

Cefepime

Introduction: Cefepime hydrochloride is a semi-synthetic, broad spectrum, cephalosporin antibiotic for parenteral administration.

Mecahnism of action: Cephalosporins are bactericidal and have the same mode of action as other beta-lactam antibiotics (such as penicillins). Cephalosporins disrupt the synthesis of the peptidoglycan layer of bacterial cell walls. The peptidoglycan layer is important for cell wall structural integrity, especially in Gram-positive organisms. The final transpeptidation step in the synthesis of the peptidoglycan is facilitated by transpeptidases known as penicillin binding proteins (PBPs).

Pharmacology: Cefepime is a fourth-generation cephalosporin antibiotic developed in 1994. Cefepime has an extended spectrum of activity against Gram-positive and Gram-negative bacteria, with greater activity against both Gram-negative and Gram-positive organisms than third-generation agents. Cefepime has good activity against important pathogens including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and multiple drug resistant *Streptococcus pneumoniae*. A particular strength is its activity against Enterobacteriaceae. Whereas other cephalosporins are degraded by many plasmid- and chromosome-mediated beta-lactamases, cefepime is stable and is a front line agent when infection with Enterobacteriaceae is known or suspected.

Indications: For the treatment of pneumonia (moderate to severe) caused by *Streptococcus pneumoniae*, including cases associated with concurrent bacteremia, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, or *Enterobacter* species. Also for empiric treatment of febrile neutropenic patients and uncomplicated and complicated urinary tract infections (including pyelonephritis) caused by *Escherichia coli* or *Klebsiella pneumoniae*, when the infection is severe, or caused by *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis*, when the infection is mild to moderate, including cases associated with concurrent bacteremia with these microorganisms. Also for the treatment of uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (methicillin-susceptible strains only) or *Streptococcus pyogenes* and complicated intra-abdominal infections (used in combination with metronidazole) caused by *Escherichia coli*, viridans group streptococci, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter* species, or *Bacteroides fragilis*.

Dosage: Most infections susceptible to cefepime therapy require a dosage regimen of 1 to 2 grams every 12 hours. However, a more definitive dosing schedule depends on the severity of the infection as well as the sensitivity of the microorganism to cefepime. Therefore, those patients with an infection caused by *P. aeruginosa* may require higher dosing, at least 2 grams every 12 hours. In addition, renal function status, determined by creatinine clearance, dictates the dose of cefepime. Those patients on hemodialysis must receive supplemental

dosing. Also, those patients undergoing CAPD therapy must receive appropriate dosing (every 48 hours) in order to prevent underdosing or overdosing the patient. Cefepime can be administered either IV via short infusion (30 minutes) or IM. Lidocaine 1% or sterile water can be used to dilute cefepime for IM use. Therapy should be continued for 48 to 72 hours post-eradication of the pathogen.

Side effects: This medication may cause headache, nausea, dizziness, vaginal yeast infection and irritation at the injection site. If any of these effects persist or worsen, notify your doctor promptly. Tell your doctor immediately if you have any of these unlikely but serious side effects: mental/mood changes, vomiting, severe stomach cramps, watery or bloody diarrhea, fever or unusual weakness, muscle twitching (myoclonus), unusual bleeding or bruising, yellowing of the eyes or skin. Tell your doctor immediately if you have any of these very unlikely but serious side effects: change in amount of urine, seizures. An allergic reaction to this drug is unlikely, but seeks immediate medical attention if it occurs. Symptoms of an allergic reaction include: skin rash, hives, severe dizziness, itching, difficulty breathing.. If you notice other effects not listed above, contact your doctor or pharmacist.

Precautions: Prescribing Cefepime in the absence of 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. As with other antimicrobials, prolonged use of Cefepime may result in overgrowth of nonsusceptible microorganisms. Repeated evaluation of the patient's condition is essential. Should superinfection occur during therapy, appropriate measures should be taken. Many cephalosporins, including cefepime, have been associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk, and exogenous vitamin K administered as indicated. Positive direct Coombs' tests have been reported during treatment with Cefepime. 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. Cefepime should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. Arginine has been shown to alter glucose metabolism and elevate serum potassium transiently when administered at 33 times the amount provided by the maximum recommended human dose of Cefepime. The effect of lower doses is not presently known.

Pregnancy: There are, however, no adequate and well-controlled studies of cefepime use in pregnant women the drug should be used during pregnancy only if clearly needed.

Nursing mothers: Cefepime is excreted in human breast milk in very low concentrations (0.5 µg/mL). Caution should be exercised when cefepime is administered to a nursing woman.

Pediatrics: The safety and effectiveness of cefepime in the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, pneumonia, and as empiric therapy for febrile neutropenic patients have been established in the age groups 2 months up to 16 years. Use of Cefepime in these age groups is supported by evidence from adequate and well-controlled studies of cefepime in adults with additional pharmacokinetic and safety data from pediatric trials. Safety and effectiveness in pediatric patients below the age of 2 months have not been established. There are insufficient clinical data to support the use of Cefepime in pediatric patients under 2 months of age or for the treatment of serious infections in the pediatric population where the suspected or proven pathogen is *Haemophilus influenzae* type b.

Geriatrics: Serious adverse events have occurred in geriatric patients with renal insufficiency given unadjusted doses of cefepime, including life-threatening or fatal occurrences of the following: encephalopathy, myoclonus, and seizures.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and renal function should be monitored.

Contraindications: Cefepime is contraindicated in patients who have shown immediate hypersensitivity reactions to cefepime or the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics.

How supplied: Customized as per request.