/hr•kg (mean ± SD). Oral clearance and elimination half-life were independent of dose and body weight over an oral dosing range from 0.25 to 10 mg/kg.

Indications:

Lamivudine is a nucleoside reverse transcriptase inhibitor structurally related to cytosine with activity against retroviruses including HIV. It is used, usually in combination with zidovudine, in the treatment of HIV infection. It is also used for the treatment of hepatitis B.

Contra-indications:

Patients known to be hypersensitive to Lamivudine.

Dosage and directions for use:

For HIV infection, the recommended dose of lamivudine for adults is 150 mg by mouth twice daily. A suggested dose for children aged between 3 months and 12 years is 4mg per kg body weight twice daily to a maximum of 150mg twice daily.
For chronic hepatitis B the recommended dose is 100mg once daily by mouth; in patients with concomitant HIV and hepatitis B infection the dosage regimen appropriate for HIV should be used.
Reduction of dosage is recommended for patients with impaired renal function.
Lamivudine should usually be taken without food. Ingestion with food reduces the C max considerably but does not alter the area under the curve (AUC). Therefore, ingestion with food might be considered when required due to clinical reasons.

Administration: Orally.

Warning:

Lamivudine is not recommended for use as monotherapy. Cases of pancreatitis have occurred rarely. However, it is not clear whether these cases were due to drug treatment or to the underlying HIV. disease. Treatment with Lamivudine should be stopped immediately if clinical signs, symptoms or laboratory abnormalities suggestive of pancreatitis occur. There are insufficient data on the use of Lamivudine in children <12 years.
Patients receiving Lamivudine or any other antiretroviral therapy may continue to develop opportunistic infection and other complications of HIV infection, and therefore should remain under close clinical observation by physicians experienced in the treatment of patients with associated HIV diseases.

Patients should be advised that current antiretroviral therapy, including Lamivudine, has not been proven to prevent the risk of transmission of HIV to others through sexual contact or blood contamination. Appropriate precautions should continue to be employed.
In patients with moderate to severe renal impairment, the terminal plasma half-life of lamivudine is increased due to decreased clearance. The dose should be adjusted.
Lamivudine should be used with caution in patients with advanced cirrhotic liver disease due to chronic Hepatitis B infection, as there is a small risk of rebound hepatitis if treatment is discontinued.

Side-effects & special precautions:

Adverse effect commonly associated with lamivudine includes abdominal pain, nausea, vomiting, diarrhoea, headache, fever, rash, malaise, insomnia, cough, nasal symptoms, and musculokeletal pain. Peripheral neuropathy and pancreatitis have been reported rarely. Neutropenia and anaemia (when given in combination with zidovudine), thrombocytopenia, and increases in liver enzymes and serum amylase have occurred.
Lamivudine therapy should be stopped in patients who develop abdominal pain, nausea, or vomiting or with abnormal biochemical test results until pancreatitis has been excluded. Dosage reduction may be necessary in patients with impaired renal function. In patients with chronic hepatitis B, there is a risk of rebound hepatitis when lamivudine is discontinued, and liver function should be monitored in such patients. The possibility of HIV infection should be excluded before beginning lamivudine therapy for hepatitis B, since the lower doses used to treat the latter may permit the development of lamivudine resistant strains of HIV.

Special precautions:

Use in Pregnancy:

The safety of lamivudine in human pregnancy has not been established. Reproductive studies in animals have not shown evidence of teratogenicity and showed no effect on male or female fertility.
Lamivudine induces early embryolethality then administered to pregnant rabbits at exposure levels comparable to those achieved in man. Lamivudine crosses the placenta in animals but there is no information on placental transfer in humans.
Although animal reproductive studies are not always predictive of the human response, administration during the first 3 months of pregnancy is not recommended.

Use in lactation:

A study in lactating rats showed that, following oral administration, lamivudine was concentrated 4-fold and excreted in the milk. It is not known if lamivudine is excreted in human breast milk. Since the drug may pass into breast milk, it is recommended that mothers taking lamivudine do not breastfeed their infants. Some health experts recommend that HIV-infected women do not breastfeed their infants under any circumstances in order to avoid transmission of HIV.

Drug Interaction:

The likelihood of metabolic interactions is low due to limited metabolism and plasma protein – binding and almost complete renal clearance. A modest increase in Cmax (28%) was observed for zidovudine when administered with lamivudine, however overall exposure (AUC) is not significantly altered. Zidovudine has no effect on the pharmacokinetics of lamivudine.

The possibility of interactions with other drugs administered concurrently should be considered, particularly when the main route of elimination is active renal secretion via the organic cationic transport system, eg trimethoprim. Other drugs (e. g, ranitidine, cimetidine) are eliminated only in part by this mechanism and were shown not to interact with lamivudine. The nucleoside analogues (e. g, didanosine and zalcitabine, like zidovudine, are not eliminated by this mechanism and are unlikely to interact with lamivudine.

The renal excretion of lamivudine may be inhibited by concomitant administration of other drugs mainly eliminated by active renal secretion, for example trimethoprim. Usual prophylactic doses of trimethoprim are unlikely to necessitate reductions in lamivudine dosage unless the patient has impaired renal function, but the co-administration of lamivudine with the high therapeutic doses of trimethoprim used in Pneumocystis carinii pneumonia and toxoplasmosis should be avoided.

Known symptoms of overdosage and particulars of its treatment:

Administration of lamivudine at very high dose levels in acute animal studies did not result in any organ toxicity. Limited data are available on the consequences of ingestion of acute overdose in humans. No fatalities occurred and the patients recovered. No specific signs or symptoms have been identified following such overdose.
If overdosage occurs, the patient should be monitored and standard supportive treatment applied as required. Since lamivudine is dialysable, continuous haemodialysis could be used in the treatment of overdosage, although this has not been studied.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

ZVD 100 TABLETS /ZVD 300 TABLETS
(Zidovudine Tablets 100mg/300mg)

Composition:

I) Each Tablet contains:
Zidovudine IP 100mg

II) Each Tablet contains:
Zidovudine IP 300mg

Presentation:
10x10's

Pharmacology:

Zidovudine is a synthetic nucleoside analogue of the naturally occurring nucleoside, thymidine, in which the 3'-hydroxy (- OH) group is replaced by an azido (- N3) group. Within cells, zidovudine is converted to the active metabolite, zidovudine 5'-triphosphate (AztTP), by the sequential action of the cellular enzymes. Zidovudine 5'-triphosphate inhibits the activity of the HIV reverse transcriptase both by competing for utilization with the natural substrate, deoxythymidine 5'- triphosphate (dTTP), and by its incorporation into viral DNA. The lack of a 3'- OH group in the incorporated nucleoside analogue prevents the formation of the 5'to 3' phosphodiester linkage essential for DNA chain elongation and therefore, the viral DNA growth is terminated. The active metabolite AztTP is also a weak inhibitor of the cellular DNA polymerase-alpha and mitochondrial polymerase-gamma and has been reported to be incorporated into the DNA of cells in culture

