Cefixime for oral Suspension 100mg/5mL

Summary of Product Characteristics

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1 NAME OF THE MEDICINAL PRODUCT

Cefixime Powder for Oral Suspension 100mg/5mL

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5mL contains
Cefixime Trihydrate USP.
Eq. to Cefixime 100 mg
Excipients Q.S.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORMS

Powder for Oral Suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indication.

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 (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 occuring pathogens including *Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Kliebsiella* 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 meticillin- 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.

Recommended Dose and Dosage Adjustment

Pediatrics (≥ 6 months):
The recommended dose of CEFIXIME is 8 mg/kg/day once daily. When necessary, a dose of 4 mg/kg given twice daily may be considered except for urinary tract infections where once daily dosing must be used.

Table 1-Pediatric dosage chart

PEDIATRIC DOSAGE CHART Doses are suggested for each weight range and rounded for ease of administration		
		Cefixime for Oral Suspension 100 mg / 5 mL
Patient Weight (Kg)	**Dose/Day (mg)**	**Dose/Day (mL)**
5 to 7.5	50	2.5
7.6 to 10	80	4
10.1 to 12.5	100	5
12.6 to 20.5	150	7.5
20.6 to 28	200	10
28.1 to 33	250	12.5
33.1 to 40	300	15
40.1 to 45	350	17.5
45.1 or greater	400	20

Children weighing more than 45 kg or older than 12 years should be treated with 400 mg CEFIXIME. Safety and effectiveness in infants aged less than six months have not been established.

Otitis media should be treated with the suspension. Clinical studies of otitis media were conducted with the suspension only and the suspension results in higher peak blood levels than the tablet when administered at the same dose. Therefore, the tablet should not be substituted for the suspension in the treatment of otitis media.

Duration of Therapy:
Duration of dosage in clinical trials was 10 to 14 days. The duration of treatment should be guided by the patient's clinical and bacteriological response.
In the treatment of infections due to *Streptococcus pyogenes*, a therapeutic dose of CEFIXIME should be administered for at least 10 days.

Renal Impairment:
Experience in children with renal impairment is very limited. The use of cefixime in these patients is not recommended.

NOTE: Neither hemodialysis, nor peritoneal dialysis remove significant amounts of cefixime from the body.

Reconstitution Directions for Oral Suspensions:
Bottle:
SIZE RECONSTITUTION DIRECTIONS
100 mL Suspend with 67 mL water.

After mixing, the suspension may be kept for 14 days at room temperature (15-25°C) or under refrigeration. Keep container tightly closed. Shake well for at least 30 seconds before using. Discard unused portion after 14 days.

4.3 Contraindications

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

4.4 Special warnings and precaution 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 such as toxic epidermal necrolysis, Stevens- Johnson syndrome and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in some patients on cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/or measures should be taken.

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.

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 product 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 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 foetus 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 Effect on the ability to drive and use machine.

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.

4.8 Undesirable effect.

Cefixime is 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
Gastrointestinal disorders:	Abdominal pain Diarrhoea* Dyspepsia Nausea Vomiting Flatulance
Hepatobiliary disorders:	Jaundice
Infections and infestations:	Pseudomembranous colitis
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:	Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition

Immune system disorders, administrative site conditions, skin and subcutaneous tissue disorders:	Anaphylactic reaction Serum sickness-like reaction Drug rash with eaosinophilia and systemic symptoms (DRESS) Pruritus Rash Drug Fever Arthralgia Erythema multiforme Stevens-Johnson syndrome Toxic epidermal necrolysis Angio-oedema Urticaria Pyrexia Face oedema Genital pruritus Vaginitis

The above mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.

4.9 Overdose.

There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics, including 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.

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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 and 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. Placetal transfer of cefixime was small in pregnant rats dosed with labelled cefixime.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Benzoate	BP
Microcrystalline Cellulose	BP
Pineapple Flavour Trusil	BP
Colloidal Silicon Dioxide	BP
Purified Talc	BP
Sodium Citrate	BP
Citric Acid (Anhydrous)	BP
Aspartame	BP
Mannitol	BP

6.2 Incompatibilities

unknown

6.3 Shelf-life
36 months

6.4 Special precautions for storage
Store in a cool dry place below 30^{o}C. Protected from Light. Keep all medicines out of reach of children.

6.5 Nature and composition of immediate packaging

100mL HDPE bottle with screw cap. Such 1 labeled bottle are packed in a carton along with a leaflet.

6.6 Special precautions for disposal and other handling.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

SAM PHARMACEUTICALS LIMITED.
8/9, OYADIRAN ESTATE,
SABO, YABA
LAGOS, NIGERIA

VAPI CARE PHARMA PRIVATE LIMITED
PLOT NO. 225/3, G.I.D.C., NEAR MORARJI CIRCLE,
VAPI-396195,
GUJARAT, INDIA.

8 MARKETING AUTHORISATION NUMBER(S)
A4-5035

9 AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

20th Feb 2024.