PIPERACILLIN-TAZOBACTAM (IV)

WATCH

CLASS and MECHANISM:

Antipseudomonal penicillin + beta-lactamase inhibitor; resistant to penicillinases and *some* beta-lactamases (only class A); binds to penicillin-binding proteins on bacterial surface → inhibition of cell wall synthesis

SPECTRUM (*predictably* susceptible)

Gram positive	Gram negative	Anaerobes	Other
*Staphylococcus aureus (MSSA)**	*Enterobacterales (susceptible strains)*	*Oral anaerobes**	
*Staphylococcus lugdunensis**	*Pseudomonas aeruginosa (S strains)*	*Bacteroides fragilis*	
*Staphylococcus saprophyticus**	*Hemophilus influenza**	*Other GI anaerobes*	
*Streptococcus Gr A/B/C/F**	*Moraxella catarrhalis**		
*Enterococcus faecalis (most)**	*Pasteurella multocida**		
Listeria monocytogenes*	*Capnocytophaga spp**		

*Piperacillin-tazobactam has class activity that may be comparable to narrower spectrum antibiotics against these bacteria but should **NOT be used as first line against these organisms** because overly broad-spectrum, less favorable toxicity profile, less direct evidence of effectiveness

MAIN USES

- Empiric therapy for hospital-associated pneumonia
- Empiric therapy for sepsis of unclear source if patient has risk factors for Pseudomonal infection
- Empiric therapy for febrile neutropenia
- Targeted therapy (if organism isolated and *not susceptible to narrower spectrum agents*) in UTI, and other infections

COMMON ADVERSE EVENTS*:*

- **Hypersensitivity reactions: Allergies to beta-lactams often mis-diagnosed.** Labeling patient as allergic can lead to treatment with less effective, more toxic or more expensive drugs. **Recommend careful history, risk stratification +/- Allergy consultation for skin testing and oral challenge to remove label.**
  - Type 1 (immediate hypersensitivity): onset < 72h, mediated by IgE; mastocyte and basophil degranulation and histamine release → anaphylaxis, edema, urticaria, bronchospasm (1-5/10,000 cases treated with penicillin)
  - Type 2 (cytotoxic reaction): onset > 72h, mediated by IgG/IgM, Antibody binds to drug-hapten complex on target cells and cell destruction via complement. Manifested by hemolytic anemia (Coombs +), thrombocytopenia, neutropenia.
  - Type 3 (immune complex reaction): onset > 72h, mediated by IgG/IgM; deposition of antigen-antibody complexes on tissues, leading to serum sickness, small vessel vasculitis (including damage to kidneys)
  - Type 4 (delayed hypersensitivity): onset > 72h, mediated by T lymphocytes – their activation leads to release of cytokines and chemokines, manifested by skin (morbilliform) eruptions; can lead to severe cutaneous drug reactions (SCARs including DRESS, AGEP, SJS/TEN)
- **GI**: abdominal cramping, nausea/vomiting, diarrhea are frequent [moderate-high risk of *C. difficile* infection]
- **Bone Marrow:** agranulocytosis, thrombocytopenia (associated with prolonged treatment)
- **Genito-urinary**: candida vaginitis

MAJOR DRUG INTERACTIONS

- High-dose Methotrexate (>500 mg/m^2): case reports of methotrexate toxicity
- Vancomycin: Possible increase in risk of nephrotoxicity.

DRUG MONITORING:

- Check for symptoms and signs compatible with hypersensitivity reactions, rash, or other adverse events
- Recommended blood tests for prolonged (> 1 week) treatment: CBC, renal function, liver profile