Pharmacokinetics:

The pharmacokinetics of zidovudine has been evaluated in 22 adult HIV-infected patients in a Phase 1 dose-escalation study. After oral dosing (capsules), zidovudine was rapidly absorbed from the gastrointestinal tract with peak serum concentrations occurring within 0.5 to 1.5 hours. Dose-independent kinetics was observed over the range of 2 mg/kg every 8 hours to 10 mg/kg every 4 hours. The mean zidovudine half-life was approximately 1 hour and ranged from 0.78 to 1.93 hours following oral dosing.
Zidovudine is rapidly metabolized to 3'-azido-3'-deoxy-5'-O- -D-glucopyra-nuronosylthymidine (GZDV) which has an apparent elimination half-life of 1 hour (range 0.61 to 1.73 hours). Following oral administration, urinary recovery of zidovudine and GZDV accounted for 14% and 74% of the dose, respectively, and the total urinary recovery averaged 90% (range 63% to 95%), indicating a high degree of absorption. However, as a result of first-pass metabolism, the average oral capsule bioavailability of zidovudine is 65% (range 52% to 75%). A second metabolite, 3-amino- 3-deoxythymidine (AMT), has been identified in the plasma following single-dose intravenous (IV) administration of zidovudine. AMT area-under-the-curve (AUC) was one fifth of the AUC of zidovudine and had a half-life of 2.7 ± 0.7 hours. In comparison, GZDV AUC was about three-fold greater than the AUC of zidovudine.
Additional pharmacokinetic data following intravenous dosing indicated dose-independent kinetics over the range of 1 to 5 mg/kg with a mean zidovudine half-life of 1.1 hours (range 0.48 to 2.86 hours). Total body clearance averaged 1900 mL/min per 70 kg and the apparent volume of distribution was 1.6 L/kg. Renal clearance is estimated to be 400 mL/min per 70 kg, indicating glomerular filtration and active tubular secretion by the kidneys.
Zidovudine plasma protein binding is 34% to 38%, indicating that drug interactions involving binding site displacement are not anticipated.
The zidovudine cerebrospinal fluid (CSF)/plasma concentration ratio was determined in 39 patients receiving chronic therapy with zidovudine. The median ratio measured in 50 paired samples drawn 1 to 8 hours after the last dose of zidovudine was 0.6.

Indications:

Zidovudine is an antiviral agent, which is highly active in vitro against retroviruses including the Human Immunodeficiency Virus (HIV).

Management of patients with advanced HIV disease, e.g. those with the Acquired Immune Deficiency Syndrome (AIDS) or AIDS-related complex (ARC).

Treatment of HIV infection when CDC count is < 500/mm3 or symptomatic. Also approved for use in HIV-infected pregnant women in 2nd and 3rd trimesters, along with IV ZDV during labor and delivery, and ZDV syrup to newborn for 6 weeks.

Contra-indications:

Zidovudine is contraindicated in patients with clinically significant hypersensitivity to any of the components.
Zidovudine should not be given to patients with abnormally low neutrophil counts ($<0.75x10^9$/L) or abnormally low heamoglobin levels (<7.5g/dL or 4.65 mmol/L).

Dosage and directions for use:

Adults:

Although broad ranges of dosage regiments have been employed, 500 or 600 mg/day in 2-5 divided doses has been commonly used worldwide. Alternatively, a daily dosage of 2000 mg in 2 dividend doses has been shown to be effective. The effectiveness of lower dosages in the treatment or prevention of HIV-associated neurological dysfunciton and malignancies is unknown.

Children:

In children >3months, the recommended starting dosage is 180 mg/m^2 body surface area every 6 hrs (720mg/m^2/day.) The maximum dosage should not exceed 200 mg every 6 hrs.

Warnings:

Before combination therapy with Zidovudine is initiated, consult the complete prescribing information for each drug. The safety profile of Zidovudine plus other antiretroviral agents reflects the individual safety profiles of each component.
The incidence of adverse reactions appears to increase with disease progression, and patients should be monitored carefully, especially as disease progression occurs.
BONE MARROW SUPPRESSION
Zidovudine should be used with caution in patients who have bone marrow compromise evidenced by granulocyte count <1000 cells/mm3 or hemoglobin <9.5 g/dL. There have been reports of pancytopenia associated with the use of zidovudine, which was reversible in most instances after discontinuance of the drug.
Frequent blood counts are strongly recommended in patients with advanced HIV disease who are treated with zidovudine. For patients with asymptomatic or early HIV disease, periodic blood counts are recommended. If anaemia or neutropenia develops, dosage adjustments may be necessary.

MYOPATHY
Myopathy and myositis with pathological changes, similar to that produced by HIV disease, have been associated with prolonged use of zidovudine.

LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS

Rare occurrences of potentially fatal lactic acidosis in the absence of hypoxemia, and severe hepatomegaly with steatosis have been reported with the use of certain antiretroviral nucleoside analogues. Therapy with Zidovudine should be suspended until the diagnosis of lactic acidosis has been excluded. Caution should be exercised when administering Zidovudine to any patient, particularly obese women, with hepatomegaly, hepatitis, or other known risk factors for liver disease. Treatment with zidovudine should be suspended in the setting of rapidly elevating aminotransferase levels, progressive hepatomegaly, or metabolic/lactic acidosis of unknown aetiology.

OTHER SERIOUS ADVERSE REACTIONS

Reports of pancreatitis, sensitization reactions, vasculitis and seizures have been rare. These adverse events, except for sensitization, have also been associated with HIV disease. Changes in skin and nail pigmentation have been associated with the use of zidovudine.

Side-effects and special precautions:

Adults

The frequency and severity of adverse events associated with the use of zidovudine in adults are greater in patients with more advanced infection at the time of initiation of therapy.
The anaemia reported in patients with advanced HIV disease receiving zidovudine appeared to be the result of impaired erythrocyte maturation. Thrombocytopenia has also been reported in patients with advanced disease. Mild drug-associated elevations in total bilirubin levels have been reported as an uncommon occurrence in patients treated for asymptomatic HIV infection.
Clinical adverse events or symptoms which occurred in at least 5% of all patients with advanced HIV disease treated with 1,500 mg/day of zidovudine were: fever, headache, nausea, vomiting, anorexia, myalgia, insomnia, dizziness, paraesthesia, dyspnoea and rash. Malaise, gastrointestinal pain, dyspepsia, and taste perversion were also reported.

Paediatrics

Anaemia and granulocytopenia among paediatric patients with advanced HIV disease receiving zidovudine occurred with similar incidence to that reported for adults with AIDS or advanced AIDS-Related complex. Macrocytosis was frequently observed.
Other adverse events were similar to that observed in adults.

Maternal-Foetal Transmission

The most commonly reported adverse experiences were anaemia and neutropenia. The long-term consequences of in vitro and infant exposure to zidovudine are unknown.

