Cefodox®

Cefpodoxime (Proxetil)

Composition
Cefodox® 100mg Tablet: Each tablet contains Cefpodoxime proxetil equivalent to 100 mg Cefpodoxime.
Cefodox® 200mg Tablet: Each tablet contains Cefpodoxime proxetil equivalent to 200 mg Cefpodoxime.
Cefodox® 50mg Dry Suspension: Each 5 ml contains Cefpodoxime proxetil equivalent to 50 mg Cefpodoxime.
Cefodox®100mg Dry Suspension: Each 5 ml contains Cefpodoxime proxetil equivalent to 100 mg Cefpodoxime.
Cefodox®40mg Dry Suspension: Each 5 ml contains Cefpodoxime proxetil equivalent to 40 mg Cefpodoxime.

Pharmacological properties
Cefodox ® (Cefpodoxime proxetil) is an orally active, broad spectrum; semisynthetic third generation cephalosporin.
Cefpodoxime proxetil is a prodrug that undergoes de-esterification to the active metabolite Cefpodoxime. Cefpodoxime proxetil is rapidly absorbed after oral administration reaching peak plasma conentration within 2-3 hours. It is widely distributed to most body tissues reaching a concentration higher than MIC_{90} of S. pyogenes in tonsil tissues for more than 7 hours & a higher conentration than MIC_{90} of Streptococcus pneumoniae & H. influenzae in lung tissues for more than 12 hours. Cefpodoxime proxetil undergoes minimal metabolism & almost 33% of the dose is excreted unchanged renally.
Cefpodoxime proxetil inhibits bacterial cell wall synthesis & exerts a bactericidal activity against a wide range of gram positive & gram negative bacteria with a high stability in the presence of beta lactamase enzymes. It is usually active against the following organisms in vitro & in clinical infections:
G +ve Aerobes
- Streptococcus pneumoniae.
- Streptococcus pyogenes.
- Staphylococcus aureus (including β lactamase producing strains).
- Staphylococcus saprophyticus.

G -ve Aerobes
- Escherichia coli.
- Haemophilus influenzae (including β lactamase producing strains).
- Klebsiella pneumoniae.
- Moraxella (Branhamella)catarrhalis (including β lactamase producing strains).
- Neisseria gonorrhea.
- Proteus mirabilis.

G +ve Anaerobes
- Peptostreptococcus magnus.

Indications
- Upper respiratory tract infections including pharyngitis, tonsillitis, otitis media and sinusitis.
- Lower respiratory tract infections including acute exacerbation of chronic bronchitis & community acquired pneumonia.
- Skin & soft tissue infections.
- Urinary tract infections.
- Acute uncomplicated urethral, cervical & anorectal gonorrhea.

Dosage & Administration
- **Cefodox ®** tablet should be taken with food to enhance the absorption due to the effect of food in increasing the bioavailability of Cefpodoxime proxetil & as this effect is limited to the tablet dosage form only, **Cefodox ®** suspension can be given without regard to food.

Type of Infection	Total Daily Dose	Dose Frequency	Duration of treatment
Adult 13 years & older			
Tonsillitis/Pharyngitis	200mg	100mg q 12 hours	5-10 days
Bronchitis & AECB	400mg	200mg q 12 hours	10 days
Acute community acquired Pneumonia	400mg	200mg q 12 hours	14 days
Skin & soft tissue infections	800mg	400mg q 12 hours	7-14 days
Uncomplicated urinary tract infections	200mg	100mg q 12 hours	7 days
Sinusitis	400 mg	200 mg q 12 hours	10 days
Uncomplicated gonorrhea	200mg	Single dose	
Children (2months to 12 years)			
Tonsillitis/Pharyngitis	10mg/kg/day (Max 200mg/day)	5mg/kg /dose q 12 h (Max 100mg/dose)	5-10 days
Otitis media	10mg/kg/day (Max 400mg/day)	10mg/kg q 24 h (Max 400mg/dose) 5mg/kg q 12 h (Max 200mg/dose)	5 days
Sinusitis	10mg/kg/day (Max 400mg/day)	5mg/kg q 12 h (Max 200mg/dose)	10 days

