Piperacillin and Tazobactam for Injection is a combination penicillin and beta-lactamase inhibitor indicated for the treatment of infections caused by susceptible isolates of the designated organisms.

1 INDICATIONS AND USAGE

1.1 Intra-abdominal Infections

1.2 Nosocomial Pneumonia

1.3 Skin and skin structure infections

1.4 Empirical Selection of Therapy

2 DOSAGE FORMS AND STRENGTHS

2.1 Powder for Injection

2.2 Injection in a Dextrose 5% Solution

2.3 Injectable Solution

3 DOSSAGE AND ADMINISTRATION

3.1 Adults

3.2 Pediatric Patients

3.3 For Injection

3.4 For Intra-abdominal Infections

3.5 For Nosocomial Pneumonia

4 ADVERSE REACTIONS

4.1 General Adverse Reactions

4.2 Skin and Soft Tissue Adverse Reactions

4.3 Gastrointestinal Adverse Reactions

4.4 Urinary Tract Adverse Reactions

4.5 Special Sensitivity Reactions

5 PRECAUTIONS

5.1 General Precautions

5.2 Laboratory Tests

5.3 Hematologic Effects

5.4 Hypersensitivity Reactions

5.5 Neurotoxic Reactions

5.6 Allergic Reactions

5.7 Development of Drug-Resistant Bacteria

5.8 Pseudomembranous Colitis

5.9 Hepatotoxicity

5.10 Serum sickness-like reactions

5.11 Photosensitivity reactions

5.12 Eosinophilia

5.13 Local Reactions

5.14 Skin and Soft Tissue Reactions

5.15 Gastrointestinal Effects

5.16 Urinary Tract Reactions

6 CLINICAL PHARMACOLOGY

6.1 Pharmacodynamic and Pharmacokinetic

6.2 Post-Marketing Experience

6.3 Additional Experience with Piperacillin

6.4 Tazobactam

6.5 Piperacillin and Tazobactam

7 DRUG INTERACTIONS

7.1 Aminoglycosides

7.2 Beta-lactam antimicrobial agents

8 PATIENT INFORMATION

8.1 General Information

8.2 Use of Drug

8.3 Risk of Allergic Reaction

8.4 Risk of Hypersensitivity Reactions

8.5 Laboratory Test Results

8.6 General Precautions

8.7 Safety and Toxicity

8.8 Patients with Cystic Fibrosis

8.9 Other Drug Interactions

8.10 Pregnancy

8.11 Incompatibilities

8.12 Storage

8.13 Patient Counseling Information

9 CONTRAINDICATIONS

10 WARNINGS AND PRECAUTIONS

10.1 General Precautions

10.2 Hypersensitivity Reactions

10.3 Laboratory Tests

10.4 Developing Fetal Therapy

10.5 Pregnancy

10.6 Allergic Reactions

10.7 Drug Interactions

10.8 Impaired Hepatic Function

10.9 Pseudomembranous Colitis

10.10 Myelosuppression

10.11 Serum sickness-like reactions

10.12 Photosensitivity Reactions

10.13 Eosinophilia

10.14 Local Reactions

10.15 Skin and Soft Tissue Reactions

10.16 Gastrointestinal Effects

10.17 Urinary Tract Reactions

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

11.2 Breastfeeding

11.3 Children

11.4 Geriatric Use

12 CLINICAL PHARMACOLOGY

12.1 Pharmacodynamics

12.2 Pharmacokinetics

12.3 Effect on laboratory parameters

13 NONCLINICAL TOXICOLOGY

13.1 Preclinical Studies

13.2 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

14.1 Monotherapy Clinical Trials

14.2 Plus Aminoglycoside Clinical Trials

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

16.2 Stability

16.3 Storage

17 PATIENT COUNSELING INFORMATION

18 CHRONOLOGY

19 MARKETING HISTORY

20 ADVERSE REACTIONS

20.1 Reported cases

20.2 Post-marketing adverse drug reactions

20.3 Therapy with piperacillin and tazobactam and aminoglycosides

21 CLINICAL STUDIES

21.2 Effects of multiple-dose regimens

22 CLINICAL PHARMACOLOGY

22.1 Pharmacodynamics

22.2 Pharmacokinetics

22.3 Effect on laboratory parameters

23 NONCLINICAL TOXICOLOGY

23.1 Preclinical Studies

23.2 Carcinogenesis, Mutagenesis, Impairment of Fertility

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24.1 Monotherapy Clinical Trials

24.2 Plus Aminoglycoside Clinical Trials

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26.2 Stability

26.3 Storage

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28 CHRONOLOGY

29 MARKETING HISTORY

30 ADVERSE REACTIONS

30.1 Reported cases

30.2 Post-marketing adverse drug reactions

30.3 Therapy with piperacillin and tazobactam and aminoglycosides

31 CLINICAL STUDIES

31.2 Effects of multiple-dose regimens

32 CLINICAL PHARMACOLOGY

32.1 Pharmacodynamics

32.2 Pharmacokinetics

33 NONCLINICAL TOXICOLOGY

33.1 Preclinical Studies

33.2 Carcinogenesis, Mutagenesis, Impairment of Fertility

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34.1 Monotherapy Clinical Trials

