SUMMARY PRODUCT CHARACTERISTICS

1. Name of drug product:

Cefixime Dispersible Tablets 100 mg

2. Qualitative and Quantitative Composition:

Each uncoated dispersible tablet contains:
Cefixime (as trihydrate) USP
Equivalent to anhydrous Cefixime 100 mg

Full list of excipients see Section 6.1.

3. Pharmaceutical form:

A Yellow coloured round shaped biconvex uncoated dispersible tablets.

4. Clinical particulars:

4.1 Therapeutic Indications:

Urinary tract infections

In uncomplicated urinary tract infections, cefixime (200 or 400 mg daily) has been shown to be comparable in efficacy with both sulfamethoxazole and trimethoprim combination (160/800 mg twice daily) and Amoxicillin (250 mg there times daily). All 76 children with urinary infection were cured in a comparative trial of once-daily cefixime (8 $mg.kg^{-1}$) and twice-daily trimethoprim/sulfamethoxazole.

Upper and lower respiratory tract infections

Good results have been obtained with cefixime in the treatment of bacterial pharyngitis and tonsillitis, mainly caused by Streptococcus pyogenes. Results compare favorably with those of Amoxicillin. Cefixime (8 $mg.kg^{-1}$ daily for 10 days) was significantly more effective in the treatment of streptococcal pharyngitis in children in the treatment of streptococcal pharyngitis in children then penicillin V (250 $mg.kg^{-1}$ every 8 h for 10 days) (45/48 versus 36/47). For acute bacterial sinusitis, a once-daily dose of amoxicillin given three times a day (50/53 versus 47/49). In acute pneumonia, acute and chronic bronchitis, and infected bronchiectasis, cefixime has been shown to be at least as effective as amoxicillin and cefaclor in terms of both clinical response and

bacteriological clearance. In a double-blind trial, cefixime shower similar efficacy to a twice-daily dose of clarithromycin (97/110 versus 89/103)

Acute otitis media

In several studies of the treatment of children suffering from acute otitis media with effusion, cefixime was found to be as effective as standard doses of cefaclor, amoxicillin, and amoxicillin-clavulanate. Other studies have not found that diarrhea and gastrointestinal symptoms are more common in patients given cefixime than cefaclor (16/58 versus 4/50, 28/134 versus 8/129). Others failed to confirm this. Cefixime was more likely than amoxicillin to cure infections caused by Haemophilus influenza.

Gonococcal urethritis

Cefixime given as a single 400 mg dose orally was found to be as effective a single intramuscular dose of ceftriaxone in gonococcal urethritis (83/93 versus 92/94) and pharyngitis. A single 800 mg dose was no more effective. Others have confirmed its efficacy but reported adverse effects (often diarrhea) in 10% of the cefixime group. Cefixime is not useful against Chlamydia trachomatis.

Typhoid

Cefixime (10 $mg.kg^{-1}$ per day for 14 days) has been found to have similar efficacy to intravenous ceftriaxone in the treatment of enteric fever caused by Salmonella typhi resistant to sulfamethoxazole and trimethoptim combination, ampicillin, and Chloramphenicol. In each group, 22 of 25 children were cured.

4.2 Posology and Method of Administration:

The usual adult dose of Cefixime is 200 – 400 mg per day administered orally, either as a single dose or in two divided doses, although lower doses may prove sufficient to treat uncomplicated urinary tract infections. For children, 8 mg.kg daily, as either a single dose or in two divided doses, in recommended. In uncomplicated gonococcal urethritis, a single oral dose of 400 mg has been found to be effective.
Dosage adjustment is only necessary in severe renal impairment, i.e. creatinine clearance < 20 ml.min, when the usual dose should be given at twice the normal dosing interval.

Method of administration : Oral

4.3 Contraindications:

Cefixime is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

4.4 Special Warnings and Precautions for Use :

Cefixime should not be given to patients who are hypersensitive to it or to other cephalosporins. About 10% of penicillin-sensitive patients may also be allergic to cephalosporins although the true incidence is uncertain; great care should be taken if Cefixime is to be given to such patients. Care is also necessary in patients with known histories of allergy.

Cefixime should be given with caution to patients with renal impairment; a dosage reduction may be necessary. Renal and haematological status should be monitored especially during prolonged and high-dose therapy.