Special Precautions:

PREGNANCY

Category C. Congenital abnormalities were found to occur with similar frequency between infants born to mothers who received zidovudine and infants born to mothers who received placebo. Abnormalities were either problems in embryogenesis (prior to 14 weeks) or were recognised on ultrasound before or immediately after initiation of study drugs.

NURSING MOTHERS

HIV infected women are advised not to breast feed to avoid postnatal transmission of HIV to a child who may not yet be infected. Zidovudine is excreted in human milk.

IMPAIRED RENAL AND HEPATIC FUNCTION

Zidovudine is eliminated from the body primarily by renal excretion following metabolism in the liver. In patients with severely impaired renal function, dosage reduction is recommended. Although very little data are available, patients with severely impaired hepatic function may be at greater risk of toxicity.

Drug Interactions:

Acyclovir, alpha interferon, dipyridamole (increased in vitro antiretroviral activity); amphotericin B, dapsone, pentamidine, TMP/SMX, acyclovir, ganciclovir, pentamidine, sulfadiazine/pyrimethamine (increased bone marrow toxicity); methadone (decreased ZDV metabolism); phenytoin (increased or decreased phenytoin levels); Nephrotoxic drugs or cytotoxic drugs, such as flucytosine, vincristine, or interferon, may increase ZDV toxicity. Acetominophen, probenecid, cimetidine, indomethacin, lorazepam, or aspirin may inhibit excretion and contribute to toxicity.

Known symptoms of overdosage and particulars of its treatment:

Limited data are available on the consequences of ingestion of acute overdoses in both adults and children. No fatalities occurred and all patients recovered. The highest recorded blood level of zidovudine was 185µM (49.4µg/Ml). No specific symptoms have been identified following such overdosage.

Dosages as high as 1250mg Zidovudine orally every 4 hrs for 4 weeks have been administered to 2 patients with advanced HIV Disease. One experienced anaemia and neutropenia while the other had no untoward effects.

Treatment:

Patients should be observed closely for evidence of toxicity and given the necessary supportive therapy.

Haemoodialysis and peritoneal dialysis appear to have a limited effect on the elimination zidovudine but enhance the elimination after glucuronide metabolite.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

D-SINE 25/50/100/200/250/400 TABLETS
(Didanosine Tablets)

Composition:

Each Tablet contains:
Didanosine 25/50/100/200/250/400mg

Presentation:

10x10's

Pharmacology:

Didanosine (formerly called dideoxyinosine-ddI) is a synthetic purine nucleoside analogue of the naturally occurring nucleoside deoxyadenosine, in which the 3' hydroxyl group is replaced by hydrogen. Intracellularly, didanosine is converted by cellular enzymes to the active metabolite, dideoxyadenosine 5'-triphosphate. This metabolite inhibits the activity of HIV-1 reverse transcriptase both by competing with the natural substrate, and by its incorporation into viral DNA. The lack of a 3'-hydroxyl group in the incorporated nucleoside analogue prevents DNA chain elongation and therefore, the viral DNA growth is terminated.

Pharmacokinetics:

Adults:

Didanosine is rapidly degraded at an acidic pH. Therefore, all oral formulations must contain or be administered with buffering agents designed to increase gastric pH. The presence of food significantly reduces the bioavailability of didanosine. Therefore, Didanosine should be administered at least 30 minutes before a meal or 2 hours after eating.
Although there is significant variability between patients, Cmax and AUC values increase in proportion to dose. The steady state volume of distribution after IV administration averages 54 litres. The concentration of didanosine in the cerebrospinal fluid (CSF), one hour after infusion, averages 21% of that of the simultaneous plasma concentration. Renal clearance in patients with normal renal function which is equivalent to approximately 400 mL/min represents an average of 50% of total body clearance, indicating that active tubular secretion, in addition to glomerular filtration is responsible for the renal elimination of didanosine. Urinary recovery of didanosine is approximately 20% of the dose after oral treatment. There is no evidence of didanosine accumulation after the administration of oral doses for 4 weeks.
The average elimination half-life is 1,6 hours.
The metabolism of didanosine in man has not been evaluated. However, based on animal studies, it is presumed that it follows the same pathways responsible for the elimination of endogenous purines. In vitro human plasma protein binding is less than 5% with didanosine, indicating that drug interactions involving binding site displacement are not anticipated.
Renal impairment: The apparent drug clearance decreased as creatinine clearance decreased. Dose adjustment is recommended in patients with impaired renal function (<60 mL/min/1.73m2).
Hepatic impairment: The metabolism of didanosine may be altered in patients with more severe or other types of hepatic impairment
The AUC of both didanosine and delaviradine are decreased (20%) when administered together. Didanosine also decreases the AUC of indinavir. No clinically significant pharmacokinetic interactions were found between nevirapine, rifabutin, stavudine and zidovudine in specific interaction studies. The effect of rifampicin on the kinetics is not known.

Children:
The average absolute bioavailability at steady state in children is 42%(+18%). Although there is significant variability between patients, Cmax and AUC values increase in proportion to dose in paediatric and adolescent patients. The volume of distribution after IV administration averages 35,6 L/m2. The average elimination half-life after oral didanosine administration is 0.8 hours. Renal clearance is approximately 243 mL/min/m2 after oral dosing and represents about 46% of the total body clearance. Urinary recovery of didanosine is approximately 17% of dose after oral treatment. There is no evidence of didanosine accumulation after oral administration for an average of 26 days. The cerebrospinal fluid didanosine concentration averages 46% (12 to 85%) of the concentration in a simultaneous plasma sample.

Indications:

Didanosine is indicated for the treatment of HIV infection when antiretroviral therapy is warranted.

Contra-indications:

Didanosine is contraindicated in patients with clinically significant hypersensitivity to any of the components.

Dosage and directions for use:

Adults Dosage:
The dosing interval should be 12 hours. Didanosine should be administered on an empty stomach, at least 30 minutes before or 2 hours after eating. Adult patients should take 2 tablets at each dose so that adequate buffering is provided to prevent gastric acid degradation of didanosine. No more than 4 tablets should be taken at each dose to reduce the risk of gastrointestinal side effects. The recommended starting dose in adults is dependent on weight, as outlined in the table below:

PATIENT WEIGHT	DIDANOSINE TABLETS
$\geq$ 60 kg	200 mg b.d.
< 60 kg	125 mg b.d.

Administration:
For full therapeutic effect, 2 tablets must be thoroughly chewed, crushed or dispersed in water before swallowing. The tablets should not be swallowed whole. To disperse the tablets, 2 tablets should be added to 2 tablespoons (30 ml) of water. The water should then be stirred until a uniform dispersion forms. The entire dispersion should be swallowed immediately.

Dose Adjustment:
Clinical signs suggestive of pancreatitis should prompt dose suspension and careful evaluation of the possibility of pancreatitis. Didanosine use should be discontinued in patients with confirmed pancreatitis.

