Rx

CEFUROXIME

DANOXIME

1.5 g Powder for Injection
(I.M. / I.V.)
ANTIBACTERIAL

FORMULATIONS:
Each vial contains:
Cefuroxime (as sodium) ..... 1.5 g

PRODUCT DESCRIPTION:
Danoxime (Cefuroxime sodium) 1.5 g Powder for Injection is available as off-white to pale yellow crystalline odorless powder, filled in clear glass vial sealed with rubber stopper and flip-off cap

INDICATIONS:
Cefuroxime sodium is a prodrug of the bactericidal cephalosphorin antibiotic cefuroxime, which is resistant to most beta-lactamases and is against a wide range of Gram-positive and Gram-negative organism. It is indicated for the treatment of infections caused by sensitive bacteria. Other indications include:

- Upper respiratory tract infections: for example: ear, nose, and throat infections (such as otitis media, sinusitis, tonsillitis and pharyngitis).
- Lower respiratory tract infections: for example: pneumonia, acute bronchitis and acute exacerbations of chronic bronchitis.
- Genito-urinary tract infections: for example: pyelonephritis, cystitis and urethritis. Gonorrhea, acute uncomplicated gonococcal urethritis and cervicitis.
- Skin and soft tissues infections: for example: furunculosis, pyoderma and impetigo.
- Treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years old.

Bacteriology
Cefuroxime sodium owes its *in vivo* bactericidal activity to the parent compound Cefuroxime. Cefuroxime sodium is well characterized and effective antibacterial agent which has bactericidal activity against a wide range of common pathogens, including β-lactamase producing strains. Cefuroxime sodium has good stability to bacterial β-lactamase and consequently is active against many ampicillin-resistant or amoxicillin-resistant strains. The bactericidal action of Cefuroxime sodium results from inhibition of cell wall synthesis by binding to essential target proteins.
Cefuroxime sodium is usually active on the following organisms *in vitro*:
Gram-negative Aerobes:
Haemophilus influenzae (including ampicillin-resistant strains); *Haemophilus parainfluenzae*; *Moraxella (Branhamella) catarrhalis*; *Neisseria gonorrhoeae* (including penicillinase and non-penicillinase producing strains); *Escherichia coli*; *Klebsiella* spp.; *Proteus mirabilis*; *Providencia* spp.; *Proteus rettgeri*;
Gram-positive Aerobes:
Staphylococcus aureus and *Staphylococcus epidermidis* (including penicillinase producing strains but excluding methicillin resistant strains).
Streptococcus pyogenes (and other beta-haemolytic streptococci).
Streptococcus pnuemoniae Group B (*Streptococcus* agalatiae)
Anaerobes:
Gram-positive and Gram-negative cocci (including *Peptococcus* and *Pepto-streptococcus* spp.)
Gram-positive bacilli (including *Clostridium* spp.)
Gram-negative bacilli (*Propionibacterium* spp.)
Other organisms:
Borrelia burgdorferi
The following organisms are not susceptible to Cefuroxime:
Clostridium difficile; *Pseudomonas* spp.; *Campylobacter* spp.; *Acinetobacter calcoaceticus*; *Listeria monocytogenes*; Methicillin-resistant strains of *Staphylococcus aureus* and *Staphylococcus epidermidis*; *Legionella* spp.
Some strains of the following genera are not susceptible to Cefuroxime sodium: *Enterococcus* (*Streptococcus*) *faecalis*. *Morganella morganii*. *Proteus vulgaris*, *Enterobacter* spp., *Citrobacter* spp., *Serratia* spp. *Bacteriodes fragilis*.

