Cefepime for Injection, USP

Indications and Usage
Cefepime for injection, USP is indicated in the treatment of the following infections caused by aerobic and anaerobic Gram-negative bacteria (see also REMARKS and CLINICAL PHARMACOKINETICS): pneumonia (in patients with and without pre-existing chronic respiratory disease) and infections of the urinary tract, including pyelonephritis; skin and skin structure infections; as well as intra-abdominal infections.

Cefepime for injection, USP has been shown to be active against most isolates of the following microorganisms, both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section.

Dosage and Administration

Intramuscular Administration

Concentrations of cefepime achieved in specific tissues and body fluids are listed in Table 3. Concentrations of cefepime achieved in specific tissues and body fluids are listed in Table 3.

Pharmacokinetic Parameters (±SD), Intramuscular Administration

<table>
<thead>
<tr>
<th>Parameter</th>
<th>500 mg IM</th>
<th>1 g IM</th>
<th>2 g IM</th>
</tr>
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<tbody>
<tr>
<td>Cmax (μg/mL)</td>
<td>9.9 (2.9)</td>
<td>20.2 (5.1)</td>
<td>37.8 (8.2)</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>2.3 (0.8)</td>
<td>1.5 (0.5)</td>
<td>1.9 (0.5)</td>
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<tr>
<td>T1/2 (h)</td>
<td>2.8 (0.7)</td>
<td>2.6 (0.6)</td>
<td>2.4 (0.6)</td>
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<td>AUC (μg·h/mL)</td>
<td>21.3 (5.6)</td>
<td>42.9 (10.5)</td>
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This table provides concentrations of cefepime on the range of the doses evaluated. The concentrations were determined from an average of at least two samples measured at various times following single 30-minute infusions (IV) of cefepime 500 mg, 1 g, and 2 g to healthy volunteers. In all instances, cefepime is co-administered with neomycin sulfate. The following intramuscular (IM) administration, cefepime is completely absorbed. The average plasma levels of cefepime are presented in Table 2. Statistical comparisons were made on the protocol-valid population, which consisted of those with a surgically confirmed complicated infection, at least 18 years of age, with no surgical debridement or concurrent antibiotic therapy, and no history of recent bone marrow transplantation, chemotherapy, or corticosteroid therapy for at least 1 month. The primary analyses were conducted on the protocol-valid population, which defined the treatment group as patients who received cefepime and/or placebo. All other treatments were completed by the 86 patients (52%). The observed differences in efficacy may have been due to the protocol-specified exclusion of patients with coagulase-negative Staphylococcus aureus bacteremia.

Contraindications

Cefepime for injection is contraindicated in patients with a history of penicillin hypersensitivity, a history of a cephalosporin or a penicillin allergy, and patients with severe hepatic impairment.

NURSING CONSIDERATIONS

Cefepime for injection is contraindicated in patients with a history of penicillin hypersensitivity, a history of cephalosporin or penicillin allergy, and patients with severe hepatic impairment. The data suggest that cefepime is not effective against anaerobic bacteria in patients with severe hepatic impairment. The efficacy of cefepime in patients with severe hepatic impairment has not been established.

Dosage and Administration

Intramuscular Administration

Concentrations of cefepime achieved in specific tissues and body fluids are listed in Table 3.

Table 3: Average Pharmacokinetic Parameters (±SD) for Intramuscular Administration

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The incidence of rash, irrespective of relationship to cefepime in those patients who received the higher recommended doses, was 32% to 42%.

Of the more than 6400 adults treated with cefepime for injection in clinical studies, 35% were elderly patients (65 years and older).

Cefepime is also indicated for the treatment of uncomplicated and complicated urinary tract infections and skin and skin structure infections due to aerobic Gram-negative bacilli, including *P. aeruginosa*, Enterococcus spp., and Methicillin-sensitive *Staphylococcus aureus* (MSSA).

Cefepime is generally well tolerated. The most frequently reported adverse reactions in clinical trials were gastrointestinal events, including diarrhea, nausea, and vomiting. Other adverse events that occurred more frequently with cefepime than with placebo included skin and subcutaneous tissue reactions, including rash, STEVENS-JOHNSON SYNDROME, and NEUTROPIA.

Cefepime was not teratogenic or embryocidal when administered during the period of organogenesis in rats and rabbits at doses up to 100 and 500 times the recommended human maximum daily dose (RDMD) based on body surface area. At a dose of 100 mg/kg/day (50 mg per kg per dose, every 8 hours for febrile neutropenic patients), for durations as given in Table 12, cefepime was positive for clastogenicity in primary human lymphocytes, and in tester strains of *Salmonella typhimurium* and *Escherichia coli*.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Cefepime was not teratogenic or embryocidal when administered during the period of organogenesis in rats and rabbits at doses up to 100 and 500 times the recommended human maximum daily dose (RDMD) based on body surface area. At a dose of 100 mg/kg/day (50 mg per kg per dose, every 8 hours for febrile neutropenic patients), for durations as given in Table 12, cefepime was positive for clastogenicity in primary human lymphocytes, and in tester strains of *Salmonella typhimurium* and *Escherichia coli*.

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