For the use of only a Registered Medical Practitioner or a Hospital or a Laboratory

Not to be sold by retail without the prescription of a Registered Medical Practitioner

Prescribing Information

1. Generic Name

Cefadroxil Dispersible Tablets
(Brand Name: BLUDROX®-250 DT)

Cefadroxil Tablets IP
(Brand Name: BLUDROX® 500 Tablets)

2. Qualitative and Quantitative Composition

BLUDROX-250 DT

Each dispersible uncoated tablet contains:
Cefadroxil IP equivalent to Anhydrous Cefadroxil ……..… 250 mg.
Excipients …….. q.s.

BLUDROX 500 Tablets

Each uncoated tablet contains:
Cefadroxil IP equivalent to Anhydrous Cefadroxil ……..… 500 mg.
Excipients …….. q.s.

3. Dosage Form and Strength

Dosage Form: Tablets.
Dosage Strength: Cefadroxil 250 mg per dispersible tablets and cefadroxil 500 mg per tablet.

4. Clinical Particulars

4.1 Therapeutic Indication

BLUDROX-250 DT and BLUDROX 500 Tablets are indicated in the treatment of following infections when caused by susceptible bacteria:

- Streptococcal pharyngitis and tonsillitis.
- Bronchopneumonia, bacterial pneumonia.
- Uncomplicated urinary tract infections such as pyelonephritis and cystitis.
- Skin and soft tissue infections such as abscesses, furunculosis, impetigo, erysipelas, pyoderma, and lymphadenitis.

4.2Posology and Method of Administration

Adults and Adolescents Weighing >40 kg With Normal Renal Function: Usual recommended dosage of cefadroxil is 500 to 1000 mg twice daily.

Depending on the severity of the infection, adults may require increased dosage. The maximum recommended dosage of cefadroxil in adults is 4 gram per day.

Adults with Renal Impairment: In adult patients with creatinine clearance of 50 ml/min or less, the dosage should be adjusted according to creatinine clearance rates as follows to prevent accumulation of cefadroxil:

Table: Dosage in Adults with Renal Impairment

Creatinine Clearance	Initial Dose	Maintenance Dose	Dosage Interval
0 to l0 ml/min	1000 mg	500 mg	36 hours
10 to 25 ml/min	1000 mg	500 mg	24 hours
25 to 50 ml/min	1000 mg	500 mg	12 hours

Patients with creatinine clearance rates over 50 ml/min may be treated as patients having normal renal function. Renal function studies should be performed as and when indicated.

Children Weighing < 40 kg with Normal Renal Function: The recommended daily dosage is 30 to 50 mg/kg/day in equally divided doses every 12 hours.

Children Weighing < 40 kg with Renal Impairment: Cefadroxil is not indicated in children suffering from renal insufficiency and children requiring hemodialysis.

Duration of therapy is 5 to 10 days, depending on type and severity of infection. Cefadroxil is acid-stable and may be administered orally without regard to meals. Administration with food may be helpful in reducing potential gastrointestinal (GI) complaints occasionally associated with oral cephalosporin class of antibiotics. BLUDROX 500 Tablets should be swallowed whole with water.

Or, as prescribed by the physician.

Directions for Reconstitution of the BLUDROX-250 Dispersible Tablets

BLUDROX-250 Dispersible Tablets should be reconstituted by the addition of adequate amount of clean potable water (5 to 10 ml) immediately before use. Stir well until the tablet gets properly dispersed and then swallowed orally.

4.3Contraindications

BLUDROX-250 DT / BLUDROX 500 Tablets are contraindicated in the following:

- Hypersensitivity to cefadroxil or to any of the cephalosporins or to any component of the formulation.
- History of severe reactions to penicillins or to any other beta-lactam drugs.

4.4Special Warnings and Precautions for Use

Hypersensitivity: 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. Special caution should be exercised in patients with history of severe allergies or asthma. If cefadroxil 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 up to 10% of 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.

***Clostridium Difficile*-Associated Diarrhea (CDAD):** CDAD has been reported with use of nearly all antibacterial agents, including cefadroxil, and may range in severity from mild diarrhea to fatal colitis. The occurrence of diarrhea may impair the resorption of other drugs and therefore, lead to an impairment of their efficacy. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*. *Clostridium difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains 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 diarrhea 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.

History of GI Disorders: Cefadroxil should be used with caution in patients with a history of GI disturbances, particularly colitis.

Super-infection: Prolonged use of cefadroxil may result in the overgrowth of non-susceptible organisms (Candida spp.). Careful observation of the patient is essential. If super-infection occurs during therapy, appropriate measures should be taken.

Antibiotic Resistance: Prescribing cefadroxil in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. To reduce the development of drug-resistant bacteria and maintain the effectiveness of cefadroxil and other antibacterial drugs, cefadroxil should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available,

they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Interference with Diagnostic Tests: The result of the Coombs' test can be transiently positive during or after treatment with cefadroxil. This also applies to Coombs' tests carried out in newborns whose mothers received treatment with cephalosporins before delivery.

