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

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1. Name of the medicinal product

XIFIX 400 TAB (Cefixime Tablets USP 400 mg)

2. Qualitative and quantitative composition

Each film-coated tablet contains cefixime trihydrate USP equivalent to 400 mg of cefixime.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Off-white to light-yellowish, caplet-shaped film-coated tablet with a break-line on one side and plain on the other.

4. Clinical particulars

4.1 Therapeutic indications

Cefixime is indicated in adults and children over 12 years of age for the treatment of infections due to susceptible organisms when oral antibiotic therapy is appropriate, in particular:

- Acute pyelonephritis without uropathy.
- Lower urinary tract infections, complicated or not, with the exception of prostatitis.
- Bacterial super-infections of acute bronchitis and exacerbations of chronic bronchitis.
- Bacterial pneumonia.
- Sinusitis and otitis media.
- Male gonococcal urethritis.

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

4.2 Posology and method of administration

Posology

The 400 mg tablet is recommended for children over 12 years of age and for adults. The dose is 400 mg/day, given in two administrations 12 hours apart. In gonococcal urethritis, efficacy is obtained with a single dose of two 400 mg tablets (800 mg).

Elderly

When renal function is normal, no dose modification is necessary in the elderly.

Renal impairment

When creatinine clearance is above 20 mL/min, no dose modification is needed. For lower values, including in haemodialysis patients, the dose should not exceed 4 mg/kg/day in one administration.

Hepatic impairment

No dose modification is necessary.

Paediatric population

In children under 12 years, the 400 mg tablet is not appropriate; a paediatric presentation should be used. In children under 6 months, the use of cefixime is not recommended.

Method of administration

For oral use.

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

The occurrence of any allergic manifestation requires discontinuation of treatment. Since penicillin allergy is cross-reactive with cephalosporin allergy in 5 to 10% of cases, cephalosporins must be used with extreme caution in penicillin-sensitive patients, with strict medical supervision from the first administration; they are contraindicated in patients with a history of immediate-type allergy to cephalosporins, as hypersensitivity (anaphylactic) reactions can be serious and sometimes fatal.

Clostridioides difficile-associated colitis

Antibacterial-associated colitis and pseudomembranous colitis have been reported with almost all antibacterials, including cefixime, ranging in severity from mild to life-threatening. This diagnosis should be considered in patients who present with diarrhoea during or after administration; cefixime should be discontinued and specific treatment for Clostridioides difficile considered. Peristalsis inhibitors should be avoided.

Serious skin reactions

Serious skin reactions such as toxic epidermal necrolysis (Lyell's syndrome), Stevens-Johnson syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP) have been reported with cefixime. Patients should be informed of the signs and symptoms; treatment should be discontinued immediately at the first appearance of rash, mucosal lesions or any other sign of hypersensitivity.

Haemolytic anaemia and encephalopathy

Serious cases of haemolytic anaemia, including fatalities, have been reported with cephalosporins (class effect); if a patient develops anaemia on cefixime, cephalosporin-associated anaemia should be considered and cefixime discontinued until the aetiology is established. Beta-lactams, including cefixime, predispose the patient to the risk of encephalopathy (which may include convulsions, confusion, disturbances of consciousness or abnormal movements), particularly in the event of overdose or renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid: combination of 1 g of probenecid with cefixime leads to a 25% reduction in the total clearance of cefixime. Antacids do not reduce the absorption of cefixime.

Oral anticoagulants: numerous cases of increased activity of oral anticoagulants have been reported in patients receiving antibiotics, including cephalosporins; the INR should be monitored.

Interference with laboratory tests: false-positive reactions for ketones and for glucose in the urine (use glucose-oxidase methods) and a false-positive Coombs test have been described during treatment with cephalosporins.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although clinical data are insufficient, animal data have not revealed any malformative or foetotoxic effect. The use of cefixime may be considered during pregnancy if necessary.

Breast-feeding

There are no data on whether cefixime passes into breast milk. Breast-feeding may be continued when taking this antibiotic; however, breast-feeding (or treatment) should be discontinued and a doctor consulted if diarrhoea, candidiasis or rash occurs in the infant.

4.7 Effects on ability to drive and use machines

If adverse reactions such as encephalopathy (which may include seizures, confusion, altered consciousness or abnormal movements) occur, the patient should not drive or use machinery.

4.8 Undesirable effects

The adverse reactions reported with cefixime 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, thrombocytosis, thrombocytopenia, leucopenia, neutropenia, granulocytopenia, agranulocytosis; very rare cases of haemolytic anaemia
Immune system disorders	Anaphylactic reaction, urticaria, angioedema, serum sickness
Nervous system disorders	Headache, dizziness; convulsions and encephalopathy (frequency not known)
Respiratory, thoracic and mediastinal disorders	Dyspnoea
Gastrointestinal disorders	Abdominal pain, diarrhoea, nausea, vomiting, dyspepsia, flatulence
Hepatobiliary disorders	Jaundice, hepatitis
Skin and subcutaneous tissue disorders	Rash, pruritus; very rare bullous eruptions — erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP)
Renal and urinary disorders	Acute renal failure due to interstitial nephritis
Investigations	Moderate and transient elevation of AST, ALT and alkaline phosphatase; slight increase in blood urea, serum creatinine and bilirubin
General disorders and administration site conditions	Fever

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

Beta-lactams, including cefixime, predispose the patient to the risk of encephalopathy, particularly in the event of overdose or renal impairment. 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 bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms and is highly stable in the presence of many beta-lactamases. The prevalence of acquired resistance may vary geographically and with time, and local information on resistance is desirable, particularly for the treatment of severe infections.

5.2 Pharmacokinetic properties

Absorption

After a single oral 400 mg dose, mean maximum serum concentrations (Cmax) are about 3–5 micrograms/mL, reached in approximately 3 to 4 hours. The absolute oral bioavailability is approximately 50% and is not modified by food, although the time to peak is delayed by about one hour. There is no accumulation on repeated dosing.

Distribution

The apparent volume of distribution is of the order of 15 litres. Binding to serum proteins is about 70%, mainly to albumin.

Elimination

The elimination half-life is between 3 and 4 hours (mean 3.3 hours). Cefixime is eliminated via the kidneys in unchanged form (16 to 20% of the ingested dose), with extra-renal (biliary) elimination of about 25%. No serum or urinary metabolites have been demonstrated. In severe renal insufficiency (creatinine clearance < 20 mL/min), the daily dose should be reduced. In hepatic insufficiency, elimination is slowed (half-life 6.4 hours) but no dose modification is necessary.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated-dose toxicity, genotoxicity and toxicity to reproduction. No metabolites of cefixime have been isolated from serum or urine in animals or humans.

6. Pharmaceutical particulars

6.1 List of excipients

Tablet core:

- Maize starch
- Microcrystalline cellulose
- Sodium starch glycolate
- Croscarmellose sodium
- Colloidal anhydrous silica
- Purified talc
- Magnesium stearate

Film coat:

- Titanium dioxide

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

National Pharmacy Ltd, Colchester Park, P.O. Box 17843-00500, Nairobi, Kenya.

8. Marketing Authorisation Number

H2017/CTD4129/224

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text