- Use in Pediatrics
Safety & efficacy in infants less than 2 months of age have not been established.
Use in Geriatric
No need to adjust the dose in elderly patients as no overall differences in effectiveness or safety were observed between elderly & younger patients.
Patients with Renal Dysfunction
Dosing intervals should be increased to be every 24 hours in patients with severe renal impairment (<30 ml/min creatinine clearance).
Patients with Cirrhosis
No need to adjust the dose in cirrhotic patients with or without ascites as the pharmacokinetic of Cefpodoxime proxetil is not affected.
Contraindications
Cefpodoxime proxetil is contraindicated in patients with known allergy to Cefpodoxime proxetil or to the cephalosporin group of antibiotics.

Side effects
Clinical Trials:
Film-coated Tablets (Multiple dose):
In clinical trials using multiple doses of Cefpodoxime proxetil film-coated tablets, 4696 patients were treated with the recommended dosages of Cefpodoxime (100 to 400 mg Q 12 hours). There were no deaths or permanent disabilities thought related to drug toxicity.
One-hundred twenty-nine (2.7%) patients discontinued medication due to adverse events thought possibly or probably related to drug toxicity. Ninety-three (52%) of the 178 patients who discontinued therapy (whether thought related to drug therapy or not) did so because of gastrointestinal disturbances, nausea, vomiting, or diarrhea. The percentage of Cefpodoxime proxetil-treated patients who discontinued study drug because of adverse events was significantly greater at a dose of 800 mg daily than at a dose of 400 mg daily or at a dose of 200 mg daily. Adverse events thought possibly or probably related to Cefpodoxime in multiple-dose clinical trials (N=4696 Cefpodoxime-treated patients) were:
Incidence Greater Than 1%:
Diarrhea 7.0%
Diarrhea or loose stools were dose-related: decreasing from 10.4% of patients receiving 800 mg per day to 5.7% for those receiving 200 mg per day. Of patients with diarrhea, 10% had C. difficile organism or toxin in the stool.
Nausea 3.3%
Vaginal Fungal Infections 1.0%
Vulvovaginal Infections 1.3%
Abdominal Pain 1.2%
Headache 1.0%

Incidence Less Than 1%: By body system in decreasing order:
Clinical Studies
Adverse events thought possibly or probably related to cefpodoxime proxetil that occurred in less than 1% of patients (N=4696)
Body - fungal infections, abdominal distention, malaise, fatigue, asthenia, fever, chest pain, back pain, chills, generalized pain, abnormal microbiological tests, moniliasis, abscess, allergic reaction, facial edema, bacterial infections, parasitic infections, localized edema, localized pain.
Cardiovascular - congestive heart failure, migraine, palpitations, vasodilation, hematoma, hypertension, hypotension.
Digestive - vomiting, dyspepsia, dry mouth, flatulence, decreased appetite, constipation, oral moniliasis, anorexia, eructation, gastritis, mouth ulcers, gastrointestinal disorders, rectal disorders, tongue disorders, tooth disorders, increased thirst, oral lesions, tenesmus, dry throat, toothache.
Hemic and Lymphatic - anemia.
Metabolic and Nutritional - dehydration, gout, peripheral edema, weight increase.
Musculo-skeletal - myalgia.
Nervous - dizziness, insomnia, somnolence, anxiety, shakiness, nervousness, cerebral infarction, change in dreams, impaired concentration, confusion, nightmares, paresthesia, vertigo.
Respiratory - asthma, cough, epistaxis, rhinitis, wheezing, bronchitis, dyspnea, pleural effusion, pneumonia, sinusitis.
Skin - urticaria, rash, pruritus non-application site, diaphoresis, maculopapular rash, fungal dermatitis, desquamation, dry skin non-application site, hair loss, vesiculobullous rash, sunburn.
Special Senses - taste alterations, eye irritation, taste loss, tinnitus.
Urogenital - hematuria, urinary tract infections, metrorrhagia, dysuria, urinary frequency, nocturia, penile infection, proteinuria, vaginal pain.
Granules for Oral Suspension (Multiple dose):
In clinical trials using multiple doses of cefpodoxime proxetil granules for oral suspension, 2128 pediatric patients (93% of whom were less than 12 years of age) were treated with the recommended dosages of cefpodoxime (10 mg/kg/day Q 24 hours or divided Q 12 hours to a maximum equivalent adult dose). There were no deaths or permanent disabilities in any of the patients in these studies. Twenty-four patients (1.1%) discontinued medication due to adverse events thought possibly or probably related to study drug. Primarily, these discontinuations were for gastrointestinal disturbances, usually diarrhea, vomiting, or rashes.

