EFICEF-400 TABLETS
(Cefixime Dispersible Tablets 400 mg)

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Eficef-400 Tablets (Cefixime Dispersible Tablets 400 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Approved Name (if any)	Quantity per tab in mg	Active / Non- active
*Cefixime (as Trihydrate) USP equivalent to Anhydrous Cefixime	400.00	Active Ingredient
**Microcrystalline Cellulose USP PH 112	208.50	Super-Disintegrant
Neomalt IH	20.00	Sweetener
Dry Flavour Orange IH	15.00	Flavouring Agent
Neosucralose IH	0.500	Sweetener
Crospovidone USP XL-10	120.00	Disintegrant
Aspartame USP	20.00	Sweetener
Polacryllin Potassium USP (Empress DT)	8.00	Super-Disintegrant
Colloidal Silicon Dioxide USP	4.00	Glidant
Magnesium Stearate USP	4.00	Lubricant

The quantity of API may vary depending on potency/assay&%LOD/water/moisture content.

*Standard quantity has been calculated based on assay of Cefixime (as Trihydrate) on "as is such basis."

**Adjust the qty. of Microcrystalline Cellulose PH 112 depending upon the quantity of Cefixime used.

1.12 mg of Cefixime (as Trihydrate) USP is equivalent to 1mg of Anhydrous Cefixime

Definitions:

USP: United States Pharmacopoeia

IH: In House Specification

3. PHARMACEUTICAL FORM

Dispersible Tablets (Oral)

4. CLINICAL PARTICULARS

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4.1 Therapeutic indications

Treatment of adults and paediatric patients six months of age or older with the following infections when caused by susceptible isolates of the designated bacteria: Uncomplicated UTI, Pharingitis, Tonsillitis, Otitis media, acute exacerbation of chronic bronchitis (AECB), and Uncomplicated gonorrhea.

4.2 Posology and method of administration

Posology

Adults: The recommended dose of Cefixime is 400mg daily. This may be given as 400mg once daily or as 200mg every 12 hours. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400mg is recommended. The tablet may be administered without regard to food. In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

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Method of administration for dispersible tablet:

Disperse one tablet in 15ml (one tablespoonful) of boiled & cooled water, immediately before use.

Method of administration: Oral use.

4.3 Contraindications

Contraindicated in patients with known allergies to Cefixime or other Cephalosporins.

4.4 Special warnings and precautions for use

Pregnancy: Pregnancy Category B. Reproduction studies have been performed in mice & rats at doses up to 40 times the human dose & have revealed no evidence of harm to the fetus due to Cefixime. There are no adequate & 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.

Labor & Delivery: Cefixime has not been studied for use during labor & delivery. Treatment should only be given if clearly needed.

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

Paediatric Use: Safety & effectiveness of Cefixime in children aged less than six months old have not been established. The incidence of gastrointestinal adverse reactions, including diarrhoea & loose stools, in the paediatric patients receiving the suspension, was comparable to the incidence seen in adult patients receiving tablets.

Geriatric Use: Clinical studies did not include sufficient numbers of subjects aged 65 & older to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in responses between the elderly & younger patients. A pharmacokinetic study in the elderly detected differences in pharmacokinetic parameters. These differences were small & do not indicate a need for dosage adjustment of the drug in the elderly.

Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock & fatalities) have been reported with the use of Cefixime. Before therapy with Cefixime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among beta-lactam antibiotics has been clearly documented & may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to Cefixime occurs, discontinue the drug.

Clostridium difficile-Associated Diarrhoea: Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefixime, & may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A & B which contribute to the development of CDAD. Hypertoxin producing isolates of C. difficile cause increased morbidity & mortality, as these infections can be refractory to antimicrobial therapy & may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid & electrolyte management, protein supplementation, antibiotic treatment of C. difficile & surgical evaluation should be instituted as clinically indicated.

Dose adjustment in Renal Impairment: The dose of Cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) & hemodialysis (HD). Patients on dialysis should be monitored carefully.

Coagulation Effects: Cephalosporins, including Cefixime, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy & patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk & exogenous vitamin K administered as indicated.

Development of Drug-Resistant Bacteria: Prescribing Cefixime in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient & increases the risk of the development of drug-resistant bacteria.

4.5 Interaction with other medicinal products and other forms of interaction

Carbamazepine: Elevated carbamazepine levels have been reported in post marketing experience when Cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

Warfarin & Anticoagulants: Increased prothrombin time, with or without clinical bleeding, has been reported when Cefixime is administered concomitantly.

