Summary of Product Characteristics
ACTICEF-400
(Cefixime 400 mg film-coated tablets)

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1. Name of the medicinal product

ACTICEF-400 (Cefixime Tablets USP 400 mg)

2. Qualitative and quantitative composition

Each film-coated tablet contains cefixime (as trihydrate) USP equivalent to 400 mg of anhydrous cefixime.

Excipient with known effect:
Each tablet contains lactose monohydrate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

White, capsule-shaped, elongated film-coated tablet with a break-line on one side and plain on the other.

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.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

The usual course of treatment is 7 days, and may be continued for up to 14 days if required. Adults and children over 10 years or weighing more than 50 kg: 200–400 mg daily according to the severity of infection, given as a single dose or in two divided doses.

Renal impairment

Normal dose and schedule may be given in patients with creatinine clearance of 20 mL/min or greater. In patients whose creatinine clearance is below 20 mL/min, and in those on haemodialysis or chronic ambulatory peritoneal dialysis, a dose of 200 mg once daily should not be exceeded.

Elderly

Elderly patients may be given the same dose as adults; renal function should be assessed.

Paediatric population

The 400 mg tablet is not appropriate for children under 10 years or weighing less than 50 kg; a paediatric presentation should be used. Safety in children under 6 months has not been established.

Method of administration

For oral use. Absorption is not significantly modified by food.

4.3 Contraindications

Hypersensitivity to cefixime, to any other cephalosporin antibiotic, or to any of the 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; 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, DRESS and acute generalised exanthematous pustulosis, 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 and haemolytic anaemia

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. Drug-induced haemolytic anaemia, including severe cases with fatal outcome, has been described for cephalosporins as a class; if a patient develops anaemia on cefixime, cephalosporin-associated anaemia should be considered and cefixime discontinued until the aetiology is established.

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.

Renal effects

As with other cephalosporins, cefixime may cause acute renal failure, including tubulointerstitial nephritis; if this occurs, cefixime should be discontinued. Cefixime should be administered with caution in patients with markedly impaired renal function.

Lactose

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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). Probenecid reduces the total clearance of cefixime. Interference with laboratory tests: a false-positive reaction for glucose in the urine may occur with copper-reduction methods (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

Animal data have not revealed malformative or foetotoxic effects, but there are no adequate and well-controlled studies in pregnant women; cefixime should be used in pregnancy only if clearly necessary. There are no data on whether cefixime passes into breast milk; caution should be exercised in nursing mothers.

4.7 Effects on ability to drive and use machines

If adverse reactions such as dizziness or encephalopathy occur, the patient should not drive or use machinery.

4.8 Undesirable effects

Cefixime is generally well tolerated, with most reactions 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
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
Nervous system disorders	Headache, dizziness; convulsions and encephalopathy (frequency not known)
Respiratory, thoracic and mediastinal disorders	Dyspnoea
Gastrointestinal disorders	Abdominal pain, diarrhoea, dyspepsia, nausea, vomiting, flatulence
Hepatobiliary disorders	Jaundice, hepatitis
Skin and subcutaneous tissue disorders	Rash, pruritus; erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP)
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

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 whose bactericidal action results from inhibition of bacterial cell-wall synthesis. It has marked in vitro activity against a wide variety of Gram-positive and Gram-negative organisms and is highly stable in the presence of many beta-lactamases. 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 22–54% and is not significantly modified by food. Typical peak serum levels are 1.5–3 micrograms/mL, with little or no accumulation on multiple dosing. Cefixime is predominantly eliminated as unchanged drug in the urine by glomerular filtration; no metabolites have been isolated from serum or urine. Serum protein binding is approximately 70%, mainly to albumin. The elimination half-life is 3–4 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated-dose toxicity, genotoxicity and reproductive toxicity.

6. Pharmaceutical particulars

6.1 List of excipients

Tablet core:

- Microcrystalline cellulose
- Lactose monohydrate
- Croscarmellose sodium
- Colloidal anhydrous silica
- Magnesium stearate

Film coat:

- Titanium dioxide
- Hypromellose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

Blister pack of 10 tablets, presented in a printed carton together with the package insert.

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 and Manufacturer

Globela Laboratories Pvt. Ltd., India.

8. Marketing Authorisation Number

H2008/18791/752

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text