Evacef™

(Cefadroxil)

Highnoon

COMPOSITION
Evacef 500mg Capsule:
Each capsule contains:
Cefadroxil (as Monohydrate) 500mg
Evacef 125mg/5mL Suspension:
Each 5mL contains:
Cefadroxil (as Monohydrate) 125mg
Evacef 250mg/5mL Suspension:
Each 5mL contains:
Cefadroxil (as Monohydrate) 250mg

DESCRIPTION
Evacef (cefadroxil monohydrate, USP) is a first generation cephalosporin antibiotic intended for oral administration.

PHARMACOLOGY
Mechanism of Action
Cefadroxil is a cephalosporin which exhibits bactericidal activity. It inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins. The result is formation of a defective cell wall that is osmotically unstable, and bacterial cell lysis.

Microbiology
Cefadroxil has been shown to be active against the following organisms:
Commonly susceptible species: Gram-positive aerobes, Streptococci Group B, C and G, Streptococcus pyogenes, Gram-negative aerobes, Moraxella catarrhalis

Species for which acquired resistance may be a problem: Gram-positive aerobes, Staphylococcus aureus (methicillin-susceptible), Staphylococcus epidermidis, Streptococcus pneumoniae, Gram-negative aerobes, Citrobacter diversus, Escherichia coli, Haemophilus influenza, Klebsiella pneumoniae, Klebsiella oxytoca, Proteus mirabilis.

Inherently resistant species: Gram-positive aerobes, Enterococcus spp., Staphylococcus aureus (methicillin-resistant), Staphylococcus epidermidis (methicillin-resistant), Streptococcus pneumoniae (penicillin-resistant), Gram-negative aerobes, Acinetobacter spp., Citrobacter freundii, Enterobacter spp., Morganella morganii, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Pseudomonas aeruginosa, Serratia marcescens

Other species: Chlamydia spp, Mykoplasma spp, Legionella spp

It has no activity against *Pseudomonas* species and *Acinetobacter calcoaceticus* (formerly *Mima and Herellea species*).

PHARMACOKINETICS
Cefadroxil is completely absorbed from the gastrointestinal tract. After oral doses of 500 mg and 1 gram peak serum concentrations of about 16 and 30 micrograms per ml respectively occur after 1.5 to 2 hours. Although peak plasma concentration are similar to those of cefalexin, plasma concentration are more sustained. Dosage with food does not appear to affect the absorption of cefadroxil. About 20% of cefadroxil is reported to be bound to plasma proteins. The plasma half-life of cefadroxil is about 1.5 hours and is prolonged in patients with renal impairment. Cefadroxil is widely distributed to body tissues and fluids, it crosses the placenta and appears in breast milk. More than 90% of a dose of cefadroxil may be excreted unchanged in the urine within 24 hours by glomerular filtration and tubular secretion; peak urinary concentrations of 1.8 mg/ml have been reported after a dose of 500 mg. cefadroxil is removed by haemodialysis.

INDICATIONS AND USAGE
It is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:
- Streptococcal pharyngitis and tonsillitis
- Bronchopneumonia, bacterial pneumonia
- Uncomplicated urinary tract infections: pyelonephritis, cystitis
- Skin and soft tissue infections: abscesses, furunculosis, impetigo, erysipelas, pyoderma, lymphadenitis Mild to moderate susceptible Gram positive and Gram negative bacterial infections
- Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

DOSAGE AND ADMINISTRATION
The recommended dosage of Evacef (Cefadroxil) is;

Indication	Adults and adolescents > 40 kg with normal renal function	Children (< 40 kg) with normal renal function
Streptococcal pharyngitis / tonsillitis	Dosage may be decreased to 1000 mg once a day over at least 10 days	30 mg/kg/day once a day over at least 10 days
Bronchopneumonia, bacterial pneumonia	1000 mg twice a day	30-50 mg/kg/day divided into two daily doses
Urinary tract infections	1000 mg twice a day	30-50 mg/kg/day divided into two daily doses
Skin & soft tissue infections	1000 mg twice a day	30-50 mg/kg/day divided into two daily doses

Children may benefit of increased posology up to 100 mg/kg/day.

Depending on the severity of the infection, adults may require increased posology. The dosage maximum is 4 g per day. Chronic urinary tract infection may require a prolonged and intensive treatment with continued testing of susceptibility and clinical monitoring.

Cefadroxil 500 mg capsules is not recommended for infants and children under 6 years. For younger children and children with a body weight < 40 kg, liquid oral forms (Cefadroxil 250 mg/ 5 ml or 500 mg/ 5 ml suspension) are available.

