Summary Product Characteristics (SPC)

1. Name of the medicinal product

Evercef Powder for Oral Suspension.

2. Qualitative and quantitative composition

Each 5mL of the reconstituted suspension contains: Cefixime (as Trihydrate) USP 50mg.

3. Pharmaceutical Form

Powder for oral suspension.

4. Clinical particulars

4.1 Therapeutic indications

Evercef is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms.

Uncomplicated urinary tract infections caused by Escherichia coli and proteus mirabilis.

Otitis media caused by Haemophilus influenzae (beta-lactamase positive and negative strains), Moraxella (Branhamella) catarrhalis, (most of which are beta-lactamase positive) and S.pyogenes*. Otitis media caused by streptococcus pneumoniae, Pharyngitis and tonsillitis, caused by S. pyogenes.

Eradication of S.pyogenes from the nasopharynx.

Acute bronchitis and Acute Exacerbations of Chronic Bronchitis, caused by streptococcus pneumoniae and Haemophilus influenzae (beta lactamase positive and negative strains)

Uncomplicated gonorrhea (cervical/urethra), caused by Neisseria gonorrhea (penicillinase-and non-penicillinase-producing strains.

Appropriate cultures and susceptibility to cefixime; however therapy may be started while awaiting the result.

4.2 Posology and method of administration

Adults: The recommended dose of cefixime is 400mg daily, be given as a 400mg tablet daily or as 200mg tablets every 12 hours. For the treatment of uncompleted cervical /urethral gonococcal infections, a single oral dose of 400mg is recommended.

Children: The recommended dose is 8mg/kg/day of the suspension, administered as a single dose or in two divided doses of 4mg/kg/day every 12 hours. Children weighing more than 50kg or older than 12years should be treated with the recommended adult dose. Otitis media should be treated with the suspension and not the tablets.

Efficacy and safety in infants aged less than six months have not been established.

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

Renal impairment: Evercef may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 60ml/min or greater. Patients whose clearance is between 21 and 60 ml/min or patients who are on renal hemodialysis may be given 75% of the standard dosage at the standard dosing interval (i.e., 300mg daily). Patients whose clearance is <20ml/min, or patients who are on continuous ambulatory peritoneal dialysis may be given half the standard dosage at the standard dosing interval (i.e., 200mg daily). Neither hemodialysis nor peritoneal dialysis remove significant amounts of drug from the body.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Hypersensitivity reactions: Special care is indicated in patients who have experienced an allergic reaction to beta-lactam antibiotics because there is a risk of cross-sensitivity. Serious and occasionally fatal hypersensitivity reactions, treatment with cefixime must be discontinued immediately and adequate emergency measures must

be initiated. Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to cefixime to other beta-lactam agents.
Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. A toxin produced by clostridium difficile is a primary cause of severe antibiotic-associated diarrhea including pseudomembranous colitis. Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Symptoms may occur during or after antibiotic treatments and may range in severity from mild to life threatening. Mild cases usually respond to drug discontinuation alone. In moderate to severe cases, management should include fluids, electrolytes and protein supplementation.
The dose of Evercef should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and haemodialysis (HD).
Patients on dialysis should be monitored carefully. Evercef should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
Cephalosporins 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.

4.5 Interaction with other medicinal products and other forms of interaction

Carbamazepine: Elevated carbamazepine levels have been reported when cefixime is administered concomitantly.
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

Reproduction studies in mice and rats have revealed no evidence of harm to the fetus due to cefixime.
There are no adequate and well-controlled studies in pregnant women. Cefixime should be used during pregnancy only if clearly needed.

Breast feeding

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

4.7 Effects on ability to drive and use machines

Cefixime has no or negligible influence on the ability to drive or use machines.
However Cefixime may cause side effects (see section 4.8) influencing the capacity of reaction and the ability to drive and use machines.

4.8 Undesirable effects.

Most adverse reactions are of a mild and transient nature. Most commonly seen are gastrointestinal events like diarrhoea, loose and frequent stools, abdominal pain, nausea, dyspepsia and flatulence. These usually respond to symptomatic therapy or cease when cefixime is discontinued. Several patients develop severe diarrhoea and/or documented pseudomembranous colitis.
Other adverse reactions: Hypersensitivity reactions: Anaphylactic /anaphylactiod 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. Hepatic: transient elevations in SGPT,SGOT, alkaline phosphate, hepatitis, jaundice. Renal: Transient elevations in BUN or creatinine, acute renal failure. Central nervous system: Headaches, dizziness, seizures. Hemic and Lymphatic systems: Transient thrombocytopenia, leukopenia and eosinophilia. Prolongation in prothrombin time seen rarely. Abnormal laboratory tests: Hyperbilirubinemia. Other: Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis. Abnormal laboratory tests: Positive direct coombs test, elevated LDH, pancytopenia agranulocytosis.