4.5 Interaction with other medicinal products, and other forms of interaction:

Carbamazepine :

Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin and Anticoagulants :

Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly.

4.6 Pregnancy and Lactation:

Pregnancy

Pregnancy Category B. Reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and have revealed no evidence of harm to the fetus due to cefixime. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation

It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

4.7 Effects on ability to drive and use machines:

Patients experiencing visual disturbances, dizziness, vertigo, somnolence, or other central nervous system disturbances while taking Cefixime dispersible tablets 100 mg should refrain from driving or using machines.

4.8 Undesirable effects:

Potentially life-threatening effects

None has been reported.

Sever or irreversible adverse effects

A few cases of pseudomembranous colitis have been reported. Of 5000 patients in clinical trials, five developed colitis, three cases of which were confirmed to be pseudomembranous colitis.

Symptomatic adverse effects

Most adverse effects, so far reported, have been relatively mild and short-lived. Alterations of bowel habit has been the most frequently described reaction. 400 mg daily produced effects ranging from stool change (8.5-15.6%) to frank diarrheat (10.3-15.3%), although in only 3.2% were symptoms severe enough to warrant cessation of therapy. Diarrhea notably occurred early in the course of treatment, i.e. within the first 24-48 h, a finding not explained by changes in bowel flora. These observations were not effected by administering the drug in two divided doses, rather than once a day. Other symptoms described are nausea and vomiting, abdominal pain, dyspepsia, headache, and dizziness.

Other effects

In a small percentage of patients, mild elevations of serum amylase have been reported, which seem to be unrelated to symptomatic adverse effects. In a volunteer study, Clostridium difficile appeared in four of six subjects given cefixime and three of six given cefaclor but it was not accompanied by clinical signs or symptoms. Three children developed Clostridium difficile–positive antibiotic associated colitis after cefixime treatment at one hospital over a period of 2 years.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and

poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose:

No human data available. Adverse reactions seen at dose levels up to 2 g in normal subjects did not differ from the profile seen in patients treated at the recommended doses. Cefixime is not removed to a significant degree by either peritoneal dialysis or hemodialysis.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

Cefixime is an orally active, broad-spectrum antibiotic. Cefixime exhibits good in vitro activity (minimum inhibitory concentration for 90% of strains (MIC90 < 1 mg.l) against most of the Enterobacteriaceae, Haemophilus influenzae and Neisseria gonorrhoeae (including β-lactamase producing strains), β-hemolytic streptococci of groups A and B and Streptococcus pneumoniae. However, Staphylococcus aureus is considerably less susceptible, and fecal streptococci, Pseudomonas aeruginosa, most anaerobes, and Chlamydia trachomatis are in susceptible. Against Enterobacteriaceae, its activity is normally superior to that of Amoxicillin, Cefaclor and Cephalexin, but inferior to that of Ciprofloxacin. It is more active than sulfamethoxazole and Trimethoprim combination against certain species (Providencia stuartii, Proteus vulgaris and Klebsiella spp.) but less active against Escherichia coli, Enterobacter cloacae, and Enterobacter aerogenes. Against H. influenzae and N. gonorrhoeae, Cefixime has been shown to be highly inhibitory to all strains tested. For H. influenzae, this included strains resistant to ampicillin, cefaclor, cephalexin, chloramphenicol, and sulfamethoxazole and trimethoprim combination.

5.2 Pharmacokinetic Properties:

Both high performance liquid chromatography (HPLC) with a sensitivity of 0.05 $mg.1^{-1}$ and microbiological agar diffusion techniques (sensitivity is 0.1 $mg.1^{-1}$) have been used to assay cefixime concentrations with good agreement between the two methods.

Oral absorption	60-80%
Presystemic metabolism	-
Plasma half-life	
range	2.5-3.8 h
mean	3 h

Volume of distribution	0.1I.kg^{-1}
Plasma protein binding	70%

Cefixime is absorbed slowly after oral administration, the time taken to reach maximum plasma concentrations (T_{max}) increasing with increasing dose. It is likely that a significant proportion remains unabsorbed, as a much higher percentage of the drug is excreted renally when administered intravenously rather than orally (64.8% as opposed to 20%).

