

Piperacillin-tazobactam:

Class: Antibiotic.

Indications:

Treatment of moderate-to-severe infections caused by susceptible organisms, including infections of the lower respiratory tract (community-acquired pneumonia, nosocomial pneumonia); uncomplicated and complicated skin and skin structures (including diabetic foot infections); gynecologic (endometritis, pelvic inflammatory disease); and intra-abdominal infections (appendicitis with rupture/abscess, peritonitis). Tazobactam expands activity of piperacillin to include beta-lactamase producing strains of *S. aureus*, *H. influenzae*, *E. coli*, *Bacteroides* spp, and other gram-positive and gram-negative aerobic and anaerobic bacteria.

Available dosage form in the hospital: PIPRACILIN 4G + TAZOBACTAM 0.5G VIAL.

Dosage:

-Usual dosage range: I.V.: 3.375 g every 6 hours **or** 4.5 g every 6-8 hours; maximum: 18 g/day

-Extended infusion method (unlabeled dosing): 3.375-4.5 g I.V. over 4 hours every 8 hours (Kim, 2007; Shea, 2009); an alternative regimen of 4.5 g I.V. over 3 hours every 6 hours has also been described (Kim, 2007)

-Indication-specific dosing: I.V.:

-Diverticulitis, intra-abdominal abscess, peritonitis: I.V.: 3.375 g every 6 hours; Note: Some clinicians use 4.5 g every 8 hours for empiric coverage since the %time>MIC is similar between the regimens for most pathogens; however, this regimen is NOT recommended for nosocomial pneumonia or *Pseudomonas* coverage.

-Intra-abdominal infection, complicated: I.V.: 3.375 g every 6 hours for 4-7 days (provided source controlled). **Note:** Increase to 3.375 g every 4 hours or 4.5 g every 6 hours if *P. aeruginosa* is suspected. Not recommended for mild-to-moderate, community-acquired intra-abdominal infections due to risk of toxicity and the development of resistant organisms (Solomkin, 2010).

-Pneumonia (nosocomial): I.V.: 4.5 g every 6 hours for 7-14 days (when used empirically, combination with an aminoglycoside or antipseudomonal fluoroquinolone is recommended; consider discontinuation of additional agent if *P. aeruginosa* is not isolated)

-Severe infections: I.V.: 3.375 g every 6 hours for 7-10 days; Note: Some clinicians use 4.5 g every 8 hours for empiric coverage since the %time>MIC is similar between the regimens for most pathogens; however, this regimen is NOT recommended for nosocomial pneumonia or *Pseudomonas* coverage.

-Skin and soft tissue infection: I.V.: 3.375 g every 6-8 hours for 7-14 days. Notes: When used for necrotizing infection of skin, fascia, or muscle, combination with clindamycin and ciprofloxacin is recommended (Stevens, 2005); for severe diabetic foot infections,

recommended treatment duration is up to 4 weeks depending on severity of infection and response to therapy (Lipsky, 2012).

Renal Impairment:

-Traditional infusion method (ie, I.V. infusion over 30 minutes): Manufacturer's labeling:

-Cl_{cr} >40 mL/minute: No dosage adjustment required.

-Cl_{cr} 20-40 mL/minute: Administer 2.25 g every 6 hours (3.375 g every 6 hours for nosocomial pneumonia)

-Cl_{cr} <20 mL/minute: Administer 2.25 g every 8 hours (2.25 g every 6 hours for nosocomial pneumonia)

Note: Some clinicians suggest adjusting the dose at Cl_{cr} ≤20 mL/minute (rather than Cl_{cr} <40 mL/minute) in patients receiving either traditional or extended-infusion methods, particularly if treating serious gram-negative infections (empirically or definitively) (Patel, 2010).

-**Extended** infusion method (unlabeled dosing): Cl_{cr} ≤20ml/min :3.375 g I.V over 4hours every 12 hours (Patel,2010).

-Intermittent hemodialysis (IHD)/peritoneal dialysis (PD): 2.25 g every 12 hours (2.25 g every 8 hours for nosocomial pneumonia). **Note:** Dosing dependent on the assumption of 3 times/week, complete IHD sessions. Administer scheduled doses after hemodialysis on dialysis days; if next regularly scheduled dose is not due right after dialysis session, administer an additional dose of 0.75 g after the dialysis session.

-Continuous renal replacement therapy (CRRT) (Heintz, 2009; Trotman, 2005): Drug clearance is highly dependent on the method of renal replacement, filter type, and flow rate. Appropriate dosing requires close monitoring of pharmacologic response, signs of adverse reactions due to drug accumulation, as well as drug concentrations in relation to target trough (if appropriate). The following are general recommendations only (based on dialysate flow/ultrafiltration rates of 1-2 L/hour and minimal residual renal function) and should not supersede clinical judgment (Trotman, 2005):

-CVVH: 2.25-3.375 g every 6-8 hours

-CVVHD: 2.25-3.375 g every 6 hours

-CVVHDF: 3.375 g every 6 hours

NOTE :Higher dose of 3.375g should be considered when treating resistant pathogens(especially *Pseudomonas* spp);alternative recommendations suggest dosing of 4.5g every 8 hours (Valtonen,2001);regardless of regimen , there is some concern of Tazobactam (TAZ) accumulation , given its lower clearance relative to piperacillin(PIP) .Some clinicians advocate dosing with PIP to alternate with PIP/TAZ , particularly in CVVH dependent patients , to lessen this concern.

Common side effect:

Gastrointestinal: Diarrhea

Central nervous system: Insomnia , headache , fever , agitation

Dermatologic: Rash , pruritus.

Pregnancy Risk Factor: B