Xenim®

Cefepime

Description: Cefepime (**Xenim®**) is a fourth generation cephalosporin and is active against a wide range of gram-positive and gram-negative aerobic organisms. Against gram-positive cocci, its activity is similar to that of cefotaxime and includes staphylococci (but not methicillin-resistant *Staphylococcus aureus*) and streptococci. Against Enterobacteriaceae, it has a broader spectrum of activity than other cephalosporins, including activity against organisms producing chromosomally mediated beta-lactamases such as Enterobacter species and *Proteus vulgaris*.

Mode of action: Cefepime (**Xenim®**) inhibits bacterial cell wall synthesis and thus exerts bactericidal action.

Composition: Xenim® 500 mg IM/IV Injection: Each vial contains Cefepime USP 500 mg.
Xenim® 1 g IM/IV Injection: Each vial contains Cefepime USP 1 g.

Indications: Pneumonia (moderate to severe): caused by *Streptococcus pneumoniae*, including cases associated with concurrent bacteremia, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, or Enterobacter species.
Febrile neutropenia: Cefepime as monotherapy is indicated for empiric treatment of febrile neutropenic patients. In patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, with hypotension at presentation, with an underlying haematologic malignancy, or with severe or prolonged neutropenia), antimicrobial monotherapy may not be appropriate. Insufficient data exist to support the efficacy of cefepime monotherapy in such patients.
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.
Uncomplicated skin and skin structure infections: caused by *Staphylococcus aureus* (methicillin-susceptible strains only) or *Streptococcus pyogenes*.
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 & administration:

Site and type of infection	Dose	Frequency	Duration (days)
Moderate to severe pneumonia due to *S. pneumoniae**, *P. aeruginosa*, *K. pneumoniae*, or Enterobacter species	1-2 g IV	12 hourly	10
Empiric therapy for febrile neutropenia	2 g IV	8 hourly	7**
Mild to moderate uncomplicated or complicated urinary tract infections, including pyelonephritis, due to *E. coli*, *K. pneumoniae*, or *P. mirabilis**	0.5-1 g IV/IM***	12 hourly	7-10
Severe uncomplicated or complicated urinary tract infections, including pyelonephritis, due to *E. coli* or *K. pneumoniae**	2 g IV	12 hourly	10
Moderate to severe uncomplicated skin and skin structure infections due to *S. aureus or S. pyogenes*	2 g IV	12 hourly	10
Complicated intra-abdominal infections (used in combination with metronidazole) caused by *E. coli*, viridans group streptococci, *P. aeruginosa*, *K. pneumoniae*, Enterobacter species, or *B. fragilis*	2 g IV	12 hourly	7-10
Septicemia	2 g IV	12 hourly	7-10
Paediatric patients (2 months to 16 years) Bacterial meningitis	50 mg/kg body weight	8 or 12 hourly	7-10

The maximum dose of paediatric patients should not exceed the recommended adult dose.
* including cases associated with concurrent bacteremia.
** or until resolution of neutropenia. In patients whose fever resolves but who remain neutropenic for more than 7 days, the need for continued antimicrobial therapy should be re-evaluated frequently.
*** IM route of administration is indicated only for mild to moderate, uncomplicated or complicated UTIs due to *E. coli* when IM route is considered to be the more appropriate route of drug administration.

Dosage in hepatic impairment: No adjustment is necessary for patients with impaired hepatic function.
Dosage in renal impairment: In patients with impaired renal function (creatinine clearance </=60 mL/min), the dose of cefepime should be adjusted to compensate for the slower rate of renal elimination. The recommended initial dose of cefepime should be the same as in patients with normal renal function. The recommended maintenance doses of cefepime in patients with renal insufficiency are presented in the following table.
Table: Recommended maintenance schedule in adults with renal impairment relative to normal recommended dosing schedule

Creatinine clearance (mL/min)	Recommended maintenance schedule			
> 60 & Normal recommended dosing schedule	500 mg 12-hourly	1 g 12-hourly	2 g 12-hourly	2 g 8-hourly
30 - 60	500 mg 24-hourly	1 g 24-hourly	2 g 24-hourly	2 g 12-hourly
11 - 29	500 mg 24-hourly	500 mg 24-hourly	1 g 24-hourly	2 g 24-hourly
< 11	250 mg 24-hourly	250 mg 24-hourly	500 mg 24-hourly	1 g 24-hourly

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.

