

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product:

Cef-3 Forte Powder for suspension

2. Quality and Quantitative Composition

Each 5 ml reconstituted suspension contains Cefixime Trihydrate USP equivalent to Cefixime 200 mg. For a full list of excipients, see section 6.1.

3. Pharmaceutical Form:

Before reconstitution : Off-white granular powder filled and sealed in amber color glassbottle, sealed with a LDP stopper and an aluminum ROPP Cap of white outer surface printed 'SQUARE' on the top in black ink. After reconstitution: A creamy white suspension having strawberry flavor.

4. Clinical Particulars

4.1 Therapeutic indications:

Cefixime is a 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 (URTI): e.g. otitis media; and other URTI 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. 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 .

4.2 Posology and method of administration:

Route of Administration: Oral

Adults and adolescents older than 12 years (or more than 50 kg body weight): The recommended dose is 400 mg daily, given either as a single dose or in two divided doses of 200 mg every 12 hours. (see section 4.4 and 5.1).

Powder for Suspension:

Child dose: 8 mg/kg daily as a single dose or in two divided doses for 7-14 days according to the severity of infection or for children of age 1/2-1 year: 75 mg; 1-4 years: 100 mg; 5-10 years: 200 mg; 11-12 years: 300 mg; above 12 years: adult dose.

Elderly patients

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 (See above and section 4.4).

Method of administration

For oral administration

4.3 Contraindications:

Hypersensitivity to cephalosporin antibiotics or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Encephalopathy

Beta-lactams, including cefixime, have been associated with encephalopathy risk (which may include convulsions, confusion, decreased consciousness, movement disorders), particularly in elderly patients, in patients with severe renal impairment or central nervous system disorders and in case of overdose. If cefixime-associated encephalopathy is suspected discontinuation should be considered. (see section 4.8 and 4.9)

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARS) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS) 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 (see section 4.2).

Paediatric use

Safety of cefixime in premature or newborn infant has not been established (see section 4.2).

Antibiotic-associated colitis

Treatment with broad spectrum antibiotics 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 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. If the colitis does not improve after the drug has been discontinued, or if the symptoms are severe, oral vancomycin is the drug of

choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should be excluded.

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants

In common with other cephalosporins, increases in prothrombin times have been noted in a few patients. Care should therefore 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.

4.6 Fertility, pregnancy and lactation

Reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefixime. In the rabbit, at doses up to 4 times the human dose, there was no evidence of a teratogenic effect; there was a high incidence of abortion and maternal death which is an expected consequence of the known sensitivity of rabbits to antibiotic-induced changes in the population of the microflora of the intestine. 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.

4.7 Effects on ability to drive and use machines

In the case of side effects such as encephalopathy (which may include convulsion, confusion, decreased consciousness, movement disorders), the patient should not operate machines or drive a vehicle.

4.8 Undesirable effects

Cefixime generally well tolerated. The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature.

The following adverse reaction (Preferred term# or equivalent) will be considered listed:

Blood and lymphatic system disorders:	Eosinophilia Hypereosinophilia Agranulocytosis Leucopenia Neutropenia Granulocytopenia Haemolytic anaemia Thrombocytopenia Thrombocytosis
astrointestinal 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, have been associated with encephalopathy risk (which may include convulsions, confusion, decreased consciousness, movement disorders), particularly in elderly patients, in patients with severe renal impairment or central nervous system disorders and in case of overdose. (frequency not known)**
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Renal and urinary disorders:	Acute renal failure with tubulointerstitial nephritis (see section 4.4).
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 generalised exanthematous pustulosis(AGEP) (see section 4.4)
General disorders and administrative site conditions:	Drug Fever Arthralgia Pyrexia Face oedema Genital pruritus

Reporting of suspected adverse reactions

Healthcare professionals are requested to report any suspected adverse reactions via the Pharmacy and Poisons Reporting System (PvERS)
<https://pv.pharmacyboardkenya.org>

4.9 Overdose:

There is a risk of encephalopathy associated with beta-lactam antibiotics such as cefixime, particularly in case of overdose or renal impairment.

Adverse reactions seen at dose levels up to 2 g Cefixime in normal subjects did not differ from the profile seen in patients treated at the recommended doses. Cefixime is not removed from the circulation in significant quantities by dialysis.

No specific antidote exists. General supportive measures are recommended.

5. Pharmacological Properties

5.1 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. It 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*, *Bacteroides fragilis*, *Listeria monocytogenes* and *Clostridia* are resistant to cefixime.

5.2 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.

From *in vitro* studies, serum or urine concentrations of 1 mcg/mL or greater were considered to be adequate for most common pathogens against which cefixime is active. Typically, the peak serum levels following the recommended adult or paediatric doses are between 1.5 – 3 mcg/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 400 mg 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 characterised 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.

Transfer of ^{14}C -labelled cefixime from lactating rats to their nursing offspring through breast milk was quantitatively small (approximately 1.5% of the mothers' body content of cefixime in the pup). No data are available on secretion of cefixime in human breast milk. Placental transfer of cefixime was small in pregnant rats dosed with labelled cefixime.

5.3 Preclinical Safety Data:

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6. Pharmaceutical Particulars

6.1 List of Excipients:

Gum
Sodium Benzoate
Colloidal Anhydrous Silica (Aerosil-200)
Disodium Edetate
Strawberry Flavor

6.2 Incompatibilities: None known

6.3 Shelf Life: 18 months from manufacturing date

6.4 Special Precautions for Storage:

Store below 30°C, protect from light, do not freeze, keep out of reach of children.

After reconstitution the suspension/drops can be used within 7 days if be kept at room temperature and within 14 days if be kept in refrigerator (2-8 °C). Always keep the bottle tightly closed.

6.5 Nature and Contents of Container:

50 ml Glass bottle containing powder for suspension with a measuring

6.6 Special Precautions for Disposal:

Cef-3® Forte Powder for Suspension: To prepare 50 ml suspension, 35 ml boiled and cooled water is required Shake well before using the suspension.

Do not discontinue the therapy suddenly, without consulting your doctor.

Discard unused portion of reconstituted suspension after the above mentioned time. Keep away from the reach of the children.

7. Marketing Authorization Holder:

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8. Marketing Authorization Numbers: H2022/CTD7863/15035

9. Date of First Authorization/Renewal: --September 22nd 2022

10. Date of Revision of the Text: September 22nd 2022