Interference with Urine Glucose Tests: Urinary glucose should be determined enzymatically (e.g., with test strips) during treatment with cefadroxil since reduction tests can furnish falsely elevated values.

4.5Drug Interactions

Concomitant Use Is Contraindicated

- 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.

Concomitant Use Is Not Recommended

- Frequent checks on coagulation parameters are necessary during concomitant long-term use of anticoagulants or thrombocyte aggregation inhibitors to avoid haemorrhagic complications.

Concomitant Use Should Be With Caution

- The concomitant administration of probenecid reduces the renal elimination of cefadroxil; therefore, plasma concentrations of cefadroxil may be increased when given in combination with probenecid.
- Cefadroxil binds to cholestyramine which may lead to reduced bioavailability of cefadroxil.

Drug/Laboratory Test Interactions

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

4.6Use in Special Populations

Pregnant Women

Pregnancy Category B. Reproduction studies have been performed in mice and rats at doses up to 11 times the human dose and has revealed no evidence of impaired fertility or harm to the fetus due to cefadroxil. No adequate and well-controlled studies in pregnant women are available. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

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

Paediatric Patients
For dosage in pediatric patients, please refer 'Posology and Method of Administration' section.

Geriatric Patients
Elderly patients with normal renal function may be given the same dose as recommended for adults. 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.

Renal Impairment Patients
Cefadroxil should be used with caution in patients with markedly impaired renal function (creatinine clearance < 50 ml/min). In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy. Cefadroxil dosage must be adjusted according to the grade of renal impairment; for dosage in such patients, please refer table from 'Posology and Method of Administration' section.

Hepatic Impairment Patients
As cefadroxil is not metabolized, no adjustment of dosage is necessary in patients with impaired hepatic function.

4.7Effect on Ability to Drive and Use Machines
Cefadroxil may cause headache, dizziness, nervousness, sleeplessness and fatigue, therefore the ability to drive and use machines may be influenced.

4.8Undesirable Effects
Gastrointestinal: Onset of pseudomembranous colitis-related symptoms may occur during or after cefadroxil treatment. Diarrhea, dyspepsia, nausea, and vomiting have been reported rarely.

Hypersensitivity: Allergies (in the form of rash, urticaria, angioedema, and pruritus) have been observed. These reactions usually subsided upon discontinuation of the drug. Anaphylaxis has also been reported.

Other: Other reactions have included hepatic dysfunction including cholestasis and elevations in serum transaminases, genital pruritus, genital moniliasis, vaginitis, moderate transient neutropenia, fever. Agranulocytosis, thrombocytopenia, idiosyncratic hepatic failure, erythema multiforme, Stevens-Johnson syndrome, serum sickness, and arthralgia have been rarely reported.

Adverse Reactions of Cephalosporin-Cass Antibiotics: Following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Toxic epidermal necrolysis, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, prolonged prothrombin time, positive Coombs' test, increased BUN, increased creatinine, elevated alkaline phosphatase, elevated aspartate aminotransferase (AST), elevated alanine aminotransferase (ALT), elevated bilirubin, elevated lactate dehydrogenase (LDH), eosinophilia, pancytopenia, neutropenia, fixed drug eruption (FDE).

4.9Overdose

No clinical reports are available on cefadroxil overdose. However in view of experience gained with other cephalosporins, the following symptoms are possible: Nausea, hallucinations, hyperreflexia, extrapyramidal symptoms, clouded consciousness, or even coma and renal functional impairment.

In the event of overdose, induce vomiting at once or gastric lavage, and if necessary, haemodialysis. If necessary, monitor and correct the water and electrolyte balance. Monitoring of renal function is also suggested. In 5 anuric patients, it was demonstrated that an average of 63% of a 1 gram oral dose is extracted from the body during a 6 to 8 hour hemodialysis session.

Overdose Data in Paediatric Population: A study of children under 6 years of age suggested that ingestion of less than 250 mg/kg of cephalosporins is not associated with significant outcomes. No action is required other than general support and observation. For amounts greater than 250 mg/kg, induce gastric emptying.

5. Pharmacological Properties

5.1 Mechanism of Action

Cefadroxil inhibits bacterial cell wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). The result is formation of a defective cell wall that is osmotically unstable, and bacterial cell lysis (bactericidal effect).

5.2Pharmacodynamic Properties

Cefadroxil is a semisynthetic first-generation cephalosporin class of beta-lactam antibiotic for oral administration. *In vitro* tests demonstrate that the cephalosporins are bactericidal because of their inhibition of cell-wall synthesis. Following is the antimicrobial spectrum of cefadroxil.

Commonly Susceptible Species

Gram-Positive Aerobes

- Streptococci Group B, C and G.
- *Streptococcus pyogenes*.

Gram-Negative Aerobes

- *Moraxella catarrhalis*.