34.2 Plus Aminoglycoside Clinical Trials

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36.1 How Supplied

36.2 Stability

36.3 Storage

37 PATIENT COUNSELING INFORMATION

38 CHRONOLOGY

39 MARKETING HISTORY

40 ADVERSE REACTIONS

40.1 Reported cases

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41 CLINICAL STUDIES

41.2 Effects of multiple-dose regimens

42 CLINICAL PHARMACOLOGY

42.1 Pharmacodynamics

42.2 Pharmacokinetics

43 NONCLINICAL TOXICOLOGY

43.1 Preclinical Studies

43.2 Carcinogenesis, Mutagenesis, Impairment of Fertility
Piperacillin and tazobactam for injection is an antibacterial combination of piperacillin sodium and a disodium salt of tazobactam. Each vial contains 7.0 mEq (162 mg) of tazobactam. Each gram of the combination product contains 3.375 g of piperacillin sodium and 0.80 g of tazobactam sodium.

The chemical structure of piperacillin is 7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate. Piperacillin sodium is derived from D(-)-tartaric acid and L-threonine. Tazobactam sodium is derived from glucuronide conjugation of tazobactam. The antibacterial activity is attributed to the trisubstituted 7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid structure. Tazobactam sodium is a broad-spectrum ß-lactamase inhibitor that stabilizes piperacillin by inducing chromosomally-mediated ß-lactamases at tazobactam concentrations achieved with the recommended dosage regimen.

Piperacillin is excreted in low concentrations in human milk; however, data are insufficient to determine if tazobactam is excreted into breast milk. Pediatric studies have demonstrated that piperacillin and tazobactam are significantly excreted into the bile. Piperacillin and tazobactam have been administered to pregnant women without showing evidence of foetal toxic effects. However, the safety and effectiveness of piperacillin/tazobactam have not been established in pregnant women.

In patients with creatinine clearance ≤ 40 mL/min and who are not volume-depleted, the renal clearance of piperacillin is approximately 31% and 39%, respectively. Therefore, dosage adjustments are not required. In patients with impaired renal function, dosing frequency may be increased. Piperacillin and tazobactam are eliminated by glomerular filtration and tubular secretion. Piperacillin is highly protein-bound (99%), and tazobactam is bound to a lesser extent (70%).

In patients with hepatic impairment, piperacillin elimination is prolonged. Piperacillin is eliminated by biliary excretion. Tazobactam is metabolized by the hepatic microsomal enzymatic system, not by biliary excretion. Piperacillin and tazobactam are excreted in the bile. Piperacillin is eliminated by biliary excretion, whereas tazobactam is eliminated by the hepatic microsomal enzymatic system.

Piperacillin is approved for use in patients with creatinine clearance ≤ 40 mL/min and who are not volume-depleted. Piperacillin is not approved for use in patients with hepatic impairment.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, andimus, and of concomitant disease or other drug therapy. In elderly patients, this includes a prospective, randomized, comparative study of the efficacy and safety of piperacillin/tazobactam in Asian (n=9) and Caucasian (n=9) healthy volunteers who were administered single doses of 3.375 g of piperacillin/tazobactam. The impact of race on piperacillin and tazobactam was evaluated. The effect of race on piperacillin and tazobactam was evaluated.

Table 6: Piperacillin/Tazobactam Concentrations in Tissue and Fluids after a Single Oral Dose of Piperacillin 300 mg/kg or Piperacillin/Tazobactam 150 mg/kg

<table>
<thead>
<tr>
<th>Tissue/Fruid</th>
<th>Piperacillin (mg/L)</th>
<th>Tazobactam (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>1.4 – 2.7</td>
<td>0.7 – 1.5</td>
</tr>
<tr>
<td>Brain</td>
<td>0.18 – 0.32</td>
<td>0.03 – 0.06</td>
</tr>
<tr>
<td>Kidney</td>
<td>9.1 – 18.6</td>
<td>2.4 – 4.8</td>
</tr>
</tbody>
</table>

During treatment, patients can develop watery and bloody stools (with or without fever). This condition may be attributed to Clostridium difficile, which may be treated by discontinuing the antibiotic and supportive measures. Piperacillin and tazobactam should not be administered to patients with history of Clostridium difficile-associated diarrhea or pseudomembranous colitis.

Piperacillin and tazobactam for injection is contraindicated in patients with known allergy to any component of the formulation or to piperacillin or tazobactam. Piperacillin and tazobactam are not indicated for the treatment of gonococcal infections. Piperacillin and tazobactam are contraindicated in patients with known or suspected infection caused by an organism known to be sensitive to aminoglycosides. Piperacillin and tazobactam are contraindicated in patients with known or suspected infection caused by an organism known to be sensitive to aminoglycosides.

Piperacillin/tazobactam has been shown to be active against most isolates of the following microorganisms both in vitro and in vivo: Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumoniae, Enterobacter spp., Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, and members of the Enterobacteriaceae family. Piperacillin/tazobactam has been shown to be active against most isolates of the following microorganisms both in vitro and in vivo: Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumoniae, Enterobacter spp., Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, and members of the Enterobacteriaceae family.

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