

Cefiget™

(C E F I X I M E)

Cefixime Tablets 200mg USP

Cefixime Capsules 400mg

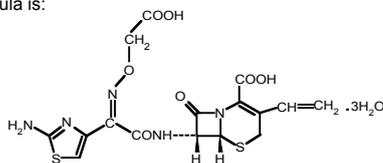
Cefixime 100mg/5mL Powder for Oral Suspension USP

Cefixime 200mg/5mL DS Powder for Oral Suspension USP

DESCRIPTION

CEFIGET (Cefixime) is a semisynthetic third generation cephalosporin antibiotic. Chemically, cefixime is described as (6*R*,7*R*)-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⁻(*Z*)-[O-(carboxymethyl)oxime] trihydrate.

The molecular formula is $C_{18}H_{15}N_5O_5S_2 \cdot 3H_2O$ and the structural formula is:



Cefixime Trihydrate

QUALITATIVE & QUANTITATIVE COMPOSITION

CEFIGET (Cefixime) is available for oral administration as:

- CEFIGET Tablets 200mg
Each film-coated tablet contains:
Cefixime USP...200mg (as Cefixime trihydrate)
- CEFIGET Capsules 400mg
Each capsule contains:
Cefixime USP...400mg (as Cefixime trihydrate)
- CEFIGET Powder for Oral Suspension 100mg/5mL
Each reconstituted 5mL contains:
Cefixime USP...100mg (as Cefixime trihydrate)
- CEFIGET DS Powder for Oral Suspension 200mg/5mL
Each reconstituted 5mL contains:
Cefixime USP...200mg (as Cefixime trihydrate)

CLINICAL PHARMACOLOGY

Mechanism of Action

Cefixime has marked *in vitro* bactericidal activity of gram positive and gram negative. Like other cephalosporins, cefixime exhibits its bactericidal action by binding to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the inhibition of the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins. The antibacterial effect of cefixime results from inhibition of mucopeptide synthesis in the bacterial cell wall.

Pharmacokinetics

Absorption & Distribution

Cefixime given orally, is 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. Cefixime is better absorbed from oral suspension than from other oral dosage forms. The plasma half life is usually about 3-4 hours.

Cefixime is approximately 65% bound to plasma proteins, independent of drug concentration. Cefixime crosses the placenta.

Metabolism & Excretion

Approximately 50% of an absorbed dose of cefixime is excreted as unchanged drug in the urine in 24 hours. Up to 60% may be eliminated by non-renal mechanism; there is no evidence of metabolism but some is probably excreted into the feces from bile.

Special Populations

Renal Insufficiency

In subjects with moderate impairment of renal function

(20 to 40mL/min creatinine clearance), the average serum half-life of cefixime is prolonged to 6.4 hours. In severe renal impairment (5 to 20mL/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.

Microbiology

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.

Spectrum of cefixime is broad and it is active against most strains of the following micro-organisms in both *in vitro* and *in vivo*. Cefixime has a longer duration of action than other cephalosporins that are active by mouth.

Gram-positive Organisms

Streptococcus pneumoniae,
Streptococcus pyogenes.

Gram-negative Organisms

Haemophilus influenzae (beta-lactamase positive and negative strains),

Moraxella (Branhamella) *catarrhalis*

(most of which are beta-lactamase positive),

Escherichia coli,

Proteus mirabilis,

Neisseria gonorrhoeae (including penicillinase- and non-penicillinase-producing strains).

Klebsiella species.

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.

THERAPEUTIC INDICATIONS

CEFIGET (Cefixime) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

- Uncomplicated urinary tract infections
- Otitis media
- Pharyngitis and tonsillitis
- Acute bronchitis and acute exacerbations of chronic bronchitis
- Uncomplicated gonorrhea (cervical/urethral)

DOSAGE AND ADMINISTRATION

Adults and children over 10 years: The recommended adult dose of CEFIGET (Cefixime) is 200 - 400mg daily according to the severity of infection, given either as a single dose or in two divided doses.