Patients who have presented with symptoms of neuropathy may tolerate a reduced dose of didanosine after resolution of these symptoms upon drug discontinuation. In adult patients with impaired renal function, the dose of didanosine should be adjusted to compensate for the slower rate of elimination. The recommended doses and dosing intervals of didanosine in adult patients with renal insufficiency are given in the table below:

CREATININE CLEARANCE (ML/MIN)	≥ 60 KG	< 60 KG	INTERVAL (HR)
≥ 60 kg	200	125	12
30-59	100	75	12
10-29	150	100	24
< 10	100	75	24

Patients requiring continuous ambulatory peritoneal dialysis (CAPD) or hemodialysis: It is recommended that one-fourth of the total daily dose of didanosine be administered once a day (See Table 2, recommended dosage for patients with CLCR < 10 mL/min). It is not necessary to administer a supplemental dose of didanosine following hemodialysis.

Warnings:

Pancreatitis

Pancreatitis, which has been fatal in some cases, has occurred during therapy with didanosine. Didanosine use should be suspended in patients with signs or symptoms of pancreatitis and discontinued in patients with confirmed pancreatitis. When treatment with other drugs known to cause pancreatic toxicity is required, suspension of didanosine therapy is recommended. In patients with risk factors for pancreatitis, didanosine should be used with extreme caution and only if clearly indicated. Patients with advanced HIV infection are at increased risk of pancreatitis and should be followed closely. Patients with renal impairment may be at greater risk for pancreatitis if treated without dose adjustment. The frequency of pancreatitis is dose-related. In phase 3 studies, incidence ranged from 1 to 10% with high dose and 1 to 7% with recommended dose.

Lactic Acidosis/Severe Hepatomegaly with Steatosis

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including didanosine. Caution should be exercised when administering didanosine to any patient, and particularly to those with known risk-factors for liver disease. Treatment with didanosine should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatoxicity.

Retinal and Visual Changes

Retinal changes and optic neuritis have been reported. Periodic retinal examinations should be considered for patients receiving didanosine.

Hyperuricemia

Didanosine has been associated with asymptomatic hyperuricemia; treatment suspension may be necessary if clinical measures aimed at reducing uric acid levels fail.

Impaired Renal Function

Patients with renal impairment (creatinine clearance < 60 mL/min) may be at greater risk of toxicity from didanosine due to decreased drug clearance. A dose reduction is recommended in these patients.

Impaired Hepatic Function

It is unknown if hepatic impairment significantly affects didanosine pharmacokinetics. Therefore, these patients should be monitored closely for evidence of didanosine toxicity.

Side-effects and special precautions:

The major toxicity of didanosine is pancreatitis. Other important toxicities include lactic acidosis/ severe hepatomegaly with steatosis and retinal/visual changes. Adults: Clinical adverse events that occurred in at least 5% of adult patients in clinical trials with didanosine monotherapy are diarrhoea, neuropathy, chills/fever, rash/pruritus, abdominal pain, asthenia, headache, pain, nausea and vomiting and pancreatitis. The incidence of adverse events has been reported to be generally lower in patients with less advanced HIV disease. The frequency of peripheral neuropathy is related to dose and stage of disease. Patients should be monitored for the development of a neuropathy that is usually characterized by numbness, tingling or pain in the feet or hands. Neuropathy has occurred more frequently in patients with a history of neuropathy or neurotoxic drug therapy and these patients may be at increased risk of neuropathy during didanosine therapy. The most frequently reported serious laboratory abnormalities with didanosine monotherapy are leukopenia, granulocytopenia and elevations of amylase, SGOT and SGPT values. Didanosine in neonates has not been established**.**

Special Precautions:

Pregnancy

Pregnancy Category B- There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation

Although it is not known if didanosine is excreted in human milk, there is the potential for adverse effects from didanosine in nursing infants. Mothers should be instructed to discontinue nursing if they are receiving didanosine. Also, it is recommended that HIV-infected mothers do not breast feed their infants to avoid risking post-natal transmission of HIV infection.

Drug Interactions:

Coadministration of didanosine with drugs that are known to cause pancreatitis may increase the risk of this toxicity and should be done with extreme caution and only if clearly indicated. Neuropathy has occurred more frequently in patients with a history of neuropathy or neurotoxic drug therapy and these patients may be at increased risk of neuropathy during didanosine therapy.

Allopurinol:

The AUC of didanosine was increased about 4-fold when allopurinol at 300 mg/day was coadministered with a single 200 mg dose of didanosine to two patients with renal impairment. The effects of allopurinol on didanosine pharmacokinetics in subjects with normal renal function are not known.

Antacids:

Concomitant administration of antacids containing magnesium or aluminium with didanosine may potentiate adverse events associated with the antacid components. Drugs whose absorption can be affected by the level of acidity in the stomach: Drugs such as ketoconazole and itraconazole should be administered at least 2 hours prior to dosing with didanosine.

Ganciclovir:

Administration of didanosine 2 hours prior to or concurrent with oral ganciclovir was associated with a 111% increase in the steady state AUC of didanosine. A 21% decrease in the steady-state AUC of

ganciclovir was observed when didanosine was administered 2 hours prior to ganciclovir, but not when the two drugs were administered simultaneously.

Quinolone antibiotics:

Plasma concentrations of quinolone antibiotics are decreased when administered with antacids containing magnesium, calcium or aluminium. The optimal dosing interval for coadministration with didanosine should be determined by consulting the appropriate quinolone package insert.
In the case of ciprofloxacin, didanosine should be administered at least 2 hours after or 6 hours before dosing with ciprofloxacin.

Protease inhibitors: Separate dosing of indinavir or delavirdine by 1 hour.

Known symptoms of overdosage and particulars of its treatment:

There is no known antidote for didanosine overdosage. Didanosine is not dialyzable by peritoneal dialysis, although there is some clearance by hemodialysis.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Shelf life is 2 years.

Package: 10 tablets packed in blister strip, 10 such blisters packed in a carton.

STV-40/30 CAPSULES
(Stavudine Capsules 40mg/30mg)

Composition:

Each Capsule contains:
Stavudine 40mg/30mg

Presentation:
10x10's

Pharmacology:

Stavudine, a nucleoside analogue of thymidine, inhibits the replication of HIV in human cells in vitro. Stavudine is phosphorylated by cellular kinases to the active metabolite stavudine triphosphate. Stavudine triphosphate inhibits the activity of HIV reverse transcriptase both by competing with the natural substrate deoxythymidine triphosphate (Ki=0.0083 to 0.032 µM), and by its incorporation into viral DNA causing a termination of DNA chain elongation because stavudine lacks the essential 3'-OH group. Stavudine triphosphate inhibits cellular DNA polymerase beta and gamma, and markedly reduces the synthesis of mitochondrial DNA.

