04-02-2023
12th Copy

180mm

Caricef®

Capsules / Tablets / Suspension

(Cefixime Trihydrate)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Caricef® Capsules (400mg)
Each capsule contains:
Cefixime Trihydrate USP
equivalent to Cefixime....400mg

Caricef® 200mg Tablets
Each film coated tablet contains:
Cefixime Trihydrate USP
equivalent to Cefixime.....200mg

Caricef® Suspension (100mg/5ml)
Each 5ml contains (reconstituted):
Cefixime Trihydrate USP
equivalent to Cefixime.....100mg

Caricef® DS Suspension (200mg/5ml)
Each 5ml of reconstituted suspension contains:
Cefixime Trihydrate USP
equivalent to Cefixime.....200mg

PHARMACEUTICAL FORM

Capsule / Tablet / Suspension.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS: Cefixime is an orally active cephalosporin antibiotic which has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms. It is indicated for the treatment of the following acute infections when caused by susceptible micro-organisms: **Upper respiratory tract infections (URTIs):** E.g. otitis media; and other URTIs where the causative organism is known or suspected to be resistant to other commonly used antibiotics, or where treatment failure may carry significant risk. **Lower respiratory tract infection:** E.g. bronchitis. **Urinary tract infections:** E.g. cystitis, cystourethritis, uncomplicated pyelonephritis. Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including *Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenzae* (beta-lactamase positive and negative), *Branhamella catarrhalis* (beta-lactamase positive and negative) and *Enterobacter species*. **Uncomplicated Gonorrhoea (cervical/urethral):** Caused by *Neisseria gonorrhoeae* (penicillinase and non-penicillinase producing isolates). Cefixime is highly stable in the presence of beta-lactamase enzymes. Most strains of *Enterococci (Streptococcus faecalis, group D Streptococci)* and *Staphylococci* (including coagulase positive and negative strains and methicillin-resistant strains) are resistant to cefixime. In addition, most strains of *Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes* and *Clostridia* are resistant to cefixime.

POSOLOGY AND METHOD OF ADMINISTRATION: The usual course of treatment is 7 days. This may be continued for up to 14 days if required. **Posology: Adults:** The recommended dose of cefixime is 400mg daily. This may be given as 400mg daily or as 200mg every 12 hours. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400mg is recommended. In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dosage of cefixime should be administered for at least 10 days. **Tablet:** ***Children under 10 years:*** Cefixime tablets 200mg are not recommended for use in children under 10 years old. ***Children less than 6 months of age:*** The safety and efficacy of cefixime has not been established in children less than 6 months of age. **Suspension:** ***Children from 6 months to 11 years of age:*** The recommended dosage is 8mg/kg/day administered as a single dose or in two divided doses based on weight, as 4mg/kg every 12 hours.

PAEDIATRIC DOSAGE CHART

		100mg/5 ml	200mg/5ml
Patient Weight (kg)	**Dose/Day (mg)**	**Dose/Day (ml)**	**Dose/Day (ml)**
5 to 6.2	50	2.5	1.25
6.3 to 12.5	100	5	2.5
12.6 to 18.8	150	7.5	3.75
18.9 to 25	200	10	5
25.1 to 31.3	250	12.5	6.25
31.4 to 37.5	300	15	7.5
37.6 to 43.8	350	17.5	8.75
43.9 to 50	400	20	10

Children weighing more than 50kg or older than 12 years should be treated with the recommended adult dose. Otitis media should be treated with the suspension. Therefore, the tablet or capsule should not be substituted for the suspension in the treatment of otitis media. In the treatment of infections due to *Streptococcus pyogenes,* a therapeutic dosage of cefixime should be administered for at least 10 days. **Elderly:** Elderly patients may be given the same dose as recommended for adults. Renal function should be assessed, and dosage should be adjusted in severe renal impairment. **Renal impairment:** 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 haemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20ml/min. **Method for administration:** For oral administration. Absorption of cefixime is not significantly modified by the presence of food.

CONTRAINDICATION: Cefixime is contraindicated in patients with known allergy to cefixime or other cephalosporins.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE: Encephalopathy: Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment. **Severe cutaneous adverse reactions:** Severe cutaneous adverse reactions (SCARS) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in association with cefixime. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Treatment should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of skin hypersensitivity. Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs. **Hypersensitivity to penicillins:** As with other cephalosporins, cefixime should be given with caution to patients with a history of hypersensitivity to penicillin, as there is some evidence of partial cross-allergenicity between the penicillins and 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. **Haemolytic anaemia:** Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime) -associated haemolytic anaemia has also been reported. **Acute renal failure:** As with other cephalosporins, cefixime may cause acute renal failure including tubulointerstitial nephritis as an underlying pathological condition. When acute renal failure occurs, cefixime should be discontinued and appropriate therapy and/or measures should be taken. **Renal impairment:** Cefixime should be administered with caution in patients with markedly impaired renal function. **Paediatric use:** Safety of cefixime in premature or newborn infant has not been established. **Antibiotic-associated colitis:** Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated diarrhoea. 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 diarrhoea in association with the use of antibiotics. Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment. Management of pseudomembranous colitis should include sigmoidoscopy, appropriate bacteriologic studies, fluids, electrolytes and protein supplementation.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION: Anticoagulants: Care should be taken in patients receiving anticoagulation therapy. Cefixime should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since cefixime may enhance effects of the anticoagulants, prolonged prothrombin time with or without bleeding may occur. **Other forms of interaction:** 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 recognised that a positive Coombs test may be due to the drug.

