

Rx Cefpirome Sulphate for Injection

 GENPIROME™

e f e m e l u e n t e

Composition:

Each vial contains
Cefpirome Sulphate
equivalent to Cefpirome.....1gm
(A sterile blend of Cefpirome Sulphate
and anhydrous Sodium Carbonate)

CLINICAL PHARMACOLOGY

Cefpirome binds to one or more of the penicillin-binding proteins (PBPs) which inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell wall, thus inhibiting biosynthesis and arresting cell wall assembly resulting in bacterial cell death. Cefpirome is rapidly and widely distributed in body fluids and achieves excellent tissue penetration reaching concentrations which exceed the minimum inhibitory concentrations for most pathogens.

Bioavailability after i.m. administration is greater than 90%. The average peak (C5min) serum level after single i.v. doses of 1.0g was 80-90 mg/L. Pharmacokinetics were dose linear. The volume of distribution was 14-19L. No accumulation was seen after multiple dosing. The elimination half-life in serum was 1.8-2.2h. Serum protein binding was less than 10% and was dose independent. Cefpirome was principally eliminated by the kidney; 80-90% of the administered drug was recovered in the urine. Radioactive counts recovered in the urine consisted of 98-99% unchanged cefpirome. Approximately 30% of a 1.0g dose was eliminated by haemodialysis

INDICATIONS

- Infections caused by Cefpirome-sensitive organisms:
- Lower respiratory tract infections
- Complicated upper and lower urinary tract infections
- Bacteraemia/Septicaemia
- Infections in neutropenic & immunocompromised patients.
- Skin and soft tissue infections.
- Severe infections in intensive care patients.

CONTRAINDICATIONS

Cefpirome must not be used in patients with hypersensitivity to antibiotics of the cephalosporin group. Cefpirome must not be used during pregnancy. Breast-feeding should be discontinued during treatment with Cefpirome.

SPECIAL WARNINGS AND PRECAUTIONS

The occurrence of any allergic reaction necessitates discontinuation of treatment. The prescription of cephalosporins requires prior interview, as cross-allergy between penicillins and cephalosporins is present in 5 to 10% of cases. Cephalosporins must be used with extreme caution in penicillin sensitive patients;

It is advisable to monitor renal function during treatment with combinations or cefpirome and diuretics of the furosemide or ethacrynic acid type and potentially nephrotoxic drugs such as certain antibiotic (aminoglycosides in particular). In cases of impaired renal function, adjust the dosage according to the creatinine clearance.

As with other beta-lactam antibiotic granulocytopenia and, more rarely, agranulocytosis may develop, particularly if Cefpirome is given over longer periods. The blood cell count should therefore be monitored for courses of treatment lasting for more than 10 days.

Severe and persistent diarrhoea may occur with broad spectrum antibiotics during treatment or in the weeks following discontinuation. These episodes may be symptomatic of pseudomembranous colitis (in most cases, due to *Clostridium difficile*). This event, which is rare with cephalosporins, may be life-threatening.

Even if pseudomembranous colitis is only suspected, administration of Cefpirome must be halted immediately. This type of colitis requires immediate and appropriate treatment by a physician. Drugs that inhibit intestinal motility (peristalsis) must not be taken in such cases. Insufficient clinical experience has been gained with Cefpirome in children

INTERACTIONS

As Cephalosporin antibiotics may potentiate the nephrotoxic effects of certain drugs (eg: aminoglycosides, loop diuretics) if administered concomitantly, the possibility of such an interaction with cefpirome must be borne in mind.

Probenicid interferes with the renal tubular transfer of cephalosporins, delaying their excretions and therefore increasing their plasma concentrations.

A false positive Coombs test result may be obtained in rare cases during treatment with cefpirome. Glycosuria must be measured by enzymatic methods during treatment, given that non-enzymatic techniques may produce a false positive reaction.

Pregnancy and lactation

The safety of cefpirome has not yet been established in pregnant women. Cefpirome must not be administered during pregnancy. Studies in several animal species have shown no teratogenic or fetotoxic action.

The safety of cefpirome has not yet been established in lactating women. Therefore, breast-feeding should be discontinued during treatment with Cefpirome

ADVERSE REACTION

Hypersensitivity reactions:

Allergic skin reactions (rash, urticaria), Itching, drug fever and severe acute allergic (anaphylactic) reactions may occur.

Gastrointestinal tract:

Nausea and vomiting, abdominal pain, diarrhoea in very rare cases pseudomembranous colitis.