Pharmacokinetics:

The pharmacokinetics of stavudine have been evaluated in HIV-infected adult and pediatric patients. Peak plasma concentrations (Cmax) and area under the plasma concentration-time curve (AUC) increased in proportion to dose after both single and multiple doses ranging from 0.03 to 4 mg/kg. There was no significant accumulation of stavudine with repeated administration every 6, 8, or 12 hours.

Absorption

Following oral administration, stavudine is rapidly absorbed, with peak plasma concentrations occurring within 1 hour after dosing. The systemic exposure to stavudine is the same following administration as capsules or solution.

Distribution

Binding of stavudine to serum proteins was negligible over the concentration range of 0.01 to 11.4 µg/mL. Stavudine distributes equally between red blood cells and plasma.

Metabolism

The metabolic fate of stavudine has not been elucidated in humans. Excretion- Renal elimination accounted for about 40% of the overall clearance regardless of the route of administration. The mean renal clearance was about twice the average endogenous creatinine clearance, indicating active tubular secretion in addition to glomerular filtration.

Indications:

Stavudine is indicated for the treatment of HIV-infected patients who have received prolonged prior zidovudine therapy.

Contra-indications:

Stavudine is contraindicated in patients with clinically significant hypersensitivity to stavudine or to any of the components contained in the formulation. It should not be used in combination with zidovudine.

Dosage and directions for use:

Adults:

The interval between oral doses should be 12 hours. Stavudine may be taken without regard to meals. The recommended starting dose based on body weight is as follows:
40 mg twice daily for patients > 60 kg
30 mg twice daily for patients < 60 kg

Paediatrics:

The recommended starting dose for paediatric patients weighing less than 30 kg is I mg/kg/dose, given every 12 hours. Paediatric patients weighing 30 kg or greater should receive the recommended adult dose.
Dosage adjustment: Patients should be monitored for the development of peripheral neuropathy, which is usually characterised by numbness, tingling or pain in the feet or hands. If these symptoms develop on treatment, stavudine therapy should be interrupted. Symptoms may resolve if therapy is withdrawn promptly. In some cases, symptoms may worsen temporarily following discontinuation of therapy. If symptoms resolve completely, resumption of treatment may be considered using the following dosage schedule.
20 mg twice daily for patients > 60 kg
15 mg twice daily for patients < 60 kg
For paediatric patients, resumption of treatment may be considered at one-half the recommended dose.
Renal Impairment:

Stavudine may be administered to adult patients with impaired renal function. The following schedule is recommended

Creatinine Clearance (mL/min)	Recommended Stavudine Dose by patient weight	
	60 kg	< 60 kg
>50	40 mg every 12 hours	30 mg every, 12 hours
26-50	20 mg every 12 hours	15 mg every 12 hours
10-25	20 mg every 24 hour	15 mg every 24 hour

Paediatrics:

There are insufficient data to recommend a specific dose adjustment of stavudine in children with renal impairment. A reduction in the dose and/or an increase in the interval between doses should be considered.

Hemodialysis Patients:

The recommended dose is 20 mg every 24 hours (>60 kg) or 15 mg every 24 hours (< 60 kg), administered after the completion of hemodialysis and at the same time of day on non-dialysis hours.

Warning:

Lactic acidosis/severe hepatomegaly with steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including stavudine. A majority of these cases have been in women. Caution should be exercised when administering stavudine to any patient and particularly to those with known risk factors for liver disease.

Treatment with stavudine should be discontinued in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or hepatotoxicity.
Peripheral Neuropathy: Stavudine therapy can be associated with severe peripheral neuropathy which is dose-related and occurs more frequently in patients with advanced HIV infection or who have previously experienced peripheral neuropathy.
Laboratory Tests: Mild to moderate increases in AST (SGOT) and (SGPT) occurred commonly in clinical trials.

Side-effects & special precautions:

The major clinical toxicity of stavudine is peri-pheral neuropathy, which is dose related. Modest elevation of hepatic transaminases was observed commonly in controlled trials. Other adverse events that occurred in adult patients included headache, chills/fever, diarrhoea, rash, nausea and vomiting, abdominal pain, pancreatitis, myalgia and insomnia.

Special caution in use:

Pregnancy:

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, stavudine should be used during pregnancy only if clearly needed.

Nursing Mothers:

It is recommended that HIV-infected mothers do not breast feed their infants to avoid risking postnatal transmission of HIV infection. It is not known whether stavudine is excreted in human milk and because of the potential for adverse reactions from stavudine in nursing infants, mothers should be instructed not to nurse if they are receiving stavudine.

Paediatric Use:

Use of stavudine in paediatric patients is supported by evidence from adequate and well-controlled studies in adults with additional safety data in 115 paediatric patients.

Renal Insufficiency:

It is recommended that the dosage of stavudine be modified in patients with reduced creatinine clearance

Drug interactions & other interactions:

Zidovudine may competitively inhibit the intracellular phosphorylation of stavudine. Therefore, use of zidovudine in combination with stavudine is not recommended

Known symptoms of overdosage and particulars of its treatment:

Experience with adults treated with 12 to 24 times the recommended daily dosage revealed no acute toxicity. Complications of chronic overdosage include peripheral neuropathy and hepatic toxicity. It is not known whether stavudine is eliminated by peritoneal dialysis or hemodialysis.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Storage life is 2 years.

Package: 10 capsules packed in blister strip, 10 such blisters packed in a carton.

E.F.200/600 CAPSULES
(Efavirenz Capsules 200mg/600mg)

Composition:

Each Capsule contains:
Efavirenz 200mg/600mg

Presentation:
10x10's

Pharmacology:

Efavirenz is a non- nucleoside reverse transcriptase (RT) inhibitor of human immunodeficiency virus type 1 (HIV-1). Efavirenz activity is mediated predominantly by non- competitive inhibition of HIV-1 RT. HIV-2 RT and human cellular DNA polymerases alpha, beta, gamma, and delta are not inhibited by efavirenz.

Pharmacokinetics:

Absorption:

