

1ST GEN: CEFADROXIL (PO), CEFAZOLIN (IV)

ACCESS

CLASS and MECHANISM:

Cephalosporins; bind 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>Staphylococcus lugdunensis</i> <i>Staphylococcus saprophyticus</i> <i>Streptococcus group A/B/C/G</i>	<i>Proteus mirabilis</i> (most) <i>E. coli</i> (most) <i>Klebsiella spp</i> (some)	Minimal activity	none

MAIN USES

- Empiric therapy for skin and soft tissue infections
- Surgical prophylaxis (cefazolin)
- Targeted therapy for infections caused by susceptible organisms (usually skin and soft tissue including surgical site; bone/joint, endocarditis)

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:** Nausea, vomiting, diarrhea [low