PENICILLIN V (PO), PENICILLIN G (IV)

ACCESS

MECHANISM:

Bind to penicillin-binding proteins on bacterial surface → inhibition of cell wall synthesis
Rendered inactive by Penicillinase (which is produced by *S. aureus* and many other bacteria)

SPECTRUM (*predictably* susceptible)

Gram positive	Gram negative	Anaerobes	Other
Streptococcus group A/B/C/G *Actinomyces spp*	*Neisseria meningitidis* *Pasteurella multocida*	*Peptostreptococcus spp* *Clostridium perfringes*	*Treponema pallidum* (syphilis) *Leptospira interrogans (leptospirosis)*

MAIN USES

- Therapy for bacterial pharyngitis
- Therapy for syphilis
- Therapy for leptospirosis
- *Targeted* therapy for skin and soft tissue infection caused by Gr A streptococcus (not for empiric management of cellulitis)
- *Targeted* therapy for pneumonia caused by penicillin-susceptible *Streptococcus pneumoniae,* or other infections caused by penicillin-susceptible organism (not empiric management)
- Prophylaxis for acute rheumatic fever

COMMON ADVERSE EVENTS*:*

- **Hypersensitivity reactions: Allergies to penicillin often mis-diagnosed.** Labeling patient as pen-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 with mastocyte and basophil degranulation and histamine release leading to anaphylaxis, edema, urticaria, bronchospasm (incidence 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)
- **GI**: Nausea, vomiting, diarrhea [relatively low risk of *C. difficile* infection]
- **CNS**: high dose of Pen G may increase risk of seizure, prudence required in Pen G dosing if renal insufficiency

MONITORING:

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