PHARMACOKINETICS:
Cefuroxime sodium is absorbed from the gastrointestinal tract and is rapidly hydrolyzed in the intestinal mucosa and blood to cefuroxime; absorption is enhanced in the presence of food. Peak plasma concentrations are reported about 2 to 3 hours after an oral dose. The sodium salt is given by intramuscular or intravenous injection. Peak plasma concentrations of about 27 micrograms/mL have been achieved in 45 minutes after an intramuscular dose of 750 mg with measurable amounts present for 8 hours after a dose. Up to 50% of cefuroxime in the circulation is bound to plasma proteins. The plasma half-life is about 70 minutes and is prolonged in patients with renal impairment and in neonates.
Cefuroxime is widely distributed in the body including pleural fluid, sputum, bone, synovial fluid, and aqueous humour, but only achieves therapeutic concentrations in the CSF when the meninges are inflamed. It crosses the placenta and has been detected in breast milk.
Cefuroxime is excreted unchanged, by glomerular filtration and renal tubular secretion, and high concentrations are achieved in the urine. On injection, most of the dose of cefuroxime is excreted within 24 hours, the majority, within 6 hours. Probenecid competes for renal tubular secretion with cefuroxime resulting in higher and more prolonged plasma concentrations of cefuroxime. Small amounts of cefuroxime are excreted in bile.

DOSAGE & ADMINISTRATION:
Cefuroxime sodium (Danoxime) may be given by deep intramuscular injection, by slow intravenous injection over 3 to 5 minutes, or by intravenous infusion. Doses of cefuroxime axetil and cefuroxime sodium are expressed in terms of the equivalent amount of cefuroxime; 1.20 g of cefuroxime axetil and 1.05 g of cefuroxime sodium are each equivalent to about 1 g of cefuroxime.

- By injection the usual adult dose is 750 mg of cefuroxime every 8 hours but in more severe infections 1.5 g may be given intravenously every 8 hours, or in some cases every 6 hours. Infants and children can be given 30 to 60 mg/kg daily, increased to 100 mg/kg daily if necessary, given in 3 or 4 divided doses.
- Neonates may be given similar total daily doses but in 2 or 3 divided doses.
- Adults with pneumonia or with acute exacerbations of chronic bronchitis may respond to sequential therapy with parenteral cefuroxime 1.5 g twice daily or 750 mg twice daily respectively, followed by oral cefuroxime 500 mg twice daily in each case.
- For Lyme disease in adults, an oral dose of 500 mg is given twice daily for 20 days.
- For the treatment of meningitis due to sensitive strains of bacteria, cefuroxime is given intravenously in adult doses of 3 g every 8 hours. Infants and children are given 200 to 240 mg/kg daily intravenously in 3 or 4 divided doses, which may be decreased to 100 mg/kg daily after 3 days or when there is clinical improvement. For neonates, a dose of 100 mg/kg daily, decreased to 50 mg/kg daily when indicated, may be used.
- In the treatment of gonorrhoea, a single dose of 1.5 g by intramuscular injection, divided between 2 injection sites, has been used. A single 1-g oral dose of cefuroxime has been given for uncomplicated gonorrhoea. In each case an oral dose of probenecid 1 g may be given with cefuroxime.
- For surgical infection prophylaxis, the usual dose is 1.5 g of cefuroxime intravenously before the procedure; this may be supplemented by 750 mg intramuscularly every 8 hours for up to 24 to 48 hours depending upon the procedure. For total joint replacement, 1.5 g of cefuroxime powder may be mixed with the methyl methacrylate cement.

Administration in patients with renal impairment:
Parenteral doses of Cefuroxime may need to be reduced in renal impairment. Licensed product information suggests the following doses based on creatinine clearance (cc):

- cc 10-20mL/minute: 750mg twice daily
- cc less than 10mL/minute: 750mg twice daily

Patients undergoing hemodialysis should receive an additional 750 mg dose following each dialysis; those undergoing continuous peritoneal dialysis may be given 750 mg twice daily.

DIRECTION FOR RECONSTITUTION:
I.M.: When constituted as directed with Sterile Water for Injection, suspensions of Cefuroxime for IM Injection maintain satisfactory potency for 6 hours at room temperature and for 24 hours potency under refrigeration.
Discard any unused suspension after periods stated.
I.V.: When 1.5 g vials are constituted as directed with 16 mL Sterile Water for Injection, solutions of Cefuroxime for IV administration maintain a satisfactory potency for 6 hours at room temperature and 24 hours under refrigeration.
More dilutions 1.5 g plus 100 mL of Sterile Water for injection, 5% Dextrose Injection, or 0.9% Sodium Chloride, also maintain satisfactory potency for 6 hours at room temperature or for 24 hours under refrigeration.

