Summary of Product Characteristics
ROFIX
(Cefixime 100 mg/5 mL powder for oral suspension)

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1. Name of the medicinal product

ROFIX (Cefixime for Oral Suspension USP)

2. Qualitative and quantitative composition

Each 5 mL of reconstituted suspension contains cefixime (as trihydrate) USP equivalent to 100 mg of anhydrous cefixime.

Excipients with known effect:

Each 5 mL contains sucrose, aspartame (a source of phenylalanine), sunset yellow FCF (E110) and sodium benzoate (E211).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for oral suspension.

A white to off-white powder that yields an orange-coloured suspension after reconstitution.

4. Clinical particulars

4.1 Therapeutic indications

Cefixime is an orally active third-generation cephalosporin antibiotic indicated for the treatment of the following acute infections caused by susceptible micro-organisms:

- Upper respiratory tract infections, e.g. otitis media.
- Lower respiratory tract infections, e.g. bronchitis.
- Urinary tract infections, e.g. cystitis, cysto-urethritis and uncomplicated pyelonephritis.

Clinical efficacy has been demonstrated against commonly occurring pathogens including Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenzae, Moraxella (Branhamella) catarrhalis and Enterobacter species. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

The recommended dose is 8 mg/kg body weight per day, administered either once daily or in two divided doses of 4 mg/kg every 12 hours. Children weighing more than 50 kg or older than 12 years should receive the adult dose of 400 mg/day. The duration of treatment is usually 7 days and may be continued for up to 14 days if required.

Renal impairment

When creatinine clearance is above 20 mL/min, no dose modification is needed. For lower values, the dose should not exceed 4 mg/kg/day. Cefixime should be administered with caution in patients with markedly impaired renal function.

Paediatric population

The safety of cefixime in premature or newborn infants has not been established.

Method of administration

For oral use. Shake well before each use. See section 6.6 for instructions on reconstitution.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Hypersensitivity

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 penicillins and cephalosporins; severe reactions (including anaphylaxis) to both classes have occurred. If an allergic reaction occurs, cefixime should be discontinued and the patient treated appropriately.

Serious skin reactions

Severe cutaneous adverse reactions, including toxic epidermal necrolysis, Stevens-Johnson syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP), have been reported with cefixime. Treatment should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of skin hypersensitivity.

Encephalopathy

Beta-lactams, including cefixime, predispose the patient to the risk of encephalopathy (which may include convulsions, confusion, impairment of consciousness or movement disorders), particularly in the event of overdose or renal impairment.

Antibiotic-associated colitis

Treatment with broad-spectrum antibiotics alters the normal colonic flora and may permit overgrowth of Clostridioides difficile; pseudomembranous colitis should be considered in patients who develop diarrhoea during or after treatment. If colitis is severe or does not improve after discontinuation, appropriate management, including oral vancomycin, should be considered. Peristalsis inhibitors should be avoided.

Renal effects

As with other cephalosporins, cefixime may cause acute renal failure, including tubulointerstitial nephritis; if this occurs, cefixime should be discontinued and appropriate measures taken.

Excipients

This medicine contains sucrose; patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. Sucrose may also be harmful to the teeth. It contains aspartame, a source of phenylalanine, which may be harmful for people with phenylketonuria. It contains sunset yellow FCF (E110), which may cause allergic reactions. It also contains sodium benzoate (E211).

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants: as with other cephalosporins, increases in prothrombin time have been noted; cefixime should be administered with caution to patients receiving coumarin-type anticoagulants (e.g. warfarin), and prolonged prothrombin time with or without bleeding may occur.

Interference with laboratory tests: a false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or copper-sulphate tests (but not with glucose-oxidase methods), and a false-positive direct Coombs test has been reported during treatment with cephalosporins.

4.6 Fertility, pregnancy and lactation

Reproduction studies in mice and rats at doses up to 400 times the human dose revealed no evidence of impaired fertility or harm to the foetus. 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

No studies on the effects on the ability to drive and use machines have been performed. If adverse reactions such as dizziness occur, patients should exercise caution.

4.8 Undesirable effects

Cefixime suspension is generally well tolerated, with most reactions being mild and self-limiting. The adverse reactions are listed below by System Organ Class. Frequencies are not established for most reactions.

System Organ Class	Adverse reaction
Infections and infestations	Pseudomembranous colitis, vaginitis, genital pruritus
Blood and lymphatic system disorders	Eosinophilia, hypereosinophilia, agranulocytosis, leucopenia, neutropenia, granulocytopenia, haemolytic anaemia, thrombocytopenia, thrombocytosis
Immune system disorders	Anaphylactic reaction, serum sickness-like reaction, angio-oedema, urticaria, drug fever, arthralgia
Nervous system disorders	Dizziness, headache; convulsions and encephalopathy (frequency not known)
Respiratory, thoracic and mediastinal disorders	Dyspnoea
Gastrointestinal disorders	Abdominal pain, diarrhoea, dyspepsia, nausea, vomiting, flatulence
Hepatobiliary disorders	Jaundice
Skin and subcutaneous tissue disorders	Rash, pruritus, face oedema; drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis
Renal and urinary disorders	Acute renal failure, including tubulointerstitial nephritis
Investigations	Aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, blood urea increased, blood creatinine increased
General disorders and administration site conditions	Pyrexia

Diarrhoea has been more commonly associated with higher doses; cefixime should be discontinued if marked diarrhoea occurs.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

If large quantities are ingested, symptomatic treatment should be initiated; there is no specific antidote. Haemodialysis or peritoneal dialysis does not remove cefixime from plasma.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, third-generation cephalosporins. ATC code: J01DD08.

Cefixime is an oral third-generation cephalosporin with marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms, resulting from inhibition of bacterial cell-wall synthesis. It is highly stable in the presence of beta-lactamase enzymes. Most strains of enterococci and staphylococci (including meticillin-resistant strains), and 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% and is not significantly modified by food. Typical peak serum levels following recommended doses are between 1.5 and 3 micrograms/mL, with little or no accumulation on multiple dosing. Cefixime is predominantly eliminated as unchanged drug in the urine, glomerular filtration being the predominant mechanism; no metabolites have been isolated from human serum or urine. Serum protein binding is approximately 70%, mainly to albumin (mean free fraction about 30%).

5.3 Preclinical safety data

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

6. Pharmaceutical particulars

6.1 List of excipients

- Sucrose
- Xanthan gum
- Anhydrous citric acid
- Sodium benzoate (E211)
- Colloidal silicon dioxide
- Aspartame
- Orange flavour
- Lemon flavour
- Sunset yellow FCF (E110)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months (unopened). After reconstitution, the suspension should be used within 14 days.

6.4 Special precautions for storage

Store below 30°C and protect from light. After reconstitution, store below 30°C (or as stated on the label) and discard any unused suspension after 14 days. Keep out of the reach and sight of children.

6.5 Nature and contents of container

One bottle of powder for oral suspension, presented in a carton (monocarton) together with the package insert.

6.6 Special precautions for disposal and other handling

Reconstitution: shake the bottle to loosen the powder. Add the quantity of previously boiled and cooled (or freshly potable) water indicated on the label, in two portions, shaking well after each addition until the suspension reaches the mark. Shake well before each use. Discard any suspension remaining 14 days after reconstitution.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

Quest Pharmaceuticals Ltd, P.O. Box 22437-00100, Nairobi, Kenya.

8. Marketing Authorisation Number

H2015CTD2609/318

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text