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CEF-OD®

(Cefixime)

Tablet, Capsule & suspension

سیف-اوڈی

COMPOSITION:

CEF-OD Tablet 200 mg:
Each film coated tablet contains:
Cefixime Trihydrate USP equivalent to
Cefixime ..... 200 mg.

Product Specs.: USP

CEF-OD Capsule 400 mg:
Each capsule contains:
CefiximeTrihydrate JP equivalent to
Cefixime..... 400 mg.

Product Specs.: JP

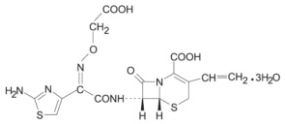
CEF-OD Suspension:
Each 5 ml of reconstituted suspension contains:
Cefixime Trihydrate USP equivalent to
Cefixime ..... 100 mg.

Product Specs.: USP

CEF-OD DS Suspension:
Each 5 ml of reconstituted suspension contains:
Cefixime Trihydrate USP equivalent to
Cefixime ..... 200 mg.

Product Specs.: USP

DESCRIPTION:
Cefixime is a semisynthetic, cephalosporin antibacterial for oral administration. Chemically, it is (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, 72-(Z)-[O-(carboxy methyl) oxime] trihydrate. Molecular weight = 507.50 as the trihydrate. Chemical Formula is $C_{16}H_{15}N_5O_7S_{2.3}H_2O$ The structural formula for cefixime trihydrate is:



CLINICAL PHARMACOLOGY:
Mechanism of action: Cefixime is a semisynthetic cephalosporin antibacterial drug. the bactericidal action of cefixime results from inhibition of cell wall synthesis. Cefixime is stable in the presence of certain beta-lactamase enzymes. As a result, certain organisms resistant to penicillins and some cephalosporins due to the presence of betalactamases may be susceptible to cefixime.
Resistance: Resistance to cefixime in isolates of Haemophilus influenzae and Neisseria gonorrhoeae is most often associated with alterations in penicillin-binding proteins (PBPs). Cefixime may have limited activity against Enterobacteriaceae producing extended spectrum beta-lactamases (ESBLs). Pseudomonas species, Enterococcus species, strains of Group D streptococci, Listeria monocytogenes, most strains of staphylococci (including methicillin-resistant strains), most strains of Enterobacter species, most strains of Bacteroides fragilis, and most strains of Clostridium species are resistant to cefixime. Cefixime has been shown to be active against most isolates of the following microorganisms, both in vitro and in clinical infections
Antibacterial activity:
- Streptococcus pneumonia
- Streptococcus pyogenes
- Gram-negative Bacteria
- Escherichia coli
- Haemophilus influenzae
- Moraxella catarrhalis
- Neisseria gonorrhoeae
- Proteus mirabilis

The following in vitro data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for cefixime against isolates of similar genus or organism group.
- Gram-positive Bacteria
- Streptococcus agalactiae
- Gram-negative Bacteria
- Citrobacter amalonaticus
- Citrobacter diversus
- Haemophilus parainfluenzae
- Klebsiella oxytoca
- Klebsiella pneumoniae
- Pasteurella multocida
- Proteus vulgaris
- Providencia species
- Salmonella species
- Serratia marcescens
- Shigella species

Pharmacokinetics:
Absorption: Cifixime 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. The area under the time versus concentration curve (AUC) is greater by approximately 10% to 25% with the oral suspension than with the tablet after doses of 100 to 400 mg. This increased absorption should be taken into consideration if the oral suspension is to be substituted for the tablet. Because of the lack of bioequivalence, tablets should not be substituted for oral suspension in the treatment of otitis media. Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200 mg tablet and a single dose of 400 mg of cefixime tablet/ suspension, between 2 and 5 hours following a single administration of 200 mg of suspension and between 3 and 8 hours following oral administration of a single 400 mg capsule.
Distribution: Serum protein binding is concentration independent with a bound fraction of approximately 65%. Adequate data on CSF levels of cefixime are not available.
Metabolism and elimination: There is no evidence of metabolism of cefixime in vivo. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. The serum half-life of cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours but may range up to 9 hours in some normal volunteers.
Pharmacokinetics in Special Populations:
Renal impairment: Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 60 mL/min or greater. In moderate to severe renal impairment follow the dose in dosage and administration section.

INDICATIONS AND USAGE:
Uncomplicated urinary tract infections:
CEF-OD is indicated in the treatment of adults and pediatric patients six months of age or older with uncomplicated urinary tract infections caused by susceptible isolates of Escherichia coli and Proteus mirabilis.
Otitis Media: CEF-OD is indicated in the treatment of adults and pediatric patients six months of age or older with otitis media caused by susceptible isolates of Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes.
Pharyngitis and tonsillitis: CEF-OD is indicated in the treatment of adults and pediatric patients six months of age or older with pharyngitis and tonsillitis caused by susceptible isolates of Streptococcus pyogenes.
Acute exacerbations of chronic bronchitis: CEF-OD is indicated in the treatment of adults and pediatric patients six months of age or older with acute exacerbations of chronic bronchitis caused by susceptible isolates of Streptococcus pneumoniae and Haemophilus influenzae.
Uncomplicated gonorrhea (cervical/urethral): CEF-OD is indicated in the treatment of adults and pediatric patients six months of age or older with uncomplicated gonorrhea (cervical/urethral) caused by susceptible isolates of Neisseria gonorrhoeae (penicillinase-and non-penicillinase-producing isolates).

DOSAGE AND ADMINISTRATION:
Adults: The recommended dose of cefixime is 400 mg daily. This may be given as a 400 mg tablet or capsule daily or

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the 400 mg tablet may be split and given as one half tablet every 12 hours. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule and tablet may be administered without regard to food. In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.
Pediatric patients: The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours.