Adults
Urinary Tract Infections: For uncomplicated lower urinary tract infections (i.e., cystitis) the usual dosage is 1 or 2 gram per day in a single or divided doses. For all other urinary tract infections the usual dosage is 2 gram per day in divided doses.

Skin and Skin Structure Infections: For skin and skin structure infections the usual dosage is 1 gram per day in single or divided doses.

Pharyngitis and Tonsillitis: Treatment of group A beta-haemolytic streptococcal pharyngitis and tonsillitis 1 gram per day in single or divided doses for 10 days.

Mild to moderate susceptible Gram positive and Gram negative bacterial infections: The usual dose is 1 to 2 gram daily as single dose or in two divided doses.

Children
For urinary tract infections, the recommended daily dosage for children is 30 mg/kg/day in divided doses every 12 hours. For pharyngitis, tonsillitis, and impetigo, the recommended daily dosage for children is 30 mg/kg/day in a single dose or in equally divided doses every 12 hours; for other skin and skin structure infections, the recommended daily dosage is 30 mg/kg/day in equally divided doses every 12 hours. In the treatment of beta-haemolytic streptococcal infections, a therapeutic dosage should be administered for at least 10 days. In the treatment of mild to moderate susceptible Gram positive and Gram negative bacterial infections: the usual daily dose in 30 mg/kg in 2 divided doses.

See chart for total daily dosage for children.

DAILY DOSAGE OF EVACEF SUSPENSION			
Child's Weight		**125mg / 5ml**	**250mg / 5ml**
10 lbs	4.5 kg	1 tsp	--
20 lbs	9.1 kg	2 tsp	1 tsp
30 lbs	13.6 kg	3 tsp	1 – 1 ½ tsp
40 lbs	18.2 kg	4 tsp	2 tsp
50 lbs	22.7 kg	5 tsp	2 – 2 ½ tsp
60 lbs	27.3 kg	6 tsp	3 tsp

Renal Impairment function:
In patients with renal impairment, the dosage of cefadroxil should be adjusted according to creatinine clearance rates to prevent drug accumulation. The following schedule is suggested. In adults, the initial dose is 1000 mg of cefadroxil and the maintenance dose (based on the creatinine clearance rate mL/min/1.73 M2) is 500 mg - 1000mg at the time intervals listed below:

Creatinine Clearances	Dosage Interval
00 – 10 mL/min	36 hours
10 – 25 mL/min	24 hours
25 – 50 mL/min	12 hours

Patients with creatinine clearance rates over 50 ml/min may be treated as if they were patients having normal renal function.

Children (< 40 kg) with renal impairment:
Cefadroxil is not indicated in children suffering from renal insufficiency and children requiring haemodialysis.
Dosage for haemodialysis patients:
Haemodialysis eliminates 63% of 1000 mg of cephalosporin after 6 to 8 hours of haemodialysis. Elimination half-time of cephalosporin is about 3 hours during dialysis.
Patients with haemodialysis receive one additional dose of 500 mg - 1000 mg at the end of the haemodialysis.
Hepatic impairment:
No adjustment of posology is necessary.
•□Elderly:
As cefadroxil is excreted by renal route, the dosage should be adjusted if necessary as described under□*impaired renal function*.
Cefadroxil is acid-stable and may be administered orally without regard to meals. Administration with food may be helpful in diminishing potential gastrointestinal complaints occasionally associated with oral cephalosporin therapy.

CONTRAINDICATIONS
It is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.
History of severe reactions to penicillins or to any other beta-lactam drugs.

DRUG INTERACTIONS
- Cefadroxil should not be combined with bacteriostatic antibiotics (e.g. tetracycline, erythromycin, sulfonamides, chloramphenicol) since an antagonistic effect is possible.
- Treatment with cefadroxil in combination with aminoglycoside antibiotics, polymyxin B, colistin or high-dose loop diuretics should be avoided since such combinations can potentiate nephrotoxic effects.
- Renal function should be carefully monitored, especially if higher dosages of the aminoglycosides are to be administered or if therapy is prolonged, because of additional potential nephrotoxicity and ototoxicity of aminoglycoside antibacterial drugs.
- In common with other antibacterial drugs, it may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral oestrogen/progesterone contraceptives.
- Frequent checks on coagulation parameters are necessary during concomitant long-term use of anticoagulants or thrombocyte aggregation inhibitors to avoid haemorrhagic complications.

ADVERSE REACTIONS
The following are the reported adverse events of Cefadroxil; onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment, glossitis, dyspepsia, nausea, vomiting, diarrhoea, allergies (in the form of rash, urticaria, angioedema, and pruritus), anaphylaxis, hepatic dysfunction including cholestasis, elevations in serum transaminase, genital pruritus, genital moniliasis, vaginitis, moderate transient neutropenia, fever, Agranulocytosis, thrombocytopenia, idiosyncratic hepatic failure, erythema multiforme, Stevens-Johnson syndrome, serum sickness, arthralgia, toxic epidermal necrolysis, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, aplastic anaemia, haemolytic anaemia, haemorrhage, prolonged prothrombin time, positive Coombs' test, increased BUN, increased creatinine, elevated alkaline phosphatase, elevated aspartate aminotransferase (AST), elevated alanine aminotransferase (ALT), elevated bilirubin, elevated LDH, eosinophilia, leukopenia, pancytopenia, neutropenia, seizures, growth of opportunistic organisms (fungi), such as vaginal mycoses, thrush, headache, sleeplessness, dizziness and nervousness.

WARNINGS AND PRECAUTIONS
- Before therapy with cefadroxil is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefadroxil, cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross-sensitivity among beta-lactam antibiotics has been clearly documented and may occur in patients with a history of penicillin allergy.
- If an allergic reaction to cefadroxil occurs, discontinue the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.
- Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefadroxil, and may range from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.
- Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. A toxin produced by Clostridium difficile is a primary cause of "antibiotic-associated colitis". After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug effective against Clostridium difficile.
- Cefadroxil should be used with caution in the presence of markedly impaired renal function (creatinine clearance rate of less than 50 mL/min/1.73 m^2). In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy.
- Prolonged use of cefadroxil may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.
- Cefadroxil should be prescribed with caution in individuals with history of gastrointestinal disease particularly colitis.
- Positive direct coombs' tests have been reported during treatment with the cephalosporin antibiotics.
- 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.
- Special caution should be exercised in patients with history of severe allergies or asthma.

PREGNANCY:
There are no adequate and well controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

LABOR AND DELIVERY
Cefadroxil has not been studied for use during labour and delivery. Treatment should only be given if clearly needed.

NURSING MOTHERS
Cefadroxil is present in low concentrations in breast milk; sensitization, diarrhoea or colonization of the infants' mucosa with fungi are possible. Caution should be exercised when cefadroxil is administered to a nursing mother.

PEDIATRIC USE
Please see dosage and administration section.

GERIATRIC USE
Cefadroxil is substantially excreted by the kidney, and dosage adjustment is indicated for patients with renal impairment. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Directions for Reconstitution
90 ml suspension
Shake the bottle to dislodge powder from inner surface. By using measuring cup (given inside) add freshly boiled and cooled water (30ml) into bottle and shake. Then again add freshly boiled and cooled water (30ml). Close the bottle with cap tightly and shake well to make suspension.

60 ml suspension
Shake the bottle to dislodge powder from inner surface. By using measuring cup (given inside) add freshly boiled and cooled water (20ml) into bottle and shake. Then again add freshly boiled and cooled water (20ml). Close the bottle with cap tightly and shake well to make suspension.

15 ml suspension (Physician Sample)
Shake the bottle to dislodge powder from inner surface. By using measuring cup (given inside) add freshly boiled and cooled water (5ml) into bottle and shake. Then again add freshly boiled and cooled water (5ml). Close the bottle with cap tightly and shake well to make suspension.

Reconstituted suspension should be used within 7 days when kept at room temperature and within 12 days when stored in refrigerator. Shake well before each use. Discard unused portion after 12 days.

OVER DOSAGE
Ingestion of less than 250mg/kg of cephalosporins is not associated with significant outcomes. No action is required other than general support and observation.
In view of other cephalosporins the following symptoms are possible: nausea, hallucinations, hyperreflexia, extrapyramidal symptoms, clouded consciousness, or even coma and renal functional impairment. First aid after intake of toxic doses: induce vomiting at once or gastric lavage, if necessary haemodialysis. Monitor and if necessary correct the water and electrolyte balance, monitor renal function.
For amounts greater than 250 mg/kg, induce gastric emptying.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION
Evacef 500mg Capsules: Alu. Alu. Blister pack of 2 x 6's.
Evacef 125mg/5mL Suspension: Pack of 60mL and 90ml bottle.
Evacef 250mg/5mL Suspension: Pack of 60mL and 90ml bottle.

ایواسیف™

(سیفاڈروکسل)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

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