Bosch

For Medical Professional only

Prelox

(Cefpodoxime Proxetil)

Product Specs.: U.S.P.

Tablets / Suspension

پریلوکس ٹیبلیٹس / سسپینشن

(سیفپوڈوکسیم پروکسیٹل)

DESCRIPTION:

Cefpodoxime proxetil is an orally administered, extended spectrum, semi-synthetic antibiotic of the cephalosporin class. The chemical name is (RS)-1(isopropoxycarbonyloxy) ethyl(+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl)-2-{(Z)methoxyimino}acetamido]-3-methoxymethyl-8-oxo-5-thia- 1-azabicyclo [4.2.0]oct-2-ene-2-carboxylate. Its empirical formula is $C_{21}H_{27}N_5O_9S_2$. The molecular weight of cefpodoxime proxetil is 557.6.

COMPOSITION:

Prelox 100mg Tablets

Cefpodoxime.....100mg as Cefpodoxime Proxetil U.S.P.
(Product Specs.: U.S.P.)

Prelox DS 200mg Tablets

Each film coated tablet contains:
Cefpodoxime.....200mg as Cefpodoxime Proxetil U.S.P.
(Product Specs.: U.S.P.)

Prelox 40mg/5ml Suspension

Each 5ml of reconstituted suspension contains:
Cefpodoxime.....40mg as Cefpodoxime Proxetil U.S.P.
(Product Specs.: U.S.P.)

Prelox Plus 100mg/5ml Suspension

Each 5ml of reconstituted suspension contains:
Cefpodoxime.....100mg as Cefpodoxime Proxetil U.S.P.
(Product Specs.: U.S.P.)

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Third generation cephalosporins, ATC code: J01DD13
Cefpodoxime proxetil is a beta-lactam antibiotic, a third generation oral cephalosporin. It is the prodrug of cefpodoxime.

Microbiology

Mechanism of action

Cefpodoxime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefpodoxime has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Mechanism of Resistance:

Resistance to Cefpodoxime is primarily through hydrolysis by beta-lactamase, alteration of penicillin-binding proteins (PBPs), and decreased permeability. Cefpodoxime has been shown to be active against most isolates of the following bacteria,

Antibacterial Spectrum

Commonly Susceptible Species
Aerobic Gram Positive Organisms:
Staphylococcus aureus (Methicillin susceptible)
Streptococcus pyogenes
Aerobic Gram Negative Organisms:
Haemophilus influenzae
Moraxella catarrhalis
Proteus mirabilis+
Species for which Acquired Resistance may be a Problem
Aerobic Gram Positive Organisms
Streptococcus pneumoniae
Aerobic Gram Negative Organism
Citrobacter freundi*
Enterobacter cloacae*
Escherichia coli+
Klebsiella pneumoniae+
Serratia marcescens*
Inherently Resistant Organisms
Aerobic Gram Negative Organisms
Morganella morganii
Pseudomonas aeruginosa.
Aerobic Gram Positive Organisms
Staphylococcus aureus (methicillin resistant)
Enterococcus spp.

Others
Chlamydia spp.
Chlamydophila spp.
Legionella pneumophila
Mycoplasma spp.

Pharmacokinetics:
Absorption
Cefpodoxime proxetil is taken up in the intestine and is hydrolysed to the active metabolite cefpodoxime. When cefpodoxime proxetil is administered orally to fasting subjects as a tablet corresponding to 100 mg of cefpodoxime, 51.1% is absorbed and absorption is increased by food intake.

Distribution
The volume of distribution is 32.3 l and peak levels of cefpodoxime occur 2 to 3 hours after dosing. The maximum plasma concentration is 1.2 mg/L and 2.5 mg/L after doses of 100 mg and 200 mg respectively. Following administration of 100 mg and 200 mg twice daily over 14.5 days, the plasma pharmacokinetic parameters of cefpodoxime remain unchanged.

Serum protein binding of cefpodoxime, 40% principally to albumin. This binding is non-saturable in type. Concentrations of cefpodoxime in excess of the minimum inhibitory levels (MIC) for common pathogens can be achieved in lung parenchyma, bronchial mucosa, pleural fluid, tonsils, interstitial fluid and prostate tissue.