Peak efavirenz plasma concentrations of 1.6-9.1 m M were attained by 5 hours following single oral doses of 100 mg to 1600 mg administered to uninfected volunteers. Dose- related increases in C_{max} and AUC were seen for doses up to 1600 mg; the increases were less than proportional suggesting diminished absorption at higher doses.
In HIV- infected patients at steady- state, mean C_{max} , mean C_{min} , and mean AUC were dose proportional following 200 mg, 400 mg, and 600 mg daily doses. Time- to- peak plasma concentrations were approximately 3-5 hours and steady-state plasma concentrations were reached in 6-10 days. In 35 patients receiving efavirenz 600 mg QD, steady- state C_{max} was 12.9 ± 3.7 m M (mean ± S. D.), steady-state C_{min} was 5.6 ± 3.2 m M, and AUC was 184 ± 73 m M"" h.
Effect of Food on Oral Absorption: In uninfected volunteers, meals of normal composition had no appreciable effect on the bioavailability of 100 mg of an investigational efavirenz formulation administered twice a day for 10 days with meals (Breakfast: 662 kcal, 13.8 g protein, 27.9 g fat, 94.6 g carbohydrate; Dinner: 567 kcal, 44.5 g protein, 12.5 g fat, 73.8 g carbohydrate). The relative bioavailability of a single 1200 mg dose of an investigational efavirenz formulation in uninfected volunteers (N= 5) was increased 50% (range 11%- 126%) following a high fat meal (1070 kcal, 82 g fat, 69% of calories from fat)
Distribution: Efavirenz is highly bound (approximately 99.5- 99.75%) to human plasma proteins,predominantly albumin. In HIV- 1 infected patients (N= 9) who received efavirenz 200 to 600 mg once daily for at least one month, cerebrospinal fluid concentrations ranged from 0.26 to 1.19% (mean 0.69%) of the corresponding plasma concentration. This proportion is approximately 3- fold higher than the non-protein- bound (free) fraction of efavirenz in plasma.
Metabolism: Studies in humans and *in vitro* studies using human liver microsomes have demonstrated that efavirenz is principally metabolized by the cytochrome P450 system to hydroxylated metabolites with subsequent glucuronidation of these hydroxylated metabolites. These metabolites are essentially inactive against HIV-1.

The *in vitro* studies suggest that C.P.A. and CYP2B6 are the major isozymes responsible for efavirenz metabolism. Efavirenz has been shown to induce P450 enzymes, resulting in the induction of its own metabolism. Multiple doses of 200- 400 mg per day for 10 days resulted in a lower than predicted extent of accumulation (22-42% lower) and a shorter terminal half- life of 40-55 hours (single dose half-life 52-76 hours).
Elimination: Efavirenz has a terminal half- life of 52- 76 hours after single doses and 40- 55 hours after multiple doses. A one-month mass balance/ excretion study was conducted using 400 mg per day with a 14

C-labeled dose administered on Day 8. Approximately 14- 34% of the radiolabel was recovered in the urine and 16-61% was recovered in the feces. Nearly all of the urinary excretion of the radiolabeled drug was in the form of metabolites. Efavirenz accounted for the majority of the total radioactivity measured in feces.

Indications:

Efavirenz is used for the treatment of HIV infection in children and adults. Efavirenz is most effective when used as part of a triple combination therapy regimen with two other anti-HIV drugs.

Contra-indications:

Efavirenz is contraindicated in patients with clinically significant hypersensitivity to the active substance or to any of the excipients. Efavirenz should not be used in patients with severe hepatic impairment (Child Pugh Grade C).
Efavirenz must not be administered concurrently with astemizole, cisapride, midazolam, triazolam or ergot alkaloids because competition for the cytochrome P450 3A4 enzyme by efavirenz could result in inhibition of metabolism of these drugs and create the potential for serious and/or life-threatening adverse events (for example, cardiac arrhythmias, prolonged sedation or respiratory depression).

Dosage and directions for use:

Adults:

Orally 600 mg once daily (three 200-mg capsules). It is recommended that efavirenz be taken on an empty stomach, preferably at bedtime. Increased absorption occurs when efavirenz is taken with food and may lead to adverse events. Taking efavirenz before bedtime may improve the tolerability of neurological side effects.

Pediatric:

For children older than 3 years, administer efavirenz once daily as follows: 200 mg (10 to <15 kg); 250 mg (15 to <20 kg); 300 mg (20 to <25 kg); 350 mg (25 to <32.5 kg); 400 mg (32.5 to 40 kg); 600 mg (>40 kg).
Because of efavirenz's long half-life, patients discontinuing antiretroviral therapy have been advised to stop taking efavirenz 1 or 2 days before stopping NRTIs to minimize the risk of acquiring NNRTI resistance during the washout period.

Warning:

Efavirenz must not be used as a single agent to treat HIV or added on as a sole agent to a failing regimen. As with all other non-nucleoside reverse transcriptase inhibitors, resistant virus emerges rapidly when efavirenz is administered as monotherapy. The choice of new antiretroviral agent(s) to be used in combination with efavirenz should take into consideration the potential for viral cross-resistance.

Psychiatric symptoms

Serious psychiatric adverse experiences have been reported in patients treated with efavirenz. These include severe depression, suicidal ideation/attempts, aggressive behaviour, paranoid reactions and manic reactions. Patients with a prior history of psychiatric disorders appear to be at greater risk for these psychiatric adverse experiences. Patients with serious psychiatric adverse experiences should seek immediate medical evaluation to assess the possibility that the symptoms may be related to the use of efavirenz, and if so, to determine whether the risk of continued therapy outweighs the benefits.
Rash

Rash associated with blistering, moist desquamation or ulceration has been reported in clinical trials. The incidence of erythema multiforme or Stevens-Johnson Syndrome was approximately 0.1%. The median time to onset of rash in adults was II days and the median duration 16 days. Appropriate antihistamines and/or corticosteroids may improve the tolerability and hasten the resolution of rash. Efavirenz must be discontinued in patients developing severe rash associated with blistering, desquamation, mucosal involvement or fever. If therapy with efavirenz is discontinued, consideration should also be given to interrupting therapy with other antiretroviral agents to avoid development of resistant virus.

Nervous system symptoms

These include dizziness, insomnia, impaired concentration, somnolence, abnormal dreams and hallucinations.

Nervous system symptoms usually begin during the first one or two days of therapy and generally resolve after the first 2-4 monthss. Patients should be informed that these common symptoms were likely to improve with continued therapy. Dosing at bedtime seems to improve the tolerability of these symptoms and can be recommended during the first monthss of therapy and in patients who continue to experience these symptoms. Patients should be altered to the potential for additive central nervous system effects when efavirenz is used concomitantly with alcohol or psychoactive drugs.

Patients who experience central nervous system symptoms such as dizziness, impaired concentration and/or drowsiness should avoid potentially hazardous tasks such as driving or operating machinery.

Liver enzymes

In patients with known or suspected history of hepatitis B or C infection and in patients treated with other mediations associated with liver toxicity, monitoring of liver enzymes is recommended. In patients with persistent elevations of serum transaminases to greater than 5 times the upper limit of normal, the benefit of continued therapy with efavirenz needs to be weighed against the unknown risks of significant liver toxicity.

Because of the extensive cytochrome P450-mediated metabolism of efavirenz and limited clinical experience in patients with hepatic impairment, caution must be exercised in administering efavirenz to these patients.

Renal impairment

The pharmacokinetics of efavirenz has not been studied in patients with renal insufficiency. However, less than 1% of efavirenz is excreted unchanged in the urine, so the impact of renal impairment on efavirenz elimination should be minimal.

Cholesterol

Monitoring of cholesterol should be considered in patients treated with efavirenz.

Side-effects & special precautions:

The most significant adverse events observed in patients treated with efavirenz are nervous system symptoms, psychiatric symptoms and rash.

