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Pharmacode Direction

30 mm

XXXXX
Ixime 400-(MAL)

For the use of a Qualified Health Provider or Hospital only

IXIME 400 Tablets

DESCRIPTION
Cefixime is a semisynthetic, cephalosporin antibiotic for oral administration.
White to pale yellow film coated capsule shaped tablet with "LUPIN" debossed on one side and scored on the other.

COMPOSITION
Each film coated IXIME Tablet contains Cefixime USP
equivalent to Cefixime Anhydrous 400 mg

CLINICAL PHARMACOLOGY

MICROBIOLOGY
As with other cephalosporins, bactericidal action of Cefixime results results from inhibition of cell wall synthesis. Cefixime is highly stable in the presence of ß lactamase enzymes.

As a result, many organisms resistant to Penicillins and some Cephalosporins due to the presence of ß lactamases, may be susceptible to Cefixime.

Cefixime has been shown to be active against most strains of the following organisms both *in vitro* and in clinical infections

GRAM-POSITIVE ORGANISMS
Streptococcus pneumoniae
Streptococcus pyogenes

GRAM-NEGATIVE ORGANISMS
Haemophilus influenzae (ß lactamase positive & negative strains)
Moraxella catarrhalis (mostly ß lactamase positive)
Escherichia coli
Proteus mirabilis
Salmonella typhi
Neisseria gonorrhoeae (including Penicillinase & Non Penicillinase Producing strains)

CEFIXIME has been shown to be active *in vitro* against most strains of the following organisms, however, clinical efficacy has not been established

GRAM-POSITIVE ORGANISMS
Streptococcus agalactiae

GRAM-NEGATIVE ORGANISMS
Haemophilus parainfluenzae (â lactamase positive & negative strains)
Proteus vulgaris,
Klebsiella pneumoniae
Klebsiella oxytoca
Pasteurella multocida
Providencia species
Salmonella species
Shigella species
Citrobacter amalonaticus
Citrobacter diversus
Serratia marcescens

NOTE
Pseudomonas species, strains of group D Streptococci (including *Enterococci*), *Listeria monocytogenes*, most strains of *Staphylococci* (including Methicillin Resistant Strains) and most strains of *Enterobacter* are resistant to Cefixime.
In addition, most strains of *Bacteroides fragilis* and *Clostridia* are resistant to Cefixime.

PHARMACOKINETICS
Cefixime Tablets given orally are about 40-50% absorbed whether administered with or without food, however, time to maximal absorption is increased approximately 0.8 hours when administered with food.

A single 200 mg tablet of Cefixime produced an average peak serum concentration of approximately 2 *µg/ml* (range of 1 to 4 *µg/ml*) where as a single 400 mg tablet produced an average peak concentration of approximately 3.7*µg/ml* (range of 1.3 to 7.7 *µg/ml)*

Cross over studies of tablet versus suspension have not been performed in children.

Peak serum concentrations occur between 2 and 6 hours following the administration of a single 200 mg Tablet or a single 400 mg tablet.

Serum Levels of Cefixime after Administration of Tablets *(µg/mL)*

Dose *(mg)*	1 hour	2 hours	4 hours	6 hours	8 hours	12 hours	24 hours
100 mg	0.3	0.8	1.0	0.7	0.4	0.2	0.02
200 mg	0.7	1.4	2	1.5	1	0.4	0.03
400 mg	1.2	2.5	3.5	2.7	1.7	0.6	0.04

Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours.
In animal studies it was noted that Cefixime is also excreted in the bile in excess of 10% of the administered dose.

Serum protein binding is concentration independent with a bound fraction of approximately 65%.
In a multiple dose study conducted with a research formulation which was less bioavailable than the tablet or suspension, there was little accumulation of drug in serum or urine after dosing for 14 days.

The serum half-life of Cefixime in healthy subjects is independent of dosage form and averages 3 to 4hours but may range up to 9 hours in some normal volunteers.
Average AUCs at steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults.

In subjects with moderate impairment of renal function (20 to 40 mL/min Creatinine Clearance), the average serum half-life of Cefixime is prolonged to 6.4 hours.
In severe renal impairment (5 to 20 mL/min Creatinine Clearance), the half-life increased to an average of 11.5 hours.

