For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory xxxxxxxx-8883

# TOPCEF Instause

(Cefixime Oral Suspension)

**TOPCEF Instause** is an orally active third-generation semisynthetic, cephalosporin antibiotic for oral administration ((6R, 7R)-7-[2-(2-Amino-4-thiazolyl) glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid, $7^2$(Z)-[O- (carboxymethyl) oxime]-trihydrate). which has marked in-vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms. It is indicated for the treatment respiratory tract infections (Pharyngitis, Tonsillitis, Acute bronchitis, Acute exacerbation of chronic bronchitis, Otitis media, Sinusitis), urinary tract infections (Acute uncomplicated pylonephritis, Acute uncomplicated cystitis, gonococcal urethritis) and biliary tract infections. Clinical trials have shown promising results in resistant Typhoid fever especially in children.

**CLINICAL PHARMACOLOGY**

The bactericidal action of Cefixime results from inhibition of cell-wall synthesis. Cefixime is highly beta-lactamase stable and as a result many organisms resistant to penicillins and some cephalosporins due to the presence of beta-lactamases may be susceptible to Cefixime. Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including *Streptococcus pneumoniae, Streptococcus pyogenes*, *Escherichia coli, Salmonella typhi, Proteus mirabilis, Klebsiella species, Haemophilus influenzae* (beta-lactamase positive and negative), *Morexiella catarrhalis* (beta-lactamase positive and negative) and *Enterobacter species*. Cefixime is highly stable in the presence of beta-lactamase enzymes. Cefixime is also very active both in vitro and in clinical infections caused by anaerobic bacteria such as Peptostreptococcus species, Lactobacillus species, and *Veillonella* species Most strains of enterococci (*Streptococcus faecalis, group D Streptococci*) and Staph- ylococci (including coagulase positive and negative strains and methicillin-resistant strains) are resistant to Cefixime. In addition, most strains of *Pseudomonas, Bacteroides fragilis, Listeria monocytogenes and Clostridia* are resistant to Cefixime.

Cefixime given orally is about 40% to 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 200mg administration produces an average peak serum concentration of approximately 2mcg/ml; a single 400mg produces an average peak concentration of approximately 3.7 mcg/ml. Peak serum concentration following oral administration of a single 200mg or 400mg dosage occurs between 2 and 6 hours. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. There is no evidence of drug accumulation following administration of 200 mg twice daily or 400 mg once daily for 15 days. In children the pharmacokinetics of Cefixime 8mg/kg were similar to those observed in adults given a 400 mg capsule dose. In animal studies, it was noted that Cefixime is also excreted in bile in excess of 10% of the administered dose. Serum protein binding is concentration independent with a bound fraction of approxim -ately 65%. The serum half-life of Cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours. In subjects with moderate impairment of renal function (20 to 40 mL/minute 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. There is no evidence of metabolism of Cefixime in vivo.

**CLINICAL USES**

**TOPCEF Instause** is indicated for the treatment of following infections when caused by susceptible organisms :

1. Respiratory tract infections
2. Otitis media
3. Urinary Tract infections (uncomplicated & complicated)
4. Gonococcal Urethritis
5. Sequential treatment after initial i.v chemotherapy by potential cephalosporins
6. Typhoid fever

**CONTRAINDICATIONS**

Patient with known hypersensitivity to cephalosporin antibiotics

**WARNINGS**

Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs. Cephalosporins should be given with caution to penicillin-sensitive patients, as there is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have had severe reactions (including anaphylaxis) to both classes of drugs. If an allergic effect occurs with Cefixime, the drug should be discontinued and the patient treated with appropriate agents if necessary. 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 diarrhoea including pseudomembranous colitis.

**PRECAUTIONS**

Cefixime should be administered with caution in patients with markedly impaired renal function. Cefixime should be prescribed with caution in patients with history of gastrointestinal disease particularly colitis.

**USE IN PREGNANCY, LACTATION & CHILDREN**

There are no adequate and well controlled studies in pregnant women. Cefixime should therefore not be used in pregnancy or in nursing mothers unless considered essential by the physician. The safety and efficacy of Cefixime has not been established in children aged less than 6 months.

**DOSAGE AND ADMINISTRATION**

Absorption of Cefixime is not significantly modified by the presence of food. The usual course of treatment is 7-14 days.

**Adults and Children over 12 years:** The recommended adult dosage is 400mg daily, given either as a single dose or in two divided doses.

**Children:** The recommended dosage for children is 8 mg/kg/day administered as a single dose or in two divided doses. The safety and efficacy of Cefixime has not been established in children aged less than 6 months.

**Pediatric dosage chart**

| Patient weight Kg | Dose/day mg |
|---|---|
| 6.25 | 50 |
| 12.5 | 100 |
| 18.75 | 150 |
| 25.0 | 200 |
| 31.25 | 250 |
| 37.5 | 300 |

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

**Dosage in renal impairment:** Cefixime may be administered in the presence of impaired renal function. Normal dose may be given in patients with creatinine clearances of 60 ml/ min or greater. Patients whose clearance is between 21 and 60 ml/min or patients who are on renal hemodialysis may be given 75% of the standard dosage at the standard dosing interval (i.e. 300mg daily). Patients whose clearance is < 20 ml/min, or patients who are on continuous ambulatory peritoneal dialysis may be given half the standard dosage at the standard dosing interval (i.e. 200mg daily).

**DRUG INTERACTIONS**

No significant drug interactions have been reported to date. 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 might be due to the drug.

**ADVERSE REACTIONS**

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 with Cefixime are diarrhoea and stool changes. Some cases of moderate to severe diarrhoea have been reported; this has occasionally warranted cessation of therapy. Cefixime 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.

**Hypersensitivity reactions:** Allergies in the form of rash, pruritis, urticaria, drug fever and arthralgia have been observed. These reactions usually subsided upon discontinuation of therapy.

**Haematological and clinical chemistry:** Thrombocytopenia, leukopenia and eosinophilia have been reported. These reactions were infrequent and reversible. Mild transient changes in liver and renal function tests have been observed. Occasional transient rise in serum amylase was reported.

**Miscellaneous:** Other possible reactions include genital pruritus and vaginitis.

**OVERDOSAGE**

There is no experience with overdoses of Cefixime. Adverse reactions seen at dose levels up to 2g. Cefixime in normal subjects did not differ from the profile seen in patients treated at the recommended doses. Gastric lavage may be initiated in overdosage. No specific antidote exists. TOPCEF Instause is not removed from the circulation in significant quantities by dialysis.

**INSTRUCTION FOR ADMINISTRATION: TOPCEF Instause** to be administered as such and it should not be mixed with water, fruit juice or any other liquid before administration. **TOPCEF Instause** should be shaken well before use.

**STORAGE**

Store below $30^{o}$C, Protected from moisture

**PRESENTATION:**

TOPCEF Instause is available in a 30 ml Bottle.

Topcef Instause is use for paediatric patients only

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

At : Vill. Manakpur, Teh. Nalagarh, Dist. Solan (H.P.)