FERTILITY, PREGNANCY AND LACTATION: Fertility: Cefixime has not been studied for use during labor and delivery. Treatment should only be given if clearly needed. **Pregnancy:** 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. **Breast-feeding:** It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug. **Paediatric Use:** Safety and effectiveness of cefixime in children aged less than six months old have not been established.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: In the case of side effects such as encephalopathy (which may include convulsion, confusion, impairment of consciousness, movement disorders), the patient should not operate machines or drive a vehicle.

UNDESIRABLE EFFECTS: Blood and lymphatic system disorders: Eosinophilia, hyper eosinophilia, agranulocytosis, leucopenia, neutropenia, granulocytopenia, haemolytic anemia, thrombocytopenia, thrombocytosis. **Gastrointestinal disorders:** Abdominal pain, diarrhoea*, dyspepsia, nausea, vomiting, flatulence. **Hepatobiliary disorders:** Jaundice. **Infections and infestations:** Pseudomembranous colitis, vaginitis. **Investigations:** Aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, blood urea increased, blood creatinine increased. **Nervous system disorders:** Dizziness, headache, cases of convulsions have been reported with cephalosporins including cefixime (frequency not known), beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment (frequency not known). **Respiratory, thoracic and mediastinal disorders:** Dyspnoea. **Renal and urinary disorders:** Acute renal failure with tubulointerstitial nephritis. **Immune system disorders:** Anaphylactic reaction, angio-oedema, serum sickness-like reaction. **Skin and subcutaneous tissue disorders:** Drug rash with eosinophilia and systemic symptoms (DRESS), erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria, rash, pruritus, acute generalized exanthematous pustulosis (AGEP). **General disorders and administrative site conditions:** Drug fever, arthralgia, pyrexia, face oedema, genital pruritus. *Diarrhoea has been more commonly associated with higher doses. 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.

OVERDOSE: Cefixime is not removed from the circulation in significant quantities by dialysis. No specific antidote exists. General supportive measures are recommended.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES: Pharmacotherapeutic group: Third generation cephalosporin. **ATC code:** J01DD08. Cefixime is an oral third generation cephalosporin which has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms. Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including: ● *Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenzae* (beta-lactamase positive and negative), *Branhamella catarrhalis* (beta-lactamase positive and negative) and *Enterobacter species.* ● Most strains of *Enterococci (Streptococcus faecalis, group D Streptococci)* and *Staphylococci* (including coagulase positive and negative strains and methicillin-resistant strains) are resistant to cefixime. In addition, most strains of *Pseudomonas, Bacteroides fragillis, Listeria monocytogenes and Clostridia* are resistant to cefixime.

PHARMACOKINETIC PROPERTIES: The absolute oral bioavailability of cefixime is in the range of 22-54%. Absorption is not significantly modified by the presence of food. Cefixime may therefore, be given without regard to meals. Typically, the peak serum levels following the recommended adult or paediatric doses are between 1.5-3mcg/ml. Little or no accumulation of cefixime occurs following multiple dosing. The pharmacokinetics of cefixime in healthy elderly (age >64 years) and young volunteers (11-35) compared the administration of 400mg doses once daily for 5 days. Mean C_{max} and AUC values were slightly greater in the elderly. Elderly patients may be given the same dose as the general population. Cefixime is predominantly eliminated as unchanged drug in the urine. Glomerular filtration is considered the predominant mechanism. Metabolites of cefixime have not been isolated from human serum or urine. Serum protein binding is well characterized for human and animal sera; cefixime is almost exclusively bound to the albumin fraction, the mean free fraction being approximately 30%. Protein binding of cefixime is only concentration dependent in human serum at very high concentrations which are not seen following clinical dosing.

DIRECTION FOR RECONSTITUTION: For Suspension (30ml & 60ml): Shake bottle to loosen the mass. Add freshly boiled and cooled water below the mark given on bottle label then shake to make homogeneous suspension. Add further same water upto the mark of bottle label and shake vigorously to form uniform suspension.

SHELF LIFE

See expiry on the pack

AVAILABILITY

Caricef® capsules (400mg) in a pack of 5's
Caricef® 200mg tablets in a pack of 10's
Caricef® suspension (100mg/5ml) in a pack of 30ml and 60ml
Caricef® DS suspension (200mg/5ml) in a pack of 30ml

INSTRUCTIONS

Dosage: As advised by the physician. Only to be sold on the prescription of a registered medical practitioner.
Keep out of reach of children.
Do not store over 30°C, and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.
For Suspension: The reconstituted suspension should be kept at 2 - 8°C, so that potency of the product remains stable and be used within 7 days.

Manufactured for:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
by:
Healthtek (Pvt.) Limited
Plot No.14, Sector 19, Korangi
Industrial Area Karachi - Pakistan

2000005875

کیری سیف کیپسول/ٹیبلٹ/سسپنشن

(سیفکزائم ٹرائی ہائیڈریٹ)

ہدایات:

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔
برائے سسپنشن: تیار شدہ سسپنشن کو ۲ سے ۸ ڈگری سینٹی گریڈ پر رکھیں تا کہ دوا کی تاثیر برقرار رہے اور ۱۴ یوم کے اندر استعمال کر لیں۔

R.N-06/NA/02/2023

80mm