CEFOCEF-O TABLETS
CEFIXIME

DESCRIPTION
Cefixime is a semisynthetic, broad spectrum, third generation cephalosporin antibiotic for oral administration.

COMPOSITION
Cefocef-O 200
Each film-coated tablet contains:

Cefixime USP as Trihydrate equivalent to anhydrous Cefixime	200 mg
Colour	Titanium Dioxide IP

Cefocef-O 100
Each dispersible uncoated tablet contains:

Cefixime USP as Trihydrate equivalent to anhydrous Cefixime	100 mg
Flavour	Pineapple

Cefocef-O 50
Each dispersible uncoated tablet contains:

Cefixime USP as Trihydrate equivalent to anhydrous Cefixime	50 mg
Flavour	Pineapple

CLINICAL PHARMACOLOGY & ANTI-MICROBIAL SPECTRUM
As with other cephalosporins, bactericidal action of cefixime results from inhibition of cell-wall synthesis. Cefixime is highly stable in the presence of beta-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins due to the presence of beta-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 (beta-lactamase positive & negative strains)
Moraxella (Branhamella) catarrhalis (beta-lactamase positive)
Escherichia coli
Proteus mirabilis
Neisseria gonorrhoeae (penicillinase & non-penicillinase-producing strains)

Cefixime has been shown to be active *in vitro* against most strains of the following Organisms:
Gram-positive Organisms.
Streptococcus agalactiae
Gram-negative Organisms.
Haemophilus parainfluenzae (beta-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*, *Enterobacter*, *Bacteroides fragilis* and *Clostridia* are resistant to cefixime.

PHARMACOKINETICS
Cefixime given orally, is about 40%-50% absorbed from the GI tract, whether administered with or without food. After a 200mg oral dose, peak [plasma] levels of an average of 2.7mg/l are achieved, between 3 and 4 hours post dose in fasting volunteers.

The mean volume of distribution of cefixime is 0.1 L/kg. Penetration into tissue fluid is slow (mean tmax=6.7h) but peak concentration similar to those of plasma has been achieved. Lower levels are found in palatine tonsil, maxillary sinus mucosa, sputum and middle ear discharge. Very high concentrations occur in bile. After single oral doses of 100, 200 or 400 mg, mean biliary concentrations were 135, 134 and 190 mg/ml respectively. The mean concentration in the CSF with inflamed and noninflamed meninges was reportedly 0.17mg/l and 0.22mg/l respectively. 65-70% of the drug is protein bound.

The mean elimination half-life (t1/2) of 3h is considerably longer than those of earlier oral cephalosporins such as cephalexin, cefaclor (<1h) and cefadroxil (1.5h). Urinary excretion accounts for between 12 and 34% of an orally administered dose. Upto 60% of the drug is eliminated by non-renal mechanisms**.** The t1/2 of cefixime is prolonged in patients with severely impaired renal function. Cefixime is not removed to a significant degree by either peritoneal dialysis or haemodialysis. Cefixime is mainly excreted unchanged in bile and urine.

INDICATIONS
- Urinary tract infections
- Upper and lower respiratory tract infections
- Acute otitis media
- Gonococcal urethritis

DOSAGE
Adults & Children [weighing more than 50 kg or older than 12 yr of age]:
200-400 mg in single or divided doses.

Children 6 mo to 12 yr of age [or weighing under 50 kg]:
8 mg/kg/day as a once-daily dose or in 2 divided doses of 4 mg/kg every 12 h.

Uncomplicated Gonorrhea
Adults: 400 mg as a single dose.

Dose Adjustment for Renal Function Impairment:
If creatinine clearance is between 21 and 60 mL/min or patient is on hemodialysis, give 75% of dose (300 mg/day).

If creatinine clearance is less than 20 mL/min or patient is on continuous peritoneal dialysis, give 50% of dose (200 mg/day).

NB: The prescribed dose may be administered without regard to meals.

CONTRAINDICATIONS
Cefixime is contraindicated in patients with a known hypersensitivity to cephalosporin group of antibiotics.

WARNINGS & 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. If cefixime is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among betalactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy.

If an allergic reaction to cefixime occurs, discontinue the drug. Hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated.

Treatment with broad spectrum antibiotics, including cefixime, alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *clostridium difficile* is a primary cause of severe antibiotic-associated diarrhea including pseudomembranous colitis. Therefore, it is important to consider this diagnosis in patients who develop diarrhea in association with the use of antibiotics. Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, management should include fluids, electrolytes, and protein supplementation. If the colitis does not improve oral vancomycin may be required.

Usage in Pregnancy
Pregnancy Category B: Reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and have revealed no evidence of harm to the fetus due to cefixime. 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.

Labor & Delivery
Cefixime has not been studied for use during labor and delivery. Treatment should be given only if clearly needed.

Nursing Mothers
It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

Pediatric Use
Safety and effectiveness of cefixime in children aged less than six months has not been established.

DRUG INTERACTIONS

A false positive test for glucose in urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets but not with enzymatic based tests.

False positive coomb's test: False positive reactions for ketones in urine (using nitroprusside methods) have been reported.

Probenecid may increase and prolong cephalosporin plasma levels by competitively inhibiting renal tubular secretion.

Loop Diuretics: Use cephalosporins with caution in patients receiving potent diuretics (e.g. loop diuretics).

Carbamazepine: Elevated carbamazepine levels have been reported in postmarketing studies when cefixime is administered concomitantly.

Warfarin & Anticoagulants: Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly.

ADVERSE REACTIONS

Most of the adverse reactions observed in clinical trials were of a mild and transient nature. The most commonly seen reactions were: skin rash, fever, urticaria, pruritis, erythema multiforme, Steven-Johnson syndrome, eosinophilia, leucopenia, genital pruritis, vaginitis, candidiasis, anaphylaxis, superinfection, haemolytic anaemia, diarrhoea, dyspepsia, flatulence, abdominal pain, pseudomembranous colitis, and transient elevation of SGOT, SGPT, alkaline phosphatase, BUN and creatinine.

PRESENTATION

Cefocef-O 200/ Cefocef-O 100/ Cefocef-O 50 is available in strips containing 10 tablets