

CLASS and MECHANISM:

Aminopenicillin + 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 |
|---------------------------------------|---------------------------------|-----------------------------|-------|
| <i>Staphylococcus aureus</i> (MSSA)* | <i>Hemophilus influenza</i> | <i>Oral anaerobes</i> | |
| <i>Staphylococcus lugdunensis</i> * | <i>Moraxella catarrhalis</i> | <i>Bacteroides fragilis</i> | |
| <i>Staphylococcus saprophyticus</i> * | <i>Pasteurella multocida</i> | <i>Other GI anaerobes</i> | |
| <i>Streptococcus</i> Gr A/B/C/F* | <i>Capnocytophaga</i> spp | | |
| <i>Enterococcus faecalis</i> (most)* | <i>Enterobacteriales</i> (some) | | |

*Amoxicillin-clavulanate has class activity that may be comparable to narrower spectrum antibiotics against these bacteria; should not be used as first line to treat infections caused by MSSA, Streptococcus Gr A/C/F/G

MAIN USES

- Empiric therapy for dental infections
- Empiric therapy for ENT Infections (otitis media, sinusitis)
- Empiric therapy for bronchitis/COPD exacerbations meeting criteria for antibiotic treatment
- Empiric therapy for animal bite-associated skin and soft tissue infections
- Empiric therapy for mild-moderate cholecystitis, cholangitis/liver abscess and other intraabdominal infections
- Targeted therapy (if organism isolated and susceptible) for UTI, pulmonary infections, others

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; include DRESS, AGEP, SJS/TEN)
- **Skin:** rash can occur in association with certain viral infections (EBV, HIV, CMV, ..)
- **GI:** abdominal cramping, nausea/vomiting, diarrhea are frequent [moderate risk of *C. difficile* infection]
- **Genito-urinary:** candida vaginitis

DRUG MONITORING:

- Check for symptoms and signs compatible with hypersensitivity reactions, rash, or other adverse events
- Recommended blood tests for prolonged (> 2 weeks) treatment: CBC, renal function, liver profile
- Therapeutic drug monitoring not available