A few cases of pancreatitis have been described, although a causal relationship with efavirenz has not been established. Asymptomatic increases in serum amylase levels were observed in a significantly higher number of patients treated with efavirenz 600 mg than in control patients. Increases in total cholesterol of 10-20% have been observed in some uninfected volunteers receiving efavirenz. Additional post-marketing surveillance data reveals the following side effects:

Body as a Whole: allergic reactions, asthenia

Central and Peripheral Nervous System: abnormal coordination, ataxia, convulsions, hypoesthesia, paresthesia, neuropathy, tremor

Endocrine: gynaecomastia

Gastrointestinal: constipation, malabsorption

Cardiovascular: flushing, palpitations

Liver and Biliary System: hepatic enzyme increase, hepatic failure

Metabolic and Nutritional: hypercholesterolemia, hypertriglyceridemia

Musculoskeletal: arthralgia, myalgia, myopathy

Psychiatric: aggressive reactions, agitation, delusions, emotional lability, mania, neurosis, paranoia, psychosis, suicide

Respiratory: dyspnea
Skin and Appendages: erythema multiforme, nail disorders, skin discoloration, Stevens-Johnson Syndrome.
Special Senses: abnormal vision, tinnitus

Special precautions:

Pregnancy:

Efavirenz has not been formally studied in pregnant women, but preliminary studies indicate that women should avoid becoming pregnant while on this drug. A study conducted in pregnant monkeys showed that there were malformations in fetuses after the monkeys were given a dose similar to the recommended human dose.

Lactation:

Women should also be cautious of breast-feeding while taking efavirenz because it may be passed through breast milk resulting in potential toxicity to the child. A study is planned to look at whether efavirenz can prevent or reduce the risk of transmission of HIV from mother to child.

Drug Interaction:

Grapefruit juice may effect plasma efavirenz concentration. Antibacterials: increased risk of rash with clarithromycin. Rifampicin reduces plasma concentration of efavirenz. Antidepressants: avoid concomitant use of st. john's wort Antihistaminics: increased risk of ventricular arrhythmias when used with terfenadine. Other antivirals: Efavirenz reduces plasma concentration of amprenavir, indinavir and lipinavir. Efavirenz reduces plasma concentration of saquinavir. Anxiolytics: Risk of prolonged sedation with midazolam. Oestrogen and progestogens: possibly reduced efficacy of oral contraceptives.

Known symptoms of overdosage and particulars of its treatment:

Some patients accidentally taking 600 mg twice daily have reported increased nervous system symptoms. One patient experienced involuntary muscle contractions.

Treatment of overdose with efavirenz should consist of general supportive measures, including monitoring of vital signs and observation of the patient's clinical status. Administration of activated charcoal may be used to aid removal of unabsorbed efavirenz. There is no specific antidote for overdose with efavirenz. Since efavirenz is highly protein bound, dialysis is unlikely to remove significant quantities from blood.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Storage life is 2 years.

Package: 10 capsules packed in blister strip, 10 such blisters packed in a carton.

INDA-400 CAPSULES
(Indinavir Capsules 400mg)

Composition:

Each Capsule contains:
Indinavir... 400 mg.

Presentation:
10x10's

Pharmacology:

Indinavir is an inhibitor of the human immunodeficiency virus (HIV) protease.
HIV protease is an enzyme required for the proteolytic cleavage of the viral polyprotein precursors into the individual functional proteins found in infectious HIV. Indinavir binds to the protease and inhibits the activity of the enzyme. This inhibition prevents cleavage of the viral polyproteins, resulting in the formation of immature noninfectious viral particles.

Pharmacokinetics:

Absorption:

Indinavir was rapidly absorbed in the fasted state with a time to peak plasma concentration (T_{max}) of 0.8 ± 0.3 hours (mean ± S.D.) (n=11). A greater than dose-proportional increase in indinavir plasma concentrations was observed over the 200-1000 mg dose range. At a dosing regimen of 800 mg every 8 hours, steady-state area under the plasma concentration time curve (AUC) was 30,691 ± 11,407 nM"hour (n=16), peak plasma concentration (C_{max}) was 12,617 ± 4037 nM (n=16), and plasma concentration eight hours post dose (trough) was 251 ± 178 nM (n=16).

Effect of Food on Oral Absorption:

Administration of indinavir with a meal high in calories, fat, and protein (784 kcal, 48.6 g fat, 31.3 g protein) resulted in a 77% ± 8% reduction in AUC and an 84% ± 7% reduction in C_{max} (n=10). Administration with lighter meals (e.g., a meal of dry toast with jelly, apple juice, and coffee with skim milk and sugar or a meal of corn flakes, skim milk and sugar) resulted in little or no change in A.C. C_{max} or trough concentration.

Distribution:

Indinavir was approximately 60% bound to human plasma proteins over a concentration range of 81 nM to 16,300 nM.

Metabolism:
Following a 400-mg dose of ^{14}C-indinavir, 83 ± 1% (n=4) and 19 ± 3% (n=6) of the total radioactivity was recovered in feces and urine, respectively; radioactivity due to parent drug in feces and urine was 19.1% and 9.4%, respectively. Seven metabolites have been identified, one glucuronide conjugate and six oxidative metabolites. In vitro studies indicate that cytochrome P-450 3A4 (CYP3A4) is the major enzyme responsible for formation of the oxidative metabolites.

Elimination:

Less than 20% of indinavir is excreted unchanged in the urine. Mean urinary excretion of unchanged drug was 10.4 ± 4.9% (n=10) and 12.0 ± 4.9% (n=10) following a single 700-mg and 1000-mg dose, respectively. Indinavir was rapidly eliminated with a half-life of 1.8 ± 0.4 hours (n=10). Significant accumulation was not observed after multiple dosing at 800 mg every 8 hours

Indications:

Indinavir in combination with antiretroviral agents is indicated for the treatment of HIV infection in adults only.

Contra-indications:

Indinavir is contraindicated in patients with clinically significant hypersensitivity to any of its components.
Indinavirshould not be administered concurrently with terfenadine, cisapride, astemizole, triazolam, midazolam, pimozide, or ergot derivatives. Inhibition of CYP3A4 by indinavir could result in elevated plasma concentrations of these drugs, potentially causing serious or life-threatening reactions.

Dosage and directions for use:

The recommended dosage of indinavir is 800 mg (two 400-mg capsules) orally every 8 hours.
For optimal absorption, indinavir Indinavir should be administered without food but with water 1 hour before or 2 hours after a meal. Alternatively, Indinavir may be administered with other liquids such as skim milk, juice, coffee, or tea, or with a light meal, e.g. dry toast with jelly, juice, and coffee with skim milk and sugar; or corn flakes, skim milk and sugar.
To ensure adequate hydration, it is recommended that the patient drink at least 1.5 litres (approximately 48 ounces) of liquids during the course of 24 hours.
Hepatic Insufficiency
The dosage of Indinavir should be reduced to 600 mg every 8 hours in patients with mild to moderate hepatic insufficiency due to cirrhosis.
Nephrolithiasis/Urolithiasis
In addition to adequate hydration, medical management in patients who experience nephrolithiasis/urolithiasis may include temporary interruption (e.g. 1-3 days) or discontinuation of therapy.
Delavirdine
Dose reduction of indinavir to 600 mg every 8 hours should be considered when administering delavirdine 400 mg three times a day.