CONTRAINDICATIONS:
Patients with known hypersensitivity to cephalosporin antibiotics.

PRECAUTIONS:
Cephalosporin antibiotics may in general be given safely to patients who are hypersensitive to penicillin, although cross-reactions have been reported. Special care is indicated in patients who experiences anaphylactic reactions to penicillin. As with other antibiotics, prolonged use of Cefuroxime sodium may result in the overgrowth of non-susceptible organisms (e.g. *Candida, Entrococci, Clostridium difficile*), which may require interruption of treatment. Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics; therefore, it is important to consider its diagnosis in patients who develop serious diarrhea during or after antibiotic use.
It is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving Cefuroxime sodium (Danoxime). This antibiotic does not interfere in the alkaline picrate assay for creatinine.
The Jarisch-Herxheimer reaction has been seen following Cefuroxime sodium treatment of Lyme disease. It results directly from the bactericidal activity of Cefuroxime sodium on the causative organism of Lyme disease, the spirochete *Borrelia burgdorferi*. Patients should be reassured that this is common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Pregnancy and Lactation:
There is no experimental evidence of embryopathic or teratogenic effects attribute to Cefuroxime sodium (Danoxime), but as with all drugs, it should be administered with caution during the early months of pregnancy. Cefuroxime sodium is excreted in human milk and consequently, caution should be exercised when Cefuroxime sodium is administered to a nursing mother.

ADVERSE EFFECTS:
Adverse reactions to Cefuroxime sodium (Danoxime) have been generally mild and transient in nature. As with other cephalosporins, there have been rare reports of erythema multiforme. Stevens-Johnson syndrome, toxic epidermal necrolysis (exanthematic necrolysis) and hypersensitivity reactions (including skin rashes, urticaria, pruritus, drug fever, serum sickness) and very rarely anaphylaxis. A small proportion of patients receiving Cefuroxime sodium (Danoxime) have experienced gastrointestinal disturbances, including diarrhea, nausea and vomiting. As with other broad-spectrum antibiotics, there have been reports of pseudomembranous colitis. Headache had also been reported. Eosinophilia and transient increases of hepatic enzyme levels, [ALT (SGPT), AST (SGOT) and LDH] have been noted very rarely. A positive Coombs Test has been reported during treatment with cephalosporin – this phenomenon can interfere with cross-matching of blood.

REPORTING OF SUSPECTED ADVERSE REACTIONS:
To allow continued monitoring of the benefit/risk balance of the medicinal product, reporting of suspected adverse reactions is necessary.
Healthcare professionals are encouraged to report any suspected adverse reaction/s directly to the importer/distributor and/or to FDA: www.fda.gov.ph.
Patients are advised to seek immediate medical attention at the first sign/s of adverse reactions.

DRUG INTERACTIONS:
Drugs which reduce gastric acidity may result in a lower bioavailability of Cefuroxime sodium (Danoxime) compared with that of the fasting state and tend to cancel the effect of enhanced postprandial absorption. Plasma concentrations are reduced by dialysis.

OVERDOSE AND TREATMENT:
Overdosage of cephalosporins can lead to cerebral irritation and seizures. With seizures
the drug should be discontinued and appropriate anticonvulsive and supportive therapy
administered. Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal
dialysis.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE:
Store at temperatures not exceeding 30°C. Protect from light.

AVAILABILITY:
USP Type II Clear Glass Vial with blue flip-off seal (Box of 1's)

FDA Registration Number : DRP-7062
Date of First/Renewal of Authorization : 22 July 2021
Date of Revision of Package Insert: 14 December 2022

Manufactured by:
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Guangdong, China

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