Prescribing information (Summary of Product Characteristics)

1. Name of the medicinal product

Evercef® 200

2. Qualitative and quantitative composition

Each film coated tablet contains: Cefixime Trihydrate USP equivalent to Cefixime 200mg

3. Pharmaceutical form

Tablet

White, circular biconvex film coated tablets plain in both sides. Packed in Alu-Alu blister of 1 x 10's contained in a unit box with literature insert.

4. Clinical particulars

4.1 Therapeutic indication

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/ urethral}, caused by Neisseria gonorrhoeae (penicillinase-and non-penicillinase- producing strains).

Appropriate cultures and susceptibility studies should be performed to determine the causative organism and its susceptibility to Cefixime; however, therapy may be started while awaiting the result.

4.2 Dosage and directions for use

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

Children: The recommended dose is 8 mg/kg/day of the suspension, administered as a single daily dose or in two divided doses of 4 mg/kg every 12 hours. Children weighing more than 50 kg or older than 12 years 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 60 ml/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., 300 mg 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., 200 mg 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 the 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 have been reported. In case of severe 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 cephalosporins or to any other type of beta lactam agent. Caution should be used if Cefixime is given to patients with a history of non-severe hypersensitivity 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 treatment 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 hemodialysis (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 Interactions

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 Fertility, 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.

Breastfeeding: 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 of adverse reactions are of a mild and transient nature. Most commonly seen are gastrointestinal events like diarrhea, loose or frequent stools, abdominal pain, nausea, dyspepsia, and flatulence. These usually respond to symptomatic therapy or cease when Cefixime is discontinued. Several patients develop severe diarrhea and/or documented pseudomembranous colitis.

Other adverse reactions: Hypersensitivity React ions: 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. 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 Systems: Transient thrombocytopenia, leukopenia, neutropenia, 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 Pharmacodynamics properties
Bactericidal 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 been 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 influenzae (beta lactamase positive and negative strains). *Proteus vulgaris, Klebsiella pneumoniae. Klebsiella oxytoca, Pasteurella multocida, Providencia species, Salmonella species, Shigella species, Citrobacter amalonaticus, Citrobacter diversus, Serratia rnarcescens.*
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 Bacteriodes 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 the tablets.
Peak serum concentrations occur between 2 and 6 hour s following oral administration of a single 200 mg tablet, a single 400 mg tablet or 400 mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg 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 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 40 ml/min creatinine clearance), average serum half-life is prolonged to 6.4 hours.
In severe renal impairment (5 to 20 ml/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
Patients undergoing hemodialysis have similar blood profiles as subjects with creatinine clearances of 21 - 60 ml/min. There is no evidence of metabolism of cefixime in vivo.

5.3 Preclinical safety data
Not available.

6. Pharmaceutical particulars

6.1 List of Excipients

Dicalcium Phosphate
Microcrystalline Cellulose pH 102
Sodium Lauryl Sulphate
Pregelatinized Starch
Crospovidone
Colloidal Silicon Dioxide (Aerosil)
Magnesium Stearate
Hydroxypropyl methylcellulose (5 Cps)
Titanium Dioxide
Diethyl Phthalate
Ethyl Cellulose 100 cps
Isopropyl Alcohol (70%)
Methylene Chloride

6.2 Incompatibilities

None known

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store in a dry place below 30ºC
Protect from light.
Keep all medicine out of reach of children.

6.5 Nature and contents of container

White, circular biconvex film coated tablets plain in both sides. Packed in Alu-Alu blister of 1 x 10's contained in a unit box with literature insert.

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing authorization holder

Marketing Authorization Holder:

Company Name: LABORATORY & ALLIED LTD
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa road, P.O. Box 42875 GPO 00100, Nairobi,
Country **:** Kenya
Telephone **:** +254 20 8040306
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E-Mail **:** info@laballied.com.

Manufacturing Site Address:

Company Name: LABORATORY & ALLIED LTD
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa road, P.O. Box 42875 GPO 00100, Nairobi,
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