Uncomplicated cervical/urethral gonococcal infections: For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400mg is recommended.

Children: The recommended dose is 8mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4mg/kg every 12 hours except for urinary tract infection where once daily dosing must be used. As a general guide for prescribing in children the following daily doses in terms of volume of pediatric oral suspension are suggested:

6 months up to 1 year: 3.75mL daily

Children 1-4 years: 5mL daily

Children 5-10 years: 10mL daily

Children weighing more than 50 kg or older than 10 years should be treated with the recommended adult dose

(200 - 400 mg daily depending on the severity of infection).

Otitis Media: Otitis media should be treated with the suspension.

Duration of Therapy

The usual course of treatment is 7 days. This may be continued for up to 14 days if required.

In the treatment of infections due to *S. pyogenes*, a therapeutic dosage of CEFIGET (Cefixime) should be administered for at least 10 days.

Special Populations

Renal Insufficiency

CEFIGET (Cefixime) may be administered in the presence of impaired renal function. Normal dose and schedule may be given in patients with creatinine clearances of 20mL/min or greater. In patients whose creatinine clearance is less than 20mL/min, it is recommended that a dose of 200mg once daily should not be exceeded. The dose and regimen for patients who are maintained on chronic ambulatory peritoneal dialysis or hemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20mL/min.

Directions for Preparing Oral Suspension

Fill previously boiled and cooled water up to the line mark on the bottle and shake vigorously.

The reconstituted suspension can be used for up to 7 days, when stored at room temperature and up to 14 days when refrigerated, without significant loss of potency. Keep tightly closed. Shake well before using.

Discard unused portion after 14 days.

ADVERSE REACTIONS

Cefixime is generally well tolerated and side effects are usually transient.

Gastrointestinal disturbance: Diarrhea (if severe diarrhea occurs, cefixime should be discontinued), changes in the color of stool, nausea, abdominal pain, dyspepsia, vomiting, flatulence have been reported. Pseudomembranous colitis has also been reported.

Central nervous system disturbance: Headache, dizziness, seizures.

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

Others: Hypersensitivity reactions which usually subside upon discontinuation of therapy; infrequent and reversible hematological changes; elevation of serum amylase. Increase in prothrombin time has been reported in few patients. Other possible reactions include genital pruritis and vaginitis.

CONTRAINDICATIONS

Cefixime is contraindicated in:

- Patients with hypersensitivity to any component of this medication.
- Patients with known allergy to the cephalosporin group of antibiotics.
- Children less than six months old as safety and efficacy of cefixime in these patients have not been established.

PRECAUTIONS

- Cephalosporins should be given with caution to penicillin-sensitive patients, as there is some evidence of partial cross-allergenicity between the penicillins and cephalosporins.
- Cefixime should be administered with caution in patients with markedly impaired renal function.
- Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Pseudomembranous colitis is associated with the use of broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins, lincosamides and cephalosporins); it is therefore important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment.
- Broad-spectrum antibiotics such as cefixime should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

- Do not use cefixime to treat *S. aureus* as this strain of staphylococci is resistant to cefixime.

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Cefixime should therefore not be used in pregnancy unless considered essential by the physician.

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.

Drug Interactions

Anticoagulants: Care should be exercised in patients receiving anticoagulants and cefixime concomitantly due to the possibility that cefixime may increase prothrombin time.
Carbamazepine: Elevated carbamazepine levels have been reported, when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Drug/Laboratory Interactions

- A false-positive reaction for ketones in the urine may occur with tests using nitroprusside but not with those using nitroferricyanide.
- 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.

STORAGE

Store below 30°C.

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

- CEFIGET (Cefixime) Tablets 200mg are available in blister packs of 10's.
- CEFIGET (Cefixime) Capsules 400mg are available in blister packs of 5's.
- CEFIGET (Cefixime) Powder for Oral Suspension is available in 30mL bottle.
- CEFIGET DS (Cefixime) Powder for Oral Suspension is available in 30mL bottle.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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LC-41, L.I.T.E., Landhi, Karachi,
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