Cefixime has been shown in one study to have an absolute bio availability of about 50% when compared with an intravenous dose. After a 200 mg oral dose, peak plasma levels of an average of 2.7 mg.1^{-1} are achieved between 3 and 4 h postdose in fasting volunteers. In non-fasting volunteers, a slight delay in reaching peak plasma concentrations has been noted, without alteration of other pharmacokinetic parameters. Another study showed a 1 h delay in reaching peak plasma concentration, but that peak serum levels, area under the curve (AUC) and 24 h recovery values were unchanged.

The mean volume of distribution of cefixime is 0.1 1.kg^{-1}. Penetration into tissue fluid is slow (mean T_{max} = 6.7h) but peak concentrations similar to those of plasma have been achieved. Lower levels have been found in other tissues, i.e, palatine tonsil, maxillary sinus mucosa sputum and middle ear discharge. Very high concentrations occur in bile. Between 3.5 and 12 h after single oral doses of 100, 200, or 400 mg mean biliary concentrations were 135, 134 and 190 mg.1^{-1}, respectively. The biliary recovery of cefixime in 24 h is 5% of the administered dose, suggesting it is one of the most highly bile-excreted cephalosporins. CSF penetration is poor. After an oral dose of 400 mg to patients with non-inflamed meninges, the CSF level reached 0.17 mg.1^{-1} compared with serum level of 3.1 mg.1^{-1}. For patients with meningitis, the mean CSF concentration was 0.22 mg.1^{-1}. In normal healthy volunteers cefixime is approximately 70% protein –bound. No biologically active metabolites of cefixime have yet been discovered.

The mean elimination half-life (t ½) of 3 h is somewhat longer than those of earlier oral cephalosporins. Eg. cephalexin, cephradine and cefaclor (< 1 h), and cefadroxil (1.5h). Urinary excretion accounts for between 12 and 34% of an orally administrated dose much less than that of the above-mentioned drugs, which are more than 80% renally excreted. As probenecid appears to make little difference to the rate of excretion, it is likely that elimination occurs mainly via glomerular filtration. The t ½ of cefixime is only significantly prolonged in patients with severely impaired renal function (creatinine clearance < 20ml.min^{-1}), when it is suggested

that the dosage be divided for administration over double the normal interval. old age per se is not an indication for dose adjustment.

Concentration –effects relationship

As with antibiotics, clinically effective plasma and tissue concentrations are related to the minimum concentrations inhibitory against the infecting microorganism. For most susceptible organisms (see clinical pharmacology) a dose of 200 mg given twice daily is adequate; however, for less susceptible organisms, or infections in sites where antibiotic penetration is low, higher dose may be required.

Metabolism

No metabolic pathways have yet been identified Cefixime is mainly excreted unchanged in bile and urine.

5.3 Pre-clinical safety data :

Animal studies have shown no evidence of mutagenicity or teratogenic effects in doses up to 3200 mg. kg per day in rats or 32 mg. kg per day in rabbits. Toxicity has been shown only at very high doses (over 320 mg. kg), which result in renal tubular necrosis in rabbits, although not in rats or dogs.

6. Pharmaceutical particulars:

6.1 List of Excipients:

Hypromellose	USP 34
Microcrystalline cellulose	USNF 29
Sodium starch glycolate	USNF 29
Talc	USP 34
Colloidal silicon dioxide	USNF 29
Calcium stearate	USNF 29
Tartrazine yellow supra	Inhouse
colour	USNF 29
Aspartame	Inhouse
Pineapple flavour)	

6.2 Incompatibilities:
None reported

6.3 Shelf-Life:
24 months from the date of manufacture.

6.4 Storage:
Store in a dry place below 30^0C.

6.5 Nature and Contents of Container:
10 tablets packed in one Alu Alu strip. Such 10 Alu Alu strips packed in unit printed duplex board carton along with its package insert. Such 120 cartons packed in one shipper. Shippers are sealed with BOPP tape.

6.6 Special precautions for disposal:
None reported.

7. Registrant:

Nairobi Enterprises Ltd.
P.O. Box 42367 00100

8. Manufacturer:
M/S CHIROS PHARMA
Village Loharon, P.O. Ghatti,
Tehsil & Distt. Solan (H.P),
India.

9. Date of revision of the text :
10-04-2021, 18th August 2026