Didanosine

If indinavir and didanosine are administered concomitantly, they should be administered at least one hour apart on an empty stomach.

Efavirenz

Dose increase of indinavir to 1000 mg every 8 hours is recommended when administering efavirenz concurrently.
Itraconazole
Dose reduction of indinavir to 600 mg every 8 hours is recommended when administering itraconazole 200 mg twice daily concurrently.

Ketoconazole
Dose reduction of indinavir to 600 mg every 8 hours is recommended when administering ketoconazole concurrently.
Rifabutin
Dose reduction of rifabutin to half the standard dose and a dose increase of indinavir to 1000 mg (three 333-mg capsules) every 8 hours are recommended when rifabutin and indinavir are coadministered.

Warning:

NEPHROLITHIASIS/UROLITHIASIS

Nephrolithiasis/urolithiasis has occurred with indinavir therapy. In some cases, nephrolithiasis has been associated with renal insufficiency or acute renal failure. If signs or symptoms of nephrolithiasis/urolithiasis occur, (including flank pain, with or without hematuria or microscopic hematuria), temporary interruption (e.g. 1-3 days) or discontinuation of therapy may be considered. Adequate hydration is recommended in all patients treated with indinavir.

HEMOLYTIC ANEMIA

Acute hemolytic anemia, including cases resulting in death, has been reported in patients treated with indinavir. Once a diagnosis is apparent, appropriate measures for the treatment of hemolytic anemia should be instituted, including discontinuation of indinavir.

HEPATITIS

Hepatitis including cases resulting in hepatic failure and death has been reported in patients treated with indinavir. Because the majority of these patients had confounding medical conditions and/or were receiving concomitant therapy(ies), a causal relationship between indinavir and these events has not been established.

HYPERGLYCEMIA

New onset diabetes mellitus, exacerbation of pre-existing diabetes mellitus and hyperglycemia have been reported during post-marketing surveillance in HIV-infected patients receiving protease inhibitor therapy. Some patients required either initiation or dose adjustments of insulin or oral hypoglycemic agents for treatment of these events. In some cases, diabetic ketoacidosis has occurred. In those patients who discontinued protease inhibitor therapy, hyperglycemia persisted in some case

Side-effects & special precautions:

Body As A Whole: Redistribution/accumulation of body fat.
Cardiovascular System: Cardiovascular disorders including myocardial infarction and angina pectoris.
Digestive System: Liver function abnormalities; hepatitis including reports of hepatic failure; pancreatitis; jaundice; abdominal distention; dyspepsia.
Hematologic: Increased spontaneous bleeding in patients with hemophilia; acute hemolytic anemia.
Endocrine/Metabolic: New onset diabetes mellitus, exacerbation of pre-existing diabetes mellitus, hyperglycemia.
Hypersensitivity: Anaphylactoid reactions; urticaria
Musculoskeletal System: Arthralgia
Nervous System / Psychiatric: Oral paresthesia; depression.
Skin and Skin Appendages: rash including erythema multiforme and Stevens-Johnson Syndrome; hyperpigmentation: alopecia; ingrown toenails and/or paronychia; pruritus.
Urogenital System

Nephrolithiasis/urolithiasis; in some cases resulting in renal insufficiency or acute renal failure; interstitial nephritis sometimes with indinavir crystal deposits; in some patients, the interstitial nephritis did not resolve following discontinuation of indinavir; crystalluria; dysuria.
Laboratory abnormalities: Increased serum triglycerides, increased serum cholesterol.

Special precautions:

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Indinavir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Although it is not known whether indinavir is excreted in human milk, there exists the potential for adverse effects from indinavir in nursing infants. Mothers should be instructed to discontinue nursing if they are receiving Indivan-400. It is also recommended that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Drug Interaction:

Concomitant use of indinavir with lovastatin or simvastatin is not recommended. Caution should be exercised if HIV protease inhibitors, including indinavir, are used concurrently with other HMG-CoA reductase inhibitors that are also metabolized by the CYP3A4 pathway (e.g. atorvastatin or cerivastatin). The risk of myopathy including rhabdomyolysis may be increased when HIV protease inhibitors, including indinavir, are used in combination with these drugs.
Concomitant use of indinavir and St. John's wort (Hypericum perforatum) or products containing St. John's wort is not recommended. Coadministration of indinavir and St. John's wort has been shown to substantially decrease indinavir concentrations and may lead to loss of virologic response and possible resistance to indinavir or to the class of protease inhibitors.
Delavirdine: Due to an increase in indinavir plasma concentrations (preliminary results), a dosage reduction of indinavir should be considered when ritonavir and delavirdine are coadministered.
Efavirenz: Due to a decrease in the plasma concentrations of indinavir, a dosage increase of indinavir is recommended when indinavir and efavirenz are coadministered. No adjustment of the dose of efavirenz is necessary when given with indinavir.
Itraconazole: Itraconazole is an inhibitor of P-450 3A4 that increases plasma concentrations of indinavir. Therefore, a dosage induction of indinavir is recommended when indinavir and itraconazole are co-administered.
Ketoconazole: Ketoconazole is an inhibitor of P-450 3A4 that increases plasma concentrations of indinavir. Therefore, a dosage reduction of indinavir is recommended when indinavir and itraconazole are co-administered.
Rifabutin: When rifabutin and indinavir are coadministered, there is an increase in the plasma concentrations of rifabutin and a decrease in plasma concentrations of indinavir. A dosage reduction of rifabutin and a dosage increase of indinavir are necessary when rifabutin is coadministered with indinavir. The suggested dose adjustments are expected to result in rifabutin concentrations at least 50% higher than typically observed when rifabutin is administered alone at its usual dose (300 mg/day) and indinavir concentrations which may be slightly less than typically observed when indinavir is administered alone at its usual dose (800 mg every 8 hours).

Rifampin: Rifampin is a potent inducer of P-450 3A4 that markedly diminishes plasma concentrations of indinavir. Therefore, Indinavirand rifampin should not be coadministered.

Known symptoms of overdosage and particulars of its treatment:

There have been more than 60 reports of acute or chronic human overdosage (up to 23 times the recommended total daily doses of 2400 mg) with indinavir. The most commonly reported symptoms were renal (e.g. nephrolithiasis/urolithiasis, flank pain, hematuria) and gastrointestinal (e.g. nausea, vomiting, diarrhoea).
It is not known whether indinavir is dialyzable by peritoneal or hemodialysis.

Storage conditions and period.

Store in cool, dry & dark place, preferably below 25°C. Storage life is 2 years.

Package: 10 capsules packed in blister strip, 10 such blisters packed in a carton.