As the majority of cefpodoxime is eliminated in the urine, the concentration is high. Good diffusion of cefpodoxime is also seen into renal tissue, with concentrations above MIC90 of the common urinary pathogens, 3-12 hours after an administration of a single 200 mg dose (1.6 – 3.1 µG/G). Concentrations of cefpodoxime in the medullary and cortical tissues is similar.

Metabolism
Cefpodoxime proxetil is a prodrug of cefpodoxime. Essentially the entire drug that is absorbed is desterified, pre-systemically in the small intestine to its active form. Cefpodoxime itself does not undergo any significant metabolism and is excreted unchanged, largely in the urine.

Elimination
The main route of excretion is renal, 80% is excreted unchanged in the urine with an elimination half-life of approximately 2.4 hours.

Special Population
Renal Impairment
Elimination of cefpodoxime is reduced in patients with moderate to severe renal impairment (<50 mL/min creatinine clearance). In subjects with mild impairment of renal function (50 to 80 mL/min creatinine clearance), the average plasma half-life of cefpodoxime was 3.5 hours. In subjects with moderate (30 to 49 mL/min creatinine clearance) or severe renal impairment (5 to 29 mL/min creatinine clearance), the half-life increased to 5.9 and 9.8 hours, respectively. Approximately 23% of the administered dose was cleared from the body during a standard 3-hour hemodialysis procedure.

Hepatic Impairment
Absorption was somewhat diminished and elimination unchanged in patients with cirrhosis. The mean cefpodoxime T1/2 and renal clearance in cirrhotic patients were similar to those derived in studies of healthy subjects. Ascites did not appear to affect values in cirrhotic subjects. No dosage adjustment is recommended in this patient population.

Geriatrics
Elderly subjects do not require dosage adjustments unless they have diminished renal function.

THERAPEUTIC INDICATIONS
Cefpodoxime proxetil is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

Acute otitis media caused by Streptococcus pneumoniae (excluding penicillin-resistant strains), Streptococcus pyogenes, Haemophilus influenzae (including beta-lactamase-producing strains), or Moraxella (Branhamella) catarrhalis (including beta-lactamase-producing strains)

Pharyngitis and/or tonsillitis caused by Streptococcus pyogenes.

Community-acquired pneumonia caused by S. pneumoniae or H. influenzae (including beta-lactamase-producing strains).

Acute bacterial exacerbation of chronic bronchitis caused by S.pneumoniae, H. influenzae (non-beta-lactamase-producing strains only), or M. catarrhalis. Data are insufficient at this time to establish efficacy in patients with acute bacterial exacerbations of chronic bronchitis caused by beta-lactamase-producing strains of H. influenzae.

Acute, uncomplicated urethral and cervical gonorrhea caused by Neisseria gonorrhoeae (including penicillinase-producing strains).

Acute, uncomplicated anorectal infections in women due to Neisseria gonorrhoeae (including penicillinase-producing strains).

Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (including penicillinase-producing strains) or Streptococcus pyogenes. Abscesses should be surgically drained as clinically indicated.

Acute maxillary sinusitis caused by Haemophilus influenzae (including beta-lactamase-producing strains), Streptococcus pneumoniae, and Moraxella catarrhalis.

Uncomplicated urinary tract infections (cystitis) caused by Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, or Staphylococcus saprophyticus

DOSAGE AND ADMINISTRATION:
Film coated tablets:
Prelox tablets should be administered orally with food to enhance absorption.
The recommended dosages, durations of treatment, and applicable patient population are as described in the following chart:

Adults and Adolescents (age 12 years and older)

Type of Infection	Total Daily Dose	Dose Frequency
Pharyngitis and/or tonsillitis	200mg	100mg every 12 hours
Acute community-acquired pneumonia	400mg	200mg every 12 hours
Acute bacterial exacerbations of chronic bronchitis	400mg	200mg every 12 hours
Uncomplicated gonorrhea (men and women) and rectal gonococcal infections (women)	200mg	Single dose
Skin and skin structure	800mg	400mg every 12 hours
Acute maxillary sinusitis	400mg	200mg every 12 hours
Uncomplicated urinary tract infection	200mg	100mg every 12 hours

Oral Suspension:
Prelox oral Suspension may be given without regard to food. The recommended dosages, durations of treatment, and applicable patient populations are as described in the following chart:

Adults and Adolescents (age 12 years and older):

Type of Infection	Total Daily Dose	Dose Frequency
Pharyngitis and/or tonsillitis	200mg	100 mg every 12 hours
Acute community-acquired pneumonia	400mg	200 mg every 12 hours
Uncomplicated gonorrhea (men and women) and rectal gonococcal infections (women)	200mg	Single Dose
Skin and skin structure	800mg	400 mg every 12 hours
Acute maxillary sinusitis	400mg	200 mg every 12 hours
Uncomplicated urinary tract infection	200 mg	100 mg every 12 hours

Infants and Pediatric Patients (age 2 months through 12 years):

Type of Infection	Total Daily Dose	Dose Frequency
Acute otitis media	10 mg/kg/day (Max 400 mg/day)	5 mg/kg every 12 h (Max 200 mg/dose)
Pharyngitis and/or tonsillitis	10 mg/kg/day (Max 200 mg/day)	5 mg/kg every 12 h (Max 100 mg/dose)
Acute maxillary sinusitis	10 mg/kg/day (Max 400 mg/day)	5 mg/kg every 12 h (Max 200 mg/dose)

CONTRAINDICATIONS:
- Cefpodoxime proxetil is contraindicated in patients with a known allergy to cefpodoxime or to the cephalosporin group of antibiotics or to any of the excipients.
- It is also contraindicated in patients with previous history of immediate and / or severe hypersensitivity reaction (anaphylaxis) to penicillin or other betalactam antibiotic.

Patients with Renal Dysfunction
When creatinine clearance is less than 40mL/min/1.73m2, the interval between 2 doses should be as follows:
Creatinine clearance 10 – 39mL/min/1.73m2 = 1 single dose every 24 hours Creatinine clearance <10mL/min/1.73m2 = 1 single dose every 48 hours

ADVERSE REACTIONS
Common:
Stomach upset, nausea, vomiting, loss of appetite, bloating or diarrhoea. Bloody diarrhoea may occur as a symptom of enterocolitis, Allergic reactions have been observed, mostly in the form of skin lesions with or without itching (erythema, rash, urticaria, purpura).

Uncommon:
Haemolytic anaemia, Headache, tinnitus, paresthesias and dizziness were observed. Asthenia, fatigue and discomfort (malaise).

Rare:
If severe or persistent diarrhoea during or after therapy thought to be Pseudomembranous enterocolitis (rare in children), diagnosis should be confirmed. In these rare cases, cephalosporins should be discontinued immediately and appropriate therapy initiated. Peristalsis agents are contraindicated

Very Rare:
In some cases, blood disorders (thrombocytosis, thrombocytopenia, leukopenia, neutropenia, agranulocytosis, eosinophilia, decreased haemoglobin values) were observed. These very rare changes are reversible upon discontinuation of therapy, acute pancreatitis, acute renal failure,Individual cases of bullous skin reactions (erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome) have been reported. The mediciation should be discontinued if such symptoms occur. Hypersensitivity reactions of any severity (e.g. angioedema, bronchospasm to life threatening shock) have been observed. Severe acute hypersensitivity reactions may require appropriate emergency measures.

WARNINGS AND PRECAUTIONS
Cefpodoxime is not a preferred antibiotic for the treatment of staphylococcal pneumonia and should not be used in the treatment of atypical pneumonia caused by organisms such as Legionella, Mycoplasma and Chlamydia. Cefpodoxime is not recommended for the treatment of pneumonia due to S. pneumoniae.

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefpodoxime must be discontinued immediately and adequate

emergency measures must be initiated.

Before therapy with cefpodoxime proxetil is instituted, a detailed inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefpodoxime, other cephalosporins, penicillins, or other drugs. If cefpodoxime is to be administered 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. As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with cefpodoxime must be discontinued immediately and adequate emergency measures must be initiated. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamine, and airway management, as clinically indicated. Caution should be used if cefpodoxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents.
C. 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.
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefpodoxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of cefpodoxime proxetil.
Cefpodoxime should always be prescribed with caution in patients with a history of gastrointestinal disease, particularly colitis.
As with all beta-lactam antibiotics, neutropenia and more rarely agranulocytosis may develop particularly during extended treatment. For cases of treatment lasting longer than 10 days, the blood count should be monitored and treatment discontinued if neutropenia is found.
In cases of severe renal insufficiency it may be necessary to reduce the dosage regimen dependent on the creatinine clearance.
As with other antibiotics, prolonged use of cefpodoxime may result in the overgrowth of non-susceptible organisms (candida and Clostridium difficile), which may require interruption of treatment. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

DRUG INTERACTIONS:
Antacids: Concomitant administration of high doses of antacids (sodium bicarbonate and aluminum hydroxide) or H2 blockers reduces peak plasma levels by 24% to 42% and the extent of absorption by 27% to 32%, respectively. The rate of absorption is not altered by these concomitant medications. Oral anti-cholinergics (e.g., propantheline) delay peak plasma levels (47% increase in Tmax), but do not affect the extent of absorption (AUC)
Probenecid: As with other beta-lactam antibiotics, renal excretion of cefpodoxime was inhibited by probenecid and resulted in an approximately 31% increase in AUC and 20% increase in peak cefpodoxime plasma levels
Nephrotoxic drugs: Although nephrotoxicity has not been noted when cefpodoxime proxetil was given alone, close monitoring of renal function is advised when cefpodoxime proxetil is administered concomitantly with compounds of known nephrotoxic potential
Oral Anticoagulants: Simultaneous administration of cefpodoxime with warfarin may augment its anticoagulant effects. There have been many reports of increases in oral anticoagulant activity in patients receiving antibacterial agents, including cephalosporins. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of the cephalosporins to the increase in INR (international normalised ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after coadministration of cefpodoxime with an oral anticoagulant agent.
Cephalosporins potentially enhance the anticoagulant effect of coumarins and reduce the contraceptive effect of oestrogens.

Laboratory Test Interactions:
A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Cephalosporins, including cefpodoxime proxetil, are known to occasionally induce a positive direct Coombs' test

Pregnancy
Pregnancy Category B:
There are no adequate and well-controlled studies of cefpodoxime proxetil use in pregnant women. Cefpodoxime proxetil should be used during pregnancy only if clearly needed.

Lactation:
Cefpodoxime is excreted in breast milk in small amounts. Breastfeeding should be stopped during treatment with cefpodoxime.

Paediatric Use:
Safety and efficacy in infants less than 2 months of age have not been established

Geriatric Use:
Dose adjustment in elderly patients with normal renal function is not necessary

OVERDOSAGE:
In the event of serious toxic reaction from overdosage, hemodialysis

or peritoneal dialysis may aid in the removal of cefpodoxime from the body, particularly if renal function is compromised. The toxic symptoms following an overdose of beta-lactam antibiotics may include nausea, vomiting, epigastric distress, and diarrhea. In cases of overdosage, particularly in patients with renal insufficiency, encephalopathy may occur. The encephalopathy is usually reversible once cefpodoxime plasma levels have fallen.

DIRECTION FOR RECONSTITUTION:
For the reconstitution of 50ml suspension, add 20ml Biostatic water as diluent , close the cap and Shake well. Then add remaining diluent in the bottle shake well to form uniform suspension.
50ml reconstituted suspension available after adding 45ml biostatic water. The reconstituted suspension should be kept in refrigerator and use within 10 days.

PRESENTATION:
Prelox 100mg tablets: Cold form & cold seal in pack of 10's
Prelox DS 200mg tablets: Cold form & cold seal in pack of 10's
Prelox 40mg/5ml (50ml) suspension in 90ml Amber glass bottle with 45ml Biostatic water as a diluent.
Prelox Plus 100mg/5ml (50ml) suspension in 90ml Amber glass bottle with 36ml Biostatic water as a diluent.

DIRECTION
Keep out of reach of children.
Protect from light and moisture, Store below 30ºC.
Shake well before use.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
For Oral use only.
For Suspension,After use close the cap tightly.
To be sold on prescription of a registered medical practitioner only.

ہدایات :

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan

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FIRST & ONLY CERTIFIED HALAAL

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PHARMACEUTICAL COMPANY