The drug is not cleared significantly from the blood by hemodialysis or peritoneal dialysis.
However, a study indicated that with doses of 400 mg, patients undergoing hemodialysis have similar blood profiles as subjects with Creatinine Clearances of 21-60 mL/min.

There is no evidence of metabolism of Cefixime *in vivo*.

Adequate data on CSF levels of Cefixime are not available.

INDICATIONS
IXIME is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms

Uncomplicated Urinary Tract Infections caused by *Escherichia coli & Proteus mirabilis*

Otitis Media caused by *Haemophilus influenzae* (ß lactamase positive & negative strains), *Moraxella catarrhalis* (most of which are ß lactamase positive) and *Streptococcus pyogenes*

Pharyngitis and Tonsillitis caused by *Streptococcus pyogenes*

NOTE
Penicillin is the usual drug of choice in the treatment of *Streptococcus pyogenes* infections, including the prophylaxis of Rheumatic Fever. Cefixime is generally effective in the eradication of *Streptococcus pyogenes* from the nasopharynx, however, data establishing the efficacy of Cefixime in the subsequent prevention of Rheumatic Fever are not available.

Acute Bronchitis and Acute Exacerbations of Chronic Bronchitis, caused by *Streptococcus pneumoniae* & *Haemophilus influenzae* (ß lactamase positive and negative strains)

Uncomplicated Multidrug Resistant and Quinolone Resistant Typhoid Fever caused by *Salmonella typhi.*

Uncomplicated Gonorrhea (cervical/urethral) caused by both Penicillinase and Non Penicillinase Producing Strains of *Neisseria gonorrhoeae*

DOSAGE

ADULT
The recommended dose of Cefixime is 400 mg once daily.

The recommended dose of Cefixime for Uncomplicated Multidrug Resistant Typhoid Fever is *15 to 20mg /kg bodyweight / 24 hours* for 7 to 14 days and for Quinolone Resistant Typhoid Fever is *20mg /kg bodyweight / 24 hours* for 7 to 14 days

A single oral dose of 400 mg of Cefixime is recommended for the treatment of Uncomplicated Cervical / Urethral Gonococcal Infections

CHILDREN
Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose.

In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of Cefixime should be given for at least 10 days.

RENAL IMPAIRMENT
Cefixime may be administered in the presence of impaired renal function as follows
Creatinine Clearance Dose
>60ml/min Normal Dose and Schedule
21-60ml/min 75% of the Standard Dosage at the Standard Dosing Interval
<20ml/min 50% of the Standard Dosage at the Standard Dosing Interval

CONTRAINDICATION
Cefixime is contraindicated in patients with known allergy to the Cephalosporin group of antibiotics.

Warning and Precautions
Before therapy with cefixime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with Ixime 400 Tablets, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, Ixime 400 Tablets must be discontinued immediately and

RABRO ADVERTISING & MARKETING

Market/Customer :-	Malaysia	**Location**	Mandideep
Prepared On	31/05/2023	**Tracking No.**	2
Product name	Ixime Tab (Malaysia)	**Font Size:**	5 pt.
Material code	XXXXX	**Supercedes Material code**	261647
Open Size	120 x 240 mm (W x H)	**Pharmacode value**	6366
Folded Size	120 x 30 mm (W x H)	**Component**	Leaflet
No. of Folds	NA	**GSM :**	54 ± 10% gsm Creamwove Paper
Pantone Colours	■ Black		
Reason of Revision:	Change in text matter as received from customer		

Rabro Advertising & Marketing
Artwork Same Size
Size: 120 x 240 mm (W X H)
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1st Laser Proof 31/05/2k23 2nd Laser Proof 28/08/2k23 3rd Laser Proof 30/08/2k23

appropriate alternative therapy instituted.

Prescribing Cefixime in the absence of a proven or strongly suspected bacterial infection of a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

The possibility of the emergence of resistant organisms which might result in overgrowth should be kept in mind, particularly during prolonged treatment. In such cases, careful observation of the patient is essential and if superinfection occurs during therapy appropriate measures should be taken.

The dose of Cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD).

Patients on dialysis should be monitored carefully. Cefixime should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Pseudomembraneous colitis has been reported with the use of Cefixime and other broad spectrum antibiotics including Macrolides, Semisynthetic Penicillins and Cephalosporins, therefore it is important to consider this diagnosis in patients who develop diarrhea in association with the use of antibiotics. Symptoms of Pseudomembraneous Colitis may occur during or after antibiotic treatment and may range in severity from mild to life threatening.

