

Tazobactam and Tazobactam Combinations*

Class: β lactamase inhibitor

Overview

Tazobactam is a derivative of penicillanic acid sulfone and functions as a mechanism based inhibitor of several β -lactamases, blocking the effects of non-group 1 β -lactamase mediated resistance. The drug can function either irreversibly or in a transient manner. β -lactamase inhibitors, like tazobactam, are hypoallergenic. The offending agent in an allergic reaction to β -lactam/ β -lactamase inhibitor combinations is always the β -lactam component. The following information applies to the piperacillin/tazobactam combination. (See the monograph on piperacillin.)

Resistance

Piperacillin/tazobactam is inactive *in vitro* against Gram-negative bacterial isolates that harbor AmpC β -lactamases, however the combination drug retains its activity against broad spectrum β -lactamase producing and some extended spectrum β -lactamase producing enterobacteriaceae. Emergence of class A β -lactamases of the *Klebsiella pneumoniae* carbapenemase (KPC) type primarily in strains of *K. pneumoniae* and, to a lesser extent, in other *Klebsiella*, *Enterobacter*, *Escherichia*, *Salmonella* and *Citrobacter* species, is especially important. Although β -lactamase inhibitors, like tazobactam, may inhibit KPCs *in vivo*, piperacillin/tazobactam has never been shown to be successful in treating KPC producing organisms. Laboratory detection of this type of resistance is often difficult to identify.

Effectiveness

The piperacillin/tazobactam combination is administered intravenously. The antimicrobial spectrum of this combination includes Gram-positive and Gram-negative aerobic and anaerobic bacteria. Piperacillin/tazobactam was recently reformulated and now includes ethylenediaminetetraacetic acid (EDTA) and sodium citrate. These additions facilitate *in vitro* compatibility with gentamicin and amikacin, but not tobramycin. Piperacillin/tazobactam is administered along with antipseudomonal fluoroquinolones, for example, ciprofloxacin, or amikacin in the empiric treatment of complicated pneumonias in intensive care units or pneumonias associated with long term hospitalization. Piperacillin/tazobactam is well tolerated and exhibits an excellent safety profile, retaining the low toxicity characteristics of the penicillin group.

Piperacillin is generally effective against β -lactamase producing bacteria, including *Haemophilus influenzae*, *Moraxella catarrhalis* and Gram-negative aerobic bacteria. Piperacillin/tazobactam is used in the treatment of patients with intra-

abdominal, skin, soft tissue, lower respiratory tract, complicated urinary tract and gynecological infections. This combination drug has a good probability of reaching adequate pharmacodynamic levels when used for empirical treatment of hospital acquired pneumonias not involving methicillin resistant *Staphylococcus aureus* (MRSA). Recently the drug has also been recommended for treatment of febrile neutropenia. In addition, piperacillin/tazobactam is used to treat infected animal bites in both adults and children. The drug is used in combination with anti-pseudomonal quinolones or in combination with an aminoglycoside (amikacin, gentamicin, tobramycin) and macrolide (azithromycin) in severe pneumonias in intensive care unit patients where structural lung disease or severe corticosteroid treated chronic obstructive pulmonary disease is present, thus increasing the likelihood of pseudomonal involvement. Infections secondary to diabetes are often treated with vancomycin, ceftazidime and the piperacillin/tazobactam combination; other limb threatening infections can be treated with piperacillin/tazobactam in combination with ciprofloxacin. Piperacillin/tazobactam is indicated for the treatment of complicated appendicitis (with rupture or abscess), peritonitis, postpartum endometritis or pelvic inflammatory disease when these infections are caused by piperacillin-resistant β -lactamase producing strains of *E. coli* or other organisms.

***References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**