Drug/Laboratory Test Interactions: A false-positive reaction for ketones in the urine may occur with tests using nitroprusside but not with those using nitroferricyanide. The administration of Cefixime may result in a false-positive reaction for glucose in the urine using Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions is used. A false positive direct Coombs test has been reported during treatment with other cephalosporins; therefore, it should be recognized that a positive Coombs test may be due to the drug.

4.6 Pregnancy and lactation

Pregnancy: Pregnancy Category B. Reproduction studies have been performed in mice & rats at doses up to 40 times the human dose & have revealed no evidence of harm to the fetus due to Cefixime. There are no adequate & 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.

Labor & Delivery: Cefixime has not been studied for use during labor & delivery. Treatment should only be given if clearly needed.

Nursing Mothers: 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

None known.

4.8 Undesirable effects

Incidence rates were less than 1 in 50 (less than 2%). Gastrointestinal: Several cases of documented pseudomembranous colitis were identified in clinical trials. The onset of pseudomembranous colitis symptoms may occur during or after therapy. Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock & fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema & facial edema. Erythema multiforme, Stevens-Johnson syndrome & serum sickness-like reactions have been reported. Hepatic: Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice.

Renal: Transient elevations in BUN or creatinine, acute renal failure. Central Nervous System: Headaches, dizziness, seizures. Hemic & Lymphatic System: Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, & eosinophilia. Abnormal Laboratory Tests: Hyperbilirubinemia. Other Adverse Reactions: Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis. Adverse Reactions reported for Cephalosporin-class Drugs: Allergic reactions, superinfection, renal dysfunction and toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis. Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

4.9 Overdose

Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis. Adverse reactions in small numbers of healthy adult volunteers receiving single doses up to 2g of Cefixime did not differ from the profile seen in patients treated at the recommended doses.

5. PHARMACOLOGICAL PROPERTIES

Pharmacological category: third generation cephalosporin, ATC code: J01DD08

5.1 Pharmacodynamic properties

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

Cefixime tablets are about 40% to 50% absorbed whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food. A single 200mg tablet of Cefixime produces an average peak serum concentration of approximately 2mcg/mL

(range 1-4mcg/mL); a single 400mg tablet produces an average peak concentration of approximately 3.7mcg/mL (range 1.3-7.7mcg/mL).

Distribution: Serum protein binding is concentration independent with a bound fraction of approximately 65%.

Metabolism and Excretion: There is no evidence of metabolism of Cefixime in vivo. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. In animal studies, it was noted that Cefixime is also excreted in the bile in excess of 10% of the administered dose.

The serum half-life of Cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours but may range up to 9 hours in some normal volunteers.

Special Populations: Geriatrics - Average AUCs at steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults.

However, these increases were not clinically significant.

Renal Impairment - In subjects with moderate impairment of renal function (20 to 40 mL/min creatinine clearance), the average serum half-life of Cefixime is prolonged to 6.4 hours. In severe renal impairment (5 to 20mL/min creatinine clearance), the half-life increased to an average of 11.5 hours. The drug is not cleared significantly from the blood by hemodialysis or peritoneal dialysis. However, a study indicated that with doses of 400mg, patients undergoing hemodialysis have similar blood profiles as subjects with creatinine clearances of 21 to 60mL/min.

5.3 Preclinical safety data

No additional data of relevance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose USP, Neomalt IH, Dry Flavour Orange IH, Neosucralose IH, Crospovidone USP XL-10, Aspartame USP, Polacryllin Potassium USP (Empress DT), Colloidal Silicon Dioxide USP, Magnesium Stearate USP

6.2 Incompatibilities

None.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 30°C. Protect from sunlight. Keep out of reach of children.

6.5 Nature and contents of container

Alu-PVC blister of 10 Tablets packed in Inner carton along with leaflet.

6.6 Special precautions for disposal and other handling

None

7. MARKETING AUTHORISATION HOLDER

SHALINA HEALTHCARE Nigeria Limited

19 Fatai Atere Way, Matori, Mushin Lagos, Nigeria

8. MARKETING AUTHORISATION NUMBER

Application for granting new registration certificate

9. DATE OF FIRST AUTHORISATION

Application for granting new registration certificate

10. DATE OF UPDATE OF TEXT

April 2024