Instruction for use: *Instruction for constitution:* A single vial of Xenim 500 mg and 1 g injection is constituted with the following amount of diluents (WFI/0.9% Sodium Chloride Injection/ 5% or 10 % Dextrose Injection) given in the table.

Single dose vial	Amount of diluent to be added (mL)	Approximate available volume (mL)	Approximate Cefepime concentration (mg/mL)
500 mg (IV)	5.0	5.6	100
500 mg (IM)	1.3	1.8	280
1 g (IV)	10.0	11.3	100
1 g (IM)	2.4	3.6	280

For IM administration, Cefepime is reconstituted with the following diluents: Sterile Water for Injection, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol, or 0.5% or 1% Lidocaine Hydrochloride.
For IV administration, Cefepime is compatible at concentrations between 1 and 40 mg/mL with the following IV infusion fluids: Sterile water for injection, 0.9% Sodium Chloride Injection, 5% and 10% Dextrose Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, Lactated Ringers and 5% Dextrose Injection.
Freshly constituted solutions of Cefepime will range in color from colorless to amber.

Mode of administration: Use by Intramuscular (IM) Route: IM route of administration is indicated only for mild to moderate, uncomplicated or complicated UTIs. The prepared solution is given by deep IM injection into a large muscle mass (such as the upper outer quadrant of the gluteus maximus).
Use by Intravenous (IV) Route: The IV route of administration is preferable for patients with severe or life-threatening infections. For direct IV injection, the solution reconstituted as recommended (see Instruction for constitution) should be slowly injected directly into the vein over a period of 3 to 5 minutes. Alternatively, the injection can be made into the tubing of an administration set while the patient is receiving a compatible IV fluid.
For continuous Intravenous (IV) Infusion: Reconstitute the 1g vial as recommended (see Instruction for constitution) and add an appropriate quantity of the resulting solution to one of the compatible IV fluids in an IV administration set. The resulting solution should be administered over a period of approximately 30 minutes.

Side effects: The most common adverse effects are hypersensitivity reactions, including skin rashes, urticaria, eosinophilia, fever, reactions resembling serum sickness and anaphylaxis.

Use in pregnancy & lactation: The safety of cefepime administration during pregnancy and lactation has not been established. This drug should be used during pregnancy only if clearly needed.

Precautions: Cefepime should not be given to patients who are hypersensitive to it or other cephalosporins. About 10% of penicillin sensitive patients may also be allergic to cephalosporins although the true incidence is uncertain; great care should be taken if it is to be given to such patients. Care is also necessary in patients with a history of allergy. It should be given with caution to patients with renal impairment; a dosage reduction may be necessary.

Drug interactions: Renal function should be monitored carefully if high doses of aminoglycosides are to be administered with cefepime, because of the increased potential of nephrotoxicity and ototoxicity of aminoglycoside antibiotics. Nephrotoxicity has been reported following concomitant administration of other cephalosporins with potent diuretics such as frusemide.

Overdosage: Patients who receive an overdose should be carefully observed and given supportive treatment. In the presence of renal insufficiency, hemodialysis, not peritoneal dialysis, is recommended to aid in the removal of cefepime from the body. Accidental overdosing might occur if large doses are given to patients with reduced renal function. In clinical trials, cefepime overdosage has occurred in a patient with renal failure (creatinine clearance <11 mL/min) who received 2 g 24-hourly for 7 days. The patient has exhibited seizures, encephalopathy, and neuromuscular excitability.

Storage after reconstitution: For IM/IV administration, constituted **Xenim®** (Cefepime) solution is stable for 24 hours at controlled room temperature 20 - 25 ˚C (68 - 77 ˚F) or for 7 days in a refrigerator 2 - 8 ˚C (36 - 46 ˚F). As with other cephalosporins, the color of Cefepime powder, as well as its solutions, tends to darken depending on storage conditions; however, when stored as recommended, the product potency is not adversely affected.

Packaging
Xenim® 500 mg IM/IV Injection: Each carton contains one vial with one ampoule of 5 ml water for injection in blister pack and a 5 ml disposable syringe.
Xenim® 1 g IM/IV Injection: Each carton contains one vial with one ampoule of 10 ml water for injection in blister pack and a 10 ml disposable syringe.

Opsonin Pharma
Ideas for healthcare

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Manufactured by
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