To reduce the development of drug-resistant bacteria and main...

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

• Initial presumptive treatment of patients with nosocomial infections that are proven or strongly suspected to be caused by bacteria.

2 DOSAGE AND ADMINISTRATION

- For patients on hemodialysis, the maximum dose is 2.25 g per day (2.25 g every 48 hours). It is recommended that the primary infusion solution be replaced with a nonsaline solution (e.g., dextrose or saline) following dosing. If the primary infusion solution is to be used, the maximum dose is 1.75 g per day (1.75 g every 48 hours).

3 DOSAGE FORMS AND STRENGTHS

- Piperacillin and tazobactam for injection is available in the following forms:
  - White to off-white powder in bottles of the following sizes: 2.5 g, 5 g, 7.5 g, and 10 g.

4 CONTRAINDICATIONS

- Piperacillin and tazobactam for injection is contraindicated in patients with a history of anaphylactic reaction to piperacillin or other β-lactam antibiotics.

5 ADVERSE REACTIONS

6.2 Post-Marketing Experience

- The safety and effectiveness of piperacillin and tazobactam for injection were assessed in clinical trials involving 1,462 patients. Adverse reactions were monitored throughout the treatment period.

7.3 Anticoagulants

- Increased blood levels of anticoagulants may occur when concomitant use of piperacillin and tazobactam for injection is initiated. It is recommended that the anticoagulant dose be adjusted when piperacillin and tazobactam for injection are started or stopped.

8 USE IN SPECIFIC POPULATIONS

8.3 Nursing Mothers

- Piperacillin and tazobactam for injection is excreted in human milk. Although no adverse effects on the nursing infant have been reported, it is recommended that nursing mothers discontinue nursing during treatment with piperacillin and tazobactam for injection.

9.3 Other Drugs

- Cimetidine, probenecid, and other drugs that decrease the renal excretion of piperacillin may result in increased serum levels of piperacillin and tazobactam for injection. It is recommended that the dose of piperacillin and tazobactam for injection be reduced if concomitant use with agents that decrease renal excretion is anticipated.

10.3 Special Populations

- For patients with renal impairment, the dose of piperacillin and tazobactam for injection should be reduced. In patients with a creatinine clearance of 10 to 30 mL/min, the dose should be reduced to 2.25 q6h.

11 DRUG INTERACTIONS

- Piperacillin and tazobactam for injection may increase the risk of development of drug-resistant bacteria. It is recommended that the use of piperacillin and tazobactam for injection be limited to patients with life-threatening infections where the benefits outweigh the risks.

12 CLINICAL PHARMACOLOGY

- Piperacillin and tazobactam for injection is a β-lactam antibiotic that is effective against Gram-negative bacilli. It is recommended that the use of piperacillin and tazobactam for injection be limited to patients with life-threatening infections where the benefits outweigh the risks.

13 NONCLINICAL TOXICOLOGY

- No specific data on the nonclinical toxicology of piperacillin and tazobactam for injection are available.

14 CLINICAL STUDIES

- Two trials of nosocomial lower respiratory tract infections were conducted with piperacillin and tazobactam for injection. In the piperacillin/tazobactam group, 19 (8.8%) patients were treated with piperacillin/tazobactam injection, while in the imipenem/cilastatin (500 mg/500 mg q6h) in combination with an aminoglycoside group, 28 (12.9%) patients were treated.

15 PATIENT FOCUS

- Patients should be informed about the importance of completing the full course of treatment. It is recommended that patients be instructed to report any adverse reactions to their healthcare provider.

16 HOW SUPPLIED/STORAGE AND HANDLING

- Piperacillin and tazobactam for injection is supplied in either single-dose vials or multiple-dose (plastic container) bottles. It is recommended that the containers be stored at a temperature not exceeding 30°C (86°F).

17 PATIENT COUNSELING INFORMATION

- Patients should be instructed to report any adverse reactions to their healthcare provider. It is recommended that patients be informed about the importance of completing the full course of treatment.
Piperacillin and Tazobactam for Injection is an injectable antibiotic combination. It contains piperacillin sodium (1 g, 3 g, or 4 g) and tazobactam sodium (0.5 g, 1.25 g, or 2 g)

**Pharmacokinetics**

**Spectrum of Activity**

*In vitro* activity against a range of bacteria, including:

- *Staphylococcus aureus* (methicillin susceptible iso
- *Proteus mirabilis*
- *Providencia stuartii*
- *Streptococcus pneumoniae*
- *Staphylococcus epidermidis*
- *Aeromonas hydrophila*
- *Bacteroides fragilis*
- *Bacteroides thetaiotaomicron*
- *Citrobacter freundii*
- *Klebsiella pneumoniae*
- *Proteus vulgaris*
- *Escherichia coli* (non-extended spectrum)  

**Dosage and Administration**

- **Paediatrics**
  - 2-12 years: 20 mg/kg/day in 4 divided doses every 6 hours for infections such as appendicitis.
  - Children ≥ 12 years: Adult dose.

**Contraindications**

- Hypersensitivity to piperacillin or tazobactam
- Enterobacter aerogenes or *Pseudomonas aeruginosa* infection

**Warnings and Precautions**

- Coagulation parameters should be tested more frequently when the drug is used concomitantly with other drugs that may affect the blood coagulation system or the drugs that may accelerate the breakdown of clotting factors.