Effects on Liver function:

Raise in serum liver enzymes (ASAT, ALAT, LDH, alkaline phosphatase), increase in serum bilirubin.

Effects on renal function:

Increases in serum creatinine (in rare cases necessitating discontinuation of treatment) and urea. In rare instances, interstitial nephritis may occur with cephalosporins.

Changes in blood constituents:

Thrombopenia; eosinophilia; very rarely haemolytic anemia. As with other beta-lactam antibiotics (particularly if given over long periods), granulocytopenia and, more rarely, agranulocytosis may develop.

Local infections:

Inflammatory irritation and pain at the injection site.

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Other Reactions:

Disturbance of taste may be experienced immediately after injection. Headache may develop. In very few cases, convulsion.

Administration of antibiotics-including Cefpirome- especially if prolonged, may lead to the proliferation of resistant micro organisms. The patient's condition must therefore be checked at regular intervals. Should a secondary infection occur, appropriate measures must be taken

DOSAGE AND ADMINISTRATION

Dosage and mode of administration depend on the severity of the infection, sensitivity of the pathogens, and condition of the patients.

Dosage in adult patients with normal renal function:

Indication	Single dose (g)	Dosage intervals (hours)	Daily dose (g)
Lower respiratory tract infections	1 to 2	12	2 to 4
Complicated upper and lower urinary tract infections	1	12	2
Bacteraemia/Septicaemia	2	12	4
Infections in neutropenic and immunocompromised patients.	2	12	4
Skin and soft tissue infections.	1	12	2
Severe infections in intensive care patients	2	12	4

Children: 50mg/kg body wt. 8 to 12 hourly.

Dosage in patients with impaired renal function: Cefpirome is excreted predominantly via the renal route. In case of impaired renal function, dose reduction is necessary to compensate for the slower excretion. No dose reduction is necessary in patients with a creatinine clearance below 50 ml/min. In patients with a creatinine clearance below 50ml/min, the dosage must be adjusted to the following scheme:

Creatinine clearance	Recommended daily dose in normal renal function 2 x 1 g	Recommended daily dose in normal renal function 2 x 2 g
50-20ml/min	1g loading dose, then 0.5g twice daily	2 g loading dose, then 1 g, twice daily
20-5ml/min	1g loading dose, then 0.5g once daily	2 g loading dose, then 1 g, once daily
≤ 5 ml/min (haemodialysis)	0.5 g, once daily, in addition 0.25 g immediately after dialysis	1 g, once daily, in addition 0.5 g immediately after dialysis

Dosage in elderly patients: No adjustment necessary except in cases of impaired renal function (see above).

Duration of treatment: The duration of treatment depends on the patient's clinical and bacteriological response.

Mode of administration: Intravenous route / Intramuscular route.

Intravenous injection of Cefpirome 1.0g: Dissolve the contents of one vial of Cefpirome 1.0g in 10 ml water for injections, and then inject slowly within 3 to 5 minutes.

Short intravenous infusion of Cefpirome 1.0 g: Dissolve the contents of one vial of Cefpirome 1.0 in 100 ml water for injections, and then infuse for 20 to 30 minutes. The following infusion solution can also be used alternatively for dissolution: 0.9% sodium chloride solution, Ringer's solution, standard electrolyte solutions, 5 and 10% glucose solution, 5% fructose solution, 6% glucose + 0.9% sodium chloride solution. Cefpirome must not be administered in sodium bicarbonate solution.

The vials containing the solvent and the powder for reconstitution should be held horizontally when preparing the infusion solution, and the cannula

should be inserted rapidly. The amount of 100 ml solvent must be adhered to as precisely as possible. Foaming occurs on dissolution of cefpirome and the vial must be tilted gently from side to side for about 1 minute before cefpirome is entirely dissolved.

After reconstitution, Cefpirome can be stored for up to 6 hours at room temperature or for up to 24 hours at between 2°C to 8°C without undergoing any significant physical or chemical changes. In order to avoid septic complication on injection it is recommended that care should be taken during reconstitution to ensure aseptic handling and that the solution should be used immediately after reconstitution. Aseptic handling is particularly important if the solution is not intended for immediate use.

Protect the reconstituted solution from direct sunlight. Some intensification of colour may occur during storage of the reconstituted solution. However, provided the recommended storage conditions are observed, this does not indicate a change in potency or safety.

Storage

Store in a cool dry place below 25°C. Protect from light & moisture.

How supplied

Genpirome is available as vials of 1g along with 10 ml sterile water for injection for reconstitution.

For further details, please contact:

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