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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Bacterial action of cefixime results from inhibition of cell-wall synthesis. Cefixime is highly stable in the presence of beta lactamase enzymes. As a result many organisms resistant to penicillins and some cephalosporins due to the presence of beta-lactamases may be susceptible to cefixime. Cefixime is active against most strains of the following organisms both in vitro and in clinical infections:

Gram-positive organisms: Streptococcus pneumoniae, streptococcus pyogenes.

Gram-negative organisms: Haemophilus influenzae (beta-lactamase positive and negative strains), Moraxella (Branhamella) catarrhalis (most of which are beta lactamase positive), Escherichia coli, proteus mirabilis, Neisseria gonorrhoeae (including penicillinase-and non-penicillinase-producing strains.

Cefixime has shown to be active in vitro against most strains of the following organisms; however, clinical efficacy has not been established.

Gram-positive organisms: Streptococcus agalactiae

Gram-negative organisms: Haemophilus parainfluenzae (beta-lactamase positive and negative strains), proteus vulgaris; klebsiella pneumoniae, klebsiella oxytoca, pasteurella multocida, providencia species, salmonella species, shigella species citrobacteramalonaticus, citrobacter diversus serratia marcescens.

Note: Pseudomonas species, strains of group D streptococci (including enterococci) listeria monocytogenes, most strains of staphylococci (including methicillin-resistant strains) and most strains of enterobacter are resistant to cefixime. In addition, most strains of bacteroides fragilis and clostridia are resistant to cefixime.

5.2 Pharmacokinetic properties

Evercef given orally is about 40%-50% absorbed whether administered with or without food; time to maximal absorption is increased approximately 0.8 hours when administered with food. The oral suspension produces average peak concentrations approximately 25% -50% higher than tablets. Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200mg tablet, a single 400mg tablet or 400mg tablet or 400mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200mg of suspension. Approximately 50% of the absorbed dose of cefixime is excreted unchanged in the urine in 24 hours. Over 10% of the administered dose of cefixime is excreted in the bile. Serum protein binding is concentration independent with a bound fraction of approximately 65%. There is little accumulation of drug in serum or urine after dosing for 14 days. The serum half-life of cefixime in healthy subjects averages 3-4 hours but may range up to 9 hours. Average AUCs at steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults.

In subjects with moderate impairment of renal function (20 to 40ml/min creatinine clearance), average serum half-life is prolonged to 6.4hours. In severe renal impairment (5to 20ml/min creatinine clearance) the half-life increased to an average of 11.5hours. The drug is not cleared significantly from the blood by hemodialysis or peritoneal dialysis. Patients undergoing hemodialysis have similar blood profiles as subjects with creatinine clearances of 21-60ml/min. There is no evidence of metabolism of cefixime in vivo.

Adequate data on CSF levels of cefixime are not available.

5.3 Preclinical safety data

There are no findings from chronic toxicity investigations suggesting that any side effects unknown to date could occur in humans. Furthermore, in vivo and in vitro studies did not yield any indication of a potential to cause mutagenicity. Long-term studies on carcinogenicity have not been conducted. Reproduction studies have been performed in mice and rats at does up to 400 times the human dose and have revealed no evidence of impaired fertility or harm to the foetus due to cefixime. In the rabbit, at doses up to 4 times the human dose, there was no

evidence of a teratogenic effect; there was a high incidence of abortion and maternal death, which is an expected consequence of the known hypersensitivity of rabbits to antibiotic-induced changes in the population of the microflora of the intestine.

6. Pharmaceutical particulars

6.1 List of excipients

Aspartame, Mannitol, Sucrose, Sodium Benzoate, Sodium CMC, Xanthan Gum, Colloidal silicon Dioxide &Tutti Fruity powder Flavour

6.2 Incompatibilities:

None known

6.3 Shelf life:

24 months

6.4 Special precautions for storage:

Store in a dry place below 30°C
Protect from light
Replace cap securely after use
Keep all medicines out of reach of children

6.5 Nature and contents of the container:

Packed in 60ml and 100ml glass/HDPE bottle contained in a unit box with literature.

6.6 Special precautions for disposal:

No special requirements

7. Registrant:

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