piperacillin and tazobactam for injection should be reduced to the degree of actual renal function. Use of piperacillin and tazobactam for injection in patients with renal impairment (creatinine clearance ≤ 40 mL/min) and with normal renal function should receive the adult dose.

1. Intra-abdominal infections

In patients with intra-abdominal infections caused by susceptible bacteria, the recommended piperacillin and tazobactam for injection dosage is 80 mg piperacillin/10 mg tazobactam per kilogram of body weight, administered as a continuous intravenous infusion over 60 minutes, every 6 hours. (2.1) In patients with appendicitis and/or peritonitis 9 months of age or older, weight-based dosing is recommended. (2.1) For patients with appendicitis and/or peritonitis less than 9 months of age, the recommended piperacillin and tazobactam for injection dosage is 30 mg piperacillin/4 mg tazobactam per kilogram of body weight, administered as a continuous intravenous infusion over 30 minutes, every 4 hours. (2.1)

2.2 Adult Patients

In patients with complicated intra-abdominal infections caused by susceptible bacteria, the recommended piperacillin and tazobactam for injection dosage is 80 mg piperacillin/10 mg tazobactam per kilogram of body weight, administered as a continuous intravenous infusion over 60 minutes, every 6 hours. (2.2)

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8. Nursing Mothers

Piperacillin/tazobactam is excreted in low concentrations in human milk; lactation should not be interrupted for this drug. Motion sickness may occur in infants when their mothers receive piperacillin/tazobactam.

9. Pediatric Use

Piperacillin/tazobactam is recommended for use in pediatric patients age 1 week to 1 year for treatment of complicated urinary tract infections, including pyelonephritis (see Clinical Pharmacology [12] and Table 6: Mean (CV%) Piperacillin and Tazobactam PK Parameters).

9.1 Neonates

In neonates, piperacillin/tazobactam is not significantly different from placebo in achieving clinical success in treatment of bacterial infection (see Clinical Pharmacology [12]).

10. OVERDOSAGE

There have been postmarketing reports of overdose with piperacillin/tazobactam. There is no specific antidote for overdose. Overdosage with piperacillin/tazobactam may result in a false-positive reaction for glucose in the urine using a glucose oxidase test.

11. DESCRIPTION

Piperacillin/tazobactam contains two components, piperacillin sodium and tazobactam sodium. Each vial contains 2.25 g and 4.5 g of piperacillin/tazobactam as their sodium salts. Each vial contains 9.39 mEq (216 mg) of sodium. The geriatric population may respond with a blunted natriuretic response to sodium administered as the sodium salt of piperacillin/tazobactam.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Piperacillin/tazobactam is bactericidal by inhibiting bacterial cell wall synthesis through the inhibition of bacterial cell wall synthesis. Tazobactam is a strong, broad-spectrum inhibitor of β-lactamases with a spectrum that includes all classes of β-lactamases. Piperacillin/tazobactam is active against many aerobic gram-negative bacteria, aerobic gram-positive bacteria, and anaerobic bacteria.

12.2 Pharmacodynamics

The pharmacokinetic profile of piperacillin/tazobactam is most suited for the treatment of infections caused by most aerobic gram-negative bacteria. Piperacillin and tazobactam are approximately 50% bound to plasma proteins (creatinine clearance <30 mL/min) and 35% bound to plasma proteins (creatinine clearance ≥30 mL/min). The molecular weights of piperacillin and tazobactam are 361.4 and 289.2, respectively.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Piperacillin/tazobactam was not positive in bacterial mutagenesis assays, the in vitro mammalian lymphocyte transformation assay (MTA), or the in vitro chromosomal aberration assay. However, a positive result was observed in a 21-week intraperitoneal carcinogenicity study in rats at a dose level that caused a significant decrease in body weight gain. A minor increase in the incidence of breast tumors in female rats was observed at the same dose level. In a 2-year intraperitoneal carcinogenicity study in mice, no increase in the incidence of tumors was observed. A 2-year intraperitoneal carcinogenicity study in dogs was negative. No evidence of fertility impairment was observed in fertility studies in mice, rats, and rabbits.

15. REFERENCES