**Toxicity and Overdose**

- In patients with creatinine clearance ≤ 40 mL/min and impaired renal function, lower doses should be used. Monitor renal function closely.

**Drug Interactions**

- **Aminoglycosides**: Piperacillin may inactivate aminoglycosides by converting them to inactive substances.
- **Probenecid**: When used concomitantly with piperacillin, probenecid may reduce the renal excretion of piperacillin.
- **Coagulation parameters**: Coagulation parameters should be tested more frequently when the drug is used concomitantly with other drugs that may affect the blood coagulation system.

**Dosage Form**

- For injection and tobramycin to patients with either normal or impaired renal function. The product does not contain excipients or preservatives.

**Clinical Pharmacology**

**Absorption**

Piperacillin is rapidly absorbed from the gastrointestinal tract. After oral administration, the bioavailability is approximately 60%.

**Distribution**

Piperacillin and tazobactam distribution is similar to that of aminoglycosides. Both drugs distribute to tissues and body fluids including intestinal mucosa, gallbladder, bile, and tissues with varying degrees of severity.

**Metabolism**

Piperacillin is metabolized to a minor microbiologically active metabolite, piperacillin acid, which is eliminated in urine. Tazobactam is metabolized to inactive metabolites.

**Excretion**

Piperacillin is excreted mainly in the urine as an active metabolite. Tazobactam is excreted mainly in the urine as metabolites.

**Pharmacokinetics in Special Populations**

- **婴幼儿**: 婴幼儿和儿童 (2-12 years of age) with complicated intra-abdominal infections may be supported by evidence from well-controlled studies.
- **Children ≥ 12 years**: Adult dose.
- **Geriatric Patients**: 80% of the estimated clearance is 80% of the human dose of piperacillin. Adjustments are not required for elderly patients.
- **Hepatic Impairment**: The clearance estimate is 80% of the human dose of piperacillin/tazobactam. Dosage adjustments are not required.
- **Renal Impairment**: Gentamicin dosage adjustments are not required. For patients with creatinine clearance less than 40 mL/min, lower doses are recommended. Monitor renal function closely.

**Precautions**

- Patients on carbapenem therapy for a longer duration of time than the usual dosing regimen may benefit from monitoring renal function at regular intervals.

**Nursing Mothers**

Piperacillin is excreted in low concentrations in human milk; tazobactam concentrations in human milk have not been evaluated. Piperacillin is excreted in low concentrations in human milk; tazobactam concentrations in human milk have not been evaluated. It is not known whether piperacillin or tazobactam is excreted in human milk.

**Pregnancy**

Teratology studies have been performed in mice and rats. There are no adequate and well-controlled studies of piperacillin in pregnant women. The safety of piperacillin in human pregnancy has not been established. Use piperacillin and tazobactam in pregnant women only if the potential benefit justifies the potential risk to the fetus.

**Clinical Laboratory Considerations**

- **Proxi**: The reaction has also been reported for streptococci and hantaviruses. A negative test result does not exclude infection with these agents.
- **Streptococcus pneumoniae**: The test is highly specific for Streptococcus pneumoniae. It is generally not necessary to perform this assay in patients with suspected Streptococcus pneumoniae infection.
- **A. H. E. C. S.**: The test is highly sensitive for Enterococcus faecalis. It is generally not necessary to perform this assay in patients with suspected Enterococcus faecalis infection.
- **B. F.**: The test is highly sensitive for Bacteroides fragilis. It is generally not necessary to perform this assay in patients with suspected Bacteroides fragilis infection.

**Bacterial Susceptibility Testing**

*In vitro* activity against a range of bacteria, including:

- *Staphylococcus aureus* (methicillin susceptible iso
- *Proteus mirabilis*
- *Providencia stuartii*
- *Streptococcus pneumoniae*
- *Staphylococcus epidermidis*
- *Aeromonas hydrophila*
- *Bacteroides fragilis*
- *Bacteroides thetaiotaomicron*
- *Citrobacter freundii*
- *Klebsiella pneumoniae*
- *Proteus vulgaris*
- *Escherichia coli* (non-extended spectrum)  

**Skeletal**

**Information**

- **WG Critical Care, LLC**
- **NDC 44567-804-01. (carton of 1)**
- **866943/02**

**Additional Experience with Piperacillin**

Piperacillin may be inactivated in the presence of tobramycin. The potency of tobramycin and piperacillin may be reduced by the presence of each other.

**Compatibility**

Piperacillin may be compatible with tobramycin for simultaneous Y-site infusion. Piperacillin may be compatible with tobramycin for simultaneous Y-site infusion. The following adverse reaction has also been reported for tazobactam:

**Adverse Reactions**

- **Seizures**: Seizures have been implicated in the prolongation of the neuromuscular system or the smooth muscle.
- **Coagulation abnormalities**: Coagulation parameters should be tested more frequently when the drug is used concomitantly with other drugs that may affect the blood coagulation system or the drugs that may accelerate the breakdown of clotting factors.
- **Probenecid**: Probenecid administered concomitantly with piperacillin may reduce the renal excretion of piperacillin.
- **Proteinuria**: Proteinuria may be increased in patients with impaired renal function.
- **Hepatic cirrhosis**: Hepatic cirrhosis may not be a contraindication to the use of piperacillin and tazobactam.
- **Bacterial resistance**: The use of piperacillin and tazobactam may lead to the development of bacterial resistance.

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