Age	Cefixime / Day mg	CEF-OD Suspension	CEF-OD DS Suspension
1-4 years	100	1 teaspoonful	½ teaspoon
5-9 years	200	2 teaspoonful	1 teaspoon
10-12 years	300	3 teaspoonful	1½ teaspoon

Children weighing more than 45 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 administered for at least 10 days.

DOSE MODIFICATION RECOMMENDATIONS:
Renal impairment: Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be employed 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., 300 mg 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., 200 mg daily). Neither hemodialysis nor peritoneal dialysis remove significant amounts of drug from the body.

CONTRAINDICATIONS:
CEF-OD (cefixime) is contraindicated in patients with known allergy to cefixime or other cephalosporins.

WARNINGS AND PRECAUTIONS:
Allergic reactions:
Hypersensitivity reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime. Before therapy with CEF-OD is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among beta-lactam antibacterial drugs has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to CEF-OD occurs, discontinue the drug.
Clostridium difficile-associated diarrhea: Clostridium difficile associated diarrhea (CDAD) may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial drug treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.
Dose adjustment in renal impairment: The dose of CEF-OD 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.
Coagulation effects: Cephalosporins, including CEF-OD, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.
Development of drug-resistant bacteria: Elevated carbamazepine levels have been reported with cefixime. 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 is administered concomitantly.
Drug/laboratory test interactions: A false-positive reaction for ketones in the urine may occur with tests using nitroprusside but not with those using nitroferricyanide. The administration of cefixime may result in a false-positive reaction for glucose in the urine using Clinistix®**, Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix®** or Clinistix®**) be used. A false-positive direct Coombs test has been reported during treatment with other cephalosporins; therefore, it should be recognized that a positive Coombs test may be due to the drug. ** Clinistix® and Clinistix® are registered trademarks of Ames Division, Miles Laboratories, Inc. Clinistix® is a registered trademark of Eli Lilly and Company.

USE IN SPECIFIC POPULATIONS:
Pregnancy:
Pregnancy Category B: This drug should be used during pregnancy 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: The incidence of gastrointestinal adverse reactions, including diarrhea and loose stools, in the pediatric patients receiving the suspension, was comparable to the incidence seen in adult patients receiving tablets.
Geriatric use: No need for dosage adjustment of the drug in the elderly.
Renal impairment: 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.

ADVERSE REACTIONS:
The most commonly seen adverse reactions noted were gastrointestinal events, which were reported in 30% of adult patients on either the twice daily or the once daily regimen. Five percent (5%) of patients discontinued therapy because of drug-related adverse reactions. Individual adverse reactions included diarrhea 16%, loose or frequent stools 6%, abdominal pain 3%, nausea 7%, dyspepsia 3%, and flatulence 4%. The incidence of gastrointestinal adverse reactions, including diarrhea and loose stools, in pediatric patients receiving the suspension was comparable to the incidence seen in adult patients receiving tablets.
Post-marketing experience: The following adverse reactions have been reported at Incidence rates was less than 2%
Gastrointestinal: The onset of pseudomembranous colitis symptoms may occur during or after therapy.
Hypersensitivity reactions: Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported.
Hepatic: Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice.
Renal: Transient elevations in BUN or creatinine, acute renal failure.
Central nervous system: Headaches, dizziness, seizures.
Hemic and lymphatic system: Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia.
Abnormal laboratory tests: Hyperbilirubinemia:
Other adverse reactions: Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis.

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.

DIRECTIONS FOR RECONSTITUTIONS:
Cef-OD 30 ml suspension: Shake bottle well to loosen the powder. Twist the cap of plastic ampoule of sterile distilled water and add into the bottle. Close the cap tightly and shake well to form 30 ml uniform suspension.
Cef-OD 60 ml suspension: Shake bottle well to loosen the powder. Twist the cap of plastic ampoules of sterile distilled water and add into the bottle. Close the cap tightly and shake well to form 60 ml uniform suspension.
Cef-OD DS 30 ml suspension: Shake bottle well to loosen the powder. Twist the cap of plastic ampoule of sterile distilled water and add into the bottle. Close the cap tightly and shake well to form 30 ml uniform suspension.

INSTRUCTIONS:
Store below 30ºC. Close the cap tightly after use. Avoid exposure to heat, sunlight and humidity. Improper storage may deteriorate the medicine. Keep out of the reach of children. The reconstituted suspension should be kept below 25ºC and consumed within 7 days. Do not freeze. Shake well before use. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

CEF-OD Tablet 200 mg	:	Pack of 1x10 tablets.
CEF-OD Capsule 400 mg	:	Pack of 1x5 capsules.
CEF-OD Suspension 100 mg/5 ml	:	30 ml oral suspension with sterile water ampoule.
CEF-OD Suspension 100 mg/5 ml	:	60 ml oral suspension with two sterile water ampoules.
CEF-OD DS Suspension 200 mg/5 ml	:	30 ml oral suspension with sterile water ampoule.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، دھوپ اور نمی سے بچائیں۔ استعمال کے بعد ڈھکن کو اچھی طرح بند کر دیں۔ بچوں کی پہنچ سے دور رکھیں۔ تیار شدہ سسپنشن کو ۲۵ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں اور سات یوم کے اندر استعمال کریں۔ دوا کو فریزر میں نہ رکھیں۔ استعمال سے پہلے بوتل کو اچھی طرح ہلا لیں۔ ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

Manufactured by:
Wilshire Labs (Pvt) Ltd.
124/1, Quaid-e-Azam, Industrial Estate,
Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

CCL

Manufactured for:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.