ROFIX

Cefixime for Oral Suspension USP

1. Name of the medicinal product

ROFIX

Cefixime for Oral Suspension USP

2. Qualitative and quantitative composition

Each 5 ml Reconstituted Suspension Contains:

Cefixime (as trihydrate) USP

Eq. to Cefixime anhydrous 100mg

Excipients .....q.s

3. Pharmaceutical form

An orange Coloured, suspension after reconstitution.

4. Clinical particulars

4.1 Therapeutic indications

Cefixime for Oral Suspension USP 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 occurring 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 Suspension is highly stable in the presence of betalactamase 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 Suspension. In addition, most strains of Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes and Clostridia are resistant to Cefixime Suspension.

4.2 Posology & Method of Administration Posology - As directed by physician. Method of administration:
Oral.

4.3 Contraindications

Patients with known hypersensitivity to cephalosporin antibiotics or any of the other components of the product.

4.4 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 (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 dry syrup 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 crossallergenicity between the penicillins and cephalosporins. Patients have had severe reactions (including anaphylaxis) to both classes of drugs. If an allergic effect occurs with Cefixime dry syrup the drug should be discontinued and the patient treated with appropriate agents if necessary.

Renal failure acute -

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 -

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, semisynthetic 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, 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 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 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Cefixime Suspension 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:	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
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

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

Reporting of suspected Adverse Reactions: Healthcare professionals are requested to report any suspected adverse drug reactions via the National Regulatory Agents

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: cephalosporins antibacterials, 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 meticillin-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 pediatric 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 Cmax 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.

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

1. Sucrose BP
2. Xanthan gum BP
3. Anhydrous citric acid BP
4. Sodium Benzoate BP
5. Colloidal silicon dioxide BP
6. Aspartame BP
7. Flavour – Orange IH
8. Flavour – Lemon IH
9. Colour – Sunset yellow IH
10. Sucrose BP (Additional)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C and protect from light.

6.5 Nature and contents of container

One bottle packed in carton. One such bottle packed in monocarton with package insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization

Holder QUEST

PHARMACEUTICALS LTD.

P.O. Box no – 22437 - 00100

Nairobi, Kenya

8. Marketing authorisation number(s)

H2015CTD2609/318

9. Date of first authorisation/renewal of the authorization

Renewal of the authorization-June 2026

10. Date of revision of the text

NA