Adverse events thought possibly or probably related, or of unknown relationship to cefpodoxime proxetil for oral suspension in multiple-dose clinical trials (N=2128 patients treated with cefpodoxime) were:

Incidence Greater Than 1%:
Diarrhea 6.0%
The incidence of diarrhea in infants and toddlers (age 1 month to 2 years) was 12.8%.
Diaper rash/Fungal skin rash 2.0% (includes moniliasis)
The incidence of diaper rash in infants and toddlers was 8.5%.
Other skin rashes 1.8%
Vomiting 2.3%
Incidence Less Than 1%:
Body: Localized abdominal pain, abdominal cramp, headache, monilia, generalized abdominal pain, asthenia, fever, fungal infection.
Digestive: Nausea, monilia, anorexia, dry mouth, stomatitis, pseudomembranous colitis.
Hemic & Lymphatic: Thrombocythemia, positive direct Coombs' test, eosinophilia, leukocytosis, leukopenia, prolonged partial thromboplastin time, thrombocytopenic purpura.
Metabolic & Nutritional: Increased SGPT.
Muscolo-Skeletal: Myalgia.
Nervous: Hallucination, hyperkinesia, nervousness, somnolence.
Respiratory: Epistaxis, rhinitis.
Skin: Skin moniliasis, urticaria, fungal dermatitis, acne, exfoliative dermatitis, maculopapular rash.
Special Senses: Taste perversion.
Film-coated Tablets (Single dose):
In clinical trials using a single dose of cefpodoxime proxetil film-coated tablets, 509 patients were treated with the recommended dosage of cefpodoxime (200 mg). There were no deaths or permanent disabilities thought related to drug toxicity in these studies.
Adverse events thought possibly or probably related to cefpodoxime in single-dose clinical trials conducted in the United States were:
Incidence Greater Than 1%:
Nausea 1.4%
Diarrhea 1.2%
Incidence Less Than 1%:
Central Nervous System: Dizziness, headache, syncope.
Dermatologic: Rash.
Genital: Vaginitis.
Gastrointestinal: Abdominal pain.
Psychiatric: Anxiety.

Laboratory Changes:
Significant laboratory changes that have been reported in adult and pediatric patients in clinical trials of cefpodoxime proxetil, without regard to drug relationship, were:
Hepatic: Transient increases in AST (SGOT), ALT (SGPT), GGT, alkaline phosphatase, bilirubin, and LDH.
Hematologic: Eosinophilia, leukocytosis, lymphocytosis, granulocytosis, basophilia, monocytosis, thrombocytosis, decreased hemoglobin, decreased hematocrit, leukopenia, neutropenia, lymphocytopenia, thrombocytopenia, thrombocythemia, positive Coombs' test, and prolonged PT, and PTT.
Serum Chemistry: Hyperglycemia, hypoglycemia, hypoalbuminemia, hypoproteinemia, hyperkalemia, and hyponatremia.
Renal: Increases in BUN and creatinine.
Most of these abnormalities were transient and not clinically significant.

Post-marketing Experience:
The following serious adverse experiences have been reported: allergic reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme and serum sickness-like reactions, pseudomembranous colitis, bloody diarrhea with abdominal pain, ulcerative colitis, rectorrhagia with hypotension, anaphylactic shock, acute liver injury, in utero exposure with miscarriage, purpuric nephritis, pulmonary infiltrate with eosinophilia, and eyelid dermatitis.
One death was attributed to pseudomembranous colitis and disseminated intravascular coagulation.

Cephalosporin Class Labeling:
In addition to the adverse reactions listed above which have been observed in patients treated with Cefpodoxime proxetil, the following adverse reactions and altered laboratory tests have been reported for cephalosporin class antibiotics:
Adverse Reactions and Abnormal Laboratory Tests: Renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, serum sickness-like reaction, hemorrhage, agranulocytosis, and pancytopenia.
Several cephalosporin's 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.

Warnings and precaution
- If Cefpodoxime is to administered to penicillin sensitive patients, caution should be exercised because cross hypersensitivity
Among beta-lactam antibiotics may occur in up to 10 % of patients with a history of penicillin allergy
- Clostridium difficile associated diarrhea has been reported with use of nearly all antibacterial agents and may range in severity from mild diarrhea to fetal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading overgrowth of clostridium difficile.

- Like other cephalosporin's, Cefpodoxime proxetil should be administered with caution to patients receiving concurrent treatment with potent diuretic.
- As with other antibiotics, prolonged administration of Cefpodoxime proxetil may result in overgrowth of non-susceptible microorganisms. If super infection occurs during therapy, appropriate measures should be taken.
- The total daily dose of Cefpodoxime proxetil should be reduced in patients with transient or persistent renal insufficiency because of high and prolonged serum Cefpodoxime concentration, which can occur in such individuals.
- Like other cephalosporin's, Cefpodoxime is known to induce a positive direct coombs test, and transient changes in hepatic and hematologic laboratory results which are not clinically significant.

Drug interactions
- Concomitant administration with high doses of antacids or H_2 blockers reduces peak plasma concentration by 24% to 42% & the extent of absorption by 27% to 32% but has no effect on the rate of absorption.

- As with other ß-lactam antibiotic, renal excretion of Cefpodoxime is inhibited by probenecid resulting in 20% increase in peak plasma levels & 31% in AUC.

- Close monitoring of renal function is advised when Cefpodoxime proxetil is administered concomitantly with compounds of known nephrotoxic drugs.

Overdosage
In the event of serious toxic reaction from Cefpodoxime proxetil overdosage, hemodialysis or peritoneal dialysis are indicated particularly if renal function is compromised.

Use in Pregnancy & lactation
- Pregnancy category B
No evidence of teratogenic effect is seen in animals at a dose up to 100mg/kg/day, however no adequate well controlled studies in pregnant women are available, thus Cefpodoxime proxetil should be used during pregnancy only if clearly needed.

- Nursing Mothers
Cefpodoxime proxetil, can be used by lactating women only if clearly needed according to physicians assessment to the importance of the drug to the nursing mother.

Presentations
Cefodox® 100mg Tablet: 10 tablets per pack.
Cefodox® 200mg Tablet: 10 tablets per pack.
Cefodox® 40mg Dry Suspension: 100 ml bottle.
Cefodox® 50mg Dry Suspension: 50 ml bottle.
Cefodox® 100mg Dry Suspension: 50 ml bottle, 100 ml bottle.

Marketing Authorization Holder and Manufacturer
Pharma International Company
Amman - Jordan
Tel: 00962-6-5158890 / 5157893
Fax: 00962-6-5154753
Email: marketing@pic-jo.com

(This is a medicament - keep medicaments out of reach of children)

Pharma International

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, method for use and the instructions of the pharmacist who sold the medicament .
- The doctor and the pharmacist are experts in medicine, its benefits and risks .
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Rev.Date Apr 2016 *I 021 04*