Susceptible Species Which May Acquire Resistance

Gram-Positive Aerobes

- *Staphylococcus aureus* (methicillin-susceptible).
- *Staphylococcus epidermidis*.
- *Streptococcus pneumonia*.

Gram-Negative Aerobes

- *Citrobacter diversus*.
- *Escherichia coli*.
- *Haemophilus influenza*.
- *Klebsiella pneumonia*.
- *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.

5.3Pharmacokinetic Properties

Absorption: Cefadroxil is rapidly and completely absorbed after oral administration. Food does not have any impact on absorption (AUC) of cefadroxil. Following single doses of 500 mg and 1000 mg of cefadroxil, average peak serum concentrations were approximately 16 and 28 mcg/ml respectively, obtained after 1 to 1.3 hours after administration.
Distribution: Around 18 to 20% of cefadroxil is bound to plasma proteins.
Metabolism: Cefadroxil is not metabolised.
Excretion: Half-life of cefadroxil is about 1.4 to 2.6 hours. Over 90% of the drug is excreted unchanged in the urine within 24 hours. Increase in dosage generally produces a proportionate increase in cefadroxil urinary concentration. The urine antibiotic concentration, following a 1 gram dose was maintained well above the MIC of susceptible urinary pathogens for 20 to 22 hours.

6. Nonclinical Properties

6.1 Animal Toxicology

No long-term studies have been performed to determine carcinogenic potential. No genetic toxicity tests have been performed. Reproduction studies have been performed in mice and rats at doses up to 11 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefadroxil monohydrate.

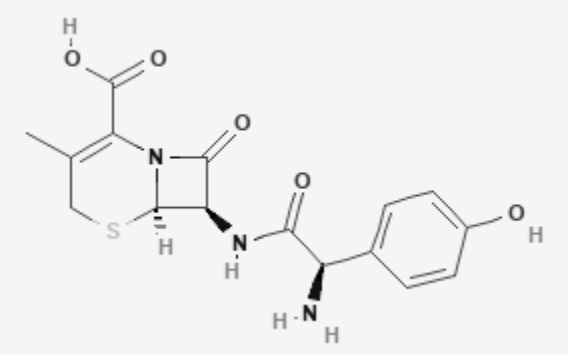
7. Description

BLUDROX-250 Dispersible Tablets are Off-white, circular, flat beveled uncoated tablet with breakline on one side and Δ engraved on other side and having strawberry flavour.

BLUDROX 500 Tablets are Off-white, circular, flat faced, beveled edged, uncoated tablet with breakline on one side and other side engraved with Δ.

BLUDROX-250 Dispersible Tablet contains 250 mg of cefadroxil for oral administration.
BLUDROX 500 Tablets contains 500 mg of cefadroxil for oral administration.

Cefadroxil is a semisynthetic cephalosporin class of antibiotic. It is a white to yellowish-white crystalline powder which is soluble in water.
Molecular Weight: 363.4 g/mol.
Molecular Formula: C16H17N3O5S.
Chemical Name: 6R,7R)-7-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.
Structural Formula:



Inactive ingredients (excipients) of BLUDROX-250 Dispersible Tablets contain Microcrystalline Cellulose, Flavour Capsorma Strawberrry, Saccharin Sodium, Colloidal Silicon Dioxide, Sodium Starch Glycollate, Magnesium Stearate & Talc.

Inactive ingredients (excipients) of BLUDROX 500 Tablets contain Microcrystalline Cellulose, Polyvinylpyrrolidone K -30, Sodium Starch Glycollate, Magnesium Stearate, Colloidal Silicon Dioxide & Talc.

8. Pharmaceutical Particulars

8.1 Incompatibilities

None known.

8.2Shelf-life

30 Months

8.3Packaging Information

10 tablets per strip.

8.4Storage and Handling Instructions

Store protected from light and moisture, at a temperature not exceeding 30°C.
Keep out of the reach of children.

9. Patient Counseling Information

Administration Instructions to Patients

- Patients should be counseled that antibacterial drugs should only be used to treat bacterial infections; not to use this medicine to treat infections caused by viruses (such as common cold).
- Patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may decrease the effectiveness of the treatment and increase the likelihood of developing antibiotic resistance.
- Inform patients that diarrhea is a common problem caused by antibacterial drugs which usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibacterials, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterial. If this occurs, patients should inform their physician as soon as possible.
- Pregnant women and lactating mothers should consult their doctor before use of this medicine.
- For BLUDROX-250 DT, remove the tablet from its original packing just before its use. Disperse the tablet in 5 to 10 ml of water and then swallow orally.

10. Details of Manufacturer

Blue Cross Laboratories Pvt. Ltd.
A – 12, MIDC, Ambad, Nashik – 422 010 .

11. Details of Permission or License Number with Date

BLUDROX -250 DT: Mfg. Lic. No. : BD/28. Date of FDA Product Permission: 20/05/2007
BLUDROX -500 Tablets:Mfg. Lic. No.:BD/28.Date of FDA Product Permission: 01/02/2009

12. Date of Revision

September 2022.