DRUG INTERACTIONS

GENERAL
A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions.

A false positive direct Coombs test has been reported during treatment with cephalosporin antibiotics, therefore it should be recognized that a positive Coombs test may be due to the drug.

In common with other cephalosporins, increases in prothrombin times have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy.

CARBAMAZEPINE
Elevated carbamazepine levels have been reported in postmarketing experience when Cefixime was administered concomitantly.
Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

WARFARIN AND ANTICOAGULANTS
Increased Prothrombin Time, with or without clinical bleeding, has been reported when Cefixime was administered concomitantly.
Care should therefore be taken in patients receiving anticoagulation therapy

PROBENECID
Concomitant administration of Probenecid increases peak serum concentrations and the AUC while decreasing the renal clearance and volume of distribution of Cefixime

OTHER DRUGS
Concomitant administration of Cefixime and Nifedipine increases the oral bioavailability of Cefixime as a result of higher peak plasma concentrations and area under the plasma concentration time curve.

In vitro, in pooled serum, Acetaminophen, Heparin, Phenytoin, Diazepam, Ibuprofen or Furosemide had no clinically important effects on the protein binding of Cefixime.

LABORATORY TEST INTERFERENCES

TESTS FOR URINARY GLUCOSE
Cefixime, like most Cephalosporins may cause false positive results in urinary glucose determinations, using cupric sulphate as in Benedict's solution, Clinitest or Fehling's slolution, but enzymatic Glucose Oxidase methods are unaffected.

IMMUNOHEMATOLOGY TESTS
A false positive direct Coombs test has been reported during treatment with Cephalosporin antibiotics, therefore it should be recognised that this reaction may interfere with hematologic studies or transfusion cross matching procedures and should be considered in patients receiving Cefixime

URINARY KETONES
Cefixime may cause false positive results for urinary ketones when tests using nitroprusside are used but not with tests using nitroferricyanide

USAGE IN PREGNANCY
Pregnancy Category B
Reproduction studies with Cefixime have been done in mice and rats at doses up to 400 times the human dose and revealed no evidence of harm to the fetus.
There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

LABOUR AND DELIVERY
Cefixime has not been studied for use during labor and delivery. Treatment should only be given if clearly needed.

NURSING MOTHERS
It is not known whether CEFIXIME TABLETS is excreted in human milk. Consideration shouldbe given to discontinuing nursing temporarily during treatment with this drug.

SIDE EFFECTS
Cefixime is generally well tolerated.
The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature.

Gastrointestinal Disturbances
The most frequent side effects seen with Cefixime are diarrhoea and stool changes with diarrhoea being been more commonly associated with higher doses.
Some cases of moderate to severe diarrhoea have been reported; this has occasionally warranted cessation of therapy. Ixime should be discontinued if marked diarrhoea occurs. Other gastrointestinal side effects seen less frequently are nausea, abdominal pain, dyspepsia, vomiting and flatulence. Pseudomembranous colitis has been reported.

Central Nervous System
Headache and dizziness
Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced.
If seizures associated with drug therapy occur, the drug should be discontinued.
Anticonvulsant therapy can be given if clinically indicated.

Hypersensitivity Reactions
Allergies in the form of rash, pruritus, urticaria, drug fever and arthralgia have been observed.
These reactions usually subsided upon discontinuation of therapy.
Rarely Erythema multiforme, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis have been reported

Haematological and Clinical Chemistry
Thrombocytopenia, leukopenia and eosinophilia have been reported though these reactions were infrequent and reversible.
Mild transient changes in liver and renal function tests too have been observed.

Hepatic Disorders
Transient rises in liver transaminases, alkaline phosphatase and jaundice can also occur

Miscellaneous
Other possible reactions include genital pruritus and vaginitis

OVERDOSAGE
Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis. Adverse reactions in small numbers of healthy adult volunteers receiving single doses up to 2 g of CEFIXIME TABLETS did not differ from the profile seen in patients treated at the recommended doses.

PRESENTATION
Avaliable as a monocarton containing a blister strip of 6 tablets.

STORAGE
Store below 25°C.

SHELF LIFE
24 months.

Date of Revision
28 August 2023

Manufactured by:
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