EFICEF 100

(Cefixime for Oral Suspension USP 100 mg)

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

EFICEF 100 (Cefixime for Oral Suspension USP 100 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ingredients	**Qty in mg/5ml**
Cefixime (As trihydrate) USP Equivalent to Anhydrous Cefixime	120.51 mg ≡ 100 mg
Xanthan Gum BP	11.66 mg
Aspartame BP	1.00 mg
Mannitol BP	91.66 mg
Colloidal Anhydrous Silica BP	20.83 mg
Flavour Strawberry IH	20.0 mg
**Sucrose BP	1667.4 mg
Sodium Citrate BP	7.13 mg
Sodium Benzoate BP	19.05 mg
Citric Acid Monohydrate BP	4.74 mg
Colloidal Anhydrous Silica BP	31.66 mg
Colour Quinoline Yellow Supra	0.33 mg
#Sucrose BP	33.33 mg

*The Quantity of API may vary depending on Potency/Assay/%LOD/Water and Moisture Content.

** The quantity of Sucrose may vary according to API.

Extra Sucrose added to compensate Loss on drying

Definitions:

USP: United States Pharmacopoeia

BP: British Pharmacopoeia

IH: In House Specification

3. PHARMACEUTICAL FORM

Powder for reconstitution for suspension

4. CLINICAL PARTICULARS

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), uncomplicated gonorrhea

4.2 Posology and method of administration

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. In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

Pediatric Patients (6 months or older): The recommended dose is 8mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4mg/kg every 12 hours. Children weighing more than 50kg or older than 12 years should be treated with the recommended adult dose. Otitis media should be treated with the suspension. Clinical trials of otitis media were conducted with the suspension, and the suspension results in higher peak blood levels than the tablet when administered at the same dose. Therefore, the tablet should not be substituted for the suspension in the treatment of otitis media. In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

Direction for reconstitution for oral suspension: Tap the bottle several times to loosen powder contents prior to reconstitution. Add boiled and cooled water to the content of the bottle up to the mark. Shake well until you obtain a homogeneous solution. If necessary, add some more water upto the mark and shake again. Use the reconstituted suspension within 14 days.

Method of administration: Oral

4.3 Contraindications

Cefixime is contraindicated in patients with known allergy to Cefixime or other Cephalosporin's.

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 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.

Labor and Delivery: Cefixime has not been studied for use during labor and 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 and effectiveness of Cefixime in children aged less than six months old have not been established. The incidence of gastrointestinal adverse reactions, including diarrhoea and 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 and older to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. A pharmacokinetic study in the elderly detected differences in pharmacokinetic parameters. These differences were small and do not indicate a need for dosage adjustment of the drug in the elderly. Hypersensitivity Reactions: Anaphylactic/anaphylactoid reactions (including shock and 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 and 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, and may range in severity from mild diarrhoea 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 and B which contribute to the development of CDAD. Hypertoxin producing isolates of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and 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 and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and 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) and 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, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and 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 and 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 and 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

This drug should be used during pregnancy only if clearly needed.

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 Adverse Reactions

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 and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and 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 and Lymphatic System: Transient thrombocytopenia, leukopenia,

neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and 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, 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.

4.8 Symptoms of Overdosage & Treatment

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

5.1 Pharmacodynamic properties

Pharmacological category: Third generation oral cephalosporin.

Pharmacological action: It is bactericidal by inhibition of the cell wall synthesis. Cefixime has been shown to be active against most isolates of the following bacteria both in vitro & in clinical infections: Gram-positive bacteria: Streptococcus pneumonia, Streptococcus pyogenes; Gram-negative bacteria: Haemophilus influenza, Moraxella catarrhalis, Escherichia coli, Proteus mirabilis, and Neisseria gonorrhoeae.

The following in vitro data are available, but their clinical significance is unknown. Cefixime exhibits in vitro MICs of 1mcg/mL or less against most (>90%) isolates of the following bacteria; however, the safety and effectiveness of Cefixime in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials. Gram-positive bacteria: Streptococcus agalactiae, Gram-negative bacteria: Haemophilus parainfluenzae, Proteus vulgaris, Klebsiella pneumonia, Klebsiella oxytoca, Pasteurella multocida, Providencia species, Salmonella species, Shigella species, Citrobacter amalonaticus, Citrobacter diversus, and Serratia marcescens.

5.2 Pharmacokinetic properties

Cefixime suspension, given orally, 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.

200 & 400mg doses of oral suspension produce average peak concentrations of 3 mcg/mL (range 1 to 4.5mcg/mL) and 4.6mcg/mL (range 1.9 to7.7mcg/mL), respectively, when tested in normal adult volunteers. The area under the time versus concentration curve (AUC) is greater by approximately 10% to 25% with the oral suspension than with the tablet after doses of 100 to 400mg, when tested in normal adult volunteers. This increased absorption should be taken into consideration if the oral suspension is to be substituted for the tablet. Because of the lack of bioequivalence, tablets should not be substituted for oral suspension in the treatment of Otitis media. Crossover studies of tablet versus suspension have not been performed in children. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200mg of suspension. Peak serum concentrations occur between 3 and 8 hours following oral administration of a single 400mg capsule. 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 preclinical findings of relevance have been reported.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Xanthan Gum BP, Aspartame BP, Mannitol BP, Colloidal Anhydrous Silica BP, Sucrose BP, Sodium Citrate BP, Sodium Benzoate BP, Citric Acid Monohydrate BP. Colour Quinoline Yellow Supra & Flavour Strawberry.

6.2 Incompatibilities

None.

6.3 Shelf life

24 months

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Eficef suspension is available in an HDPE bottle of 60ml packed in a carton along with a leaflet.

7. MARKETING AUTHORISATION HOLDER

SHALINA HEALTHCARE DMCC

30th Floor, Almas Towers,

Jumeirah Lakes Towers Dubai-UAE.

Country: UAE.

8. MARKETING AUTHORISATION IN OTHER COUNTRIES

Product is registered in Gabon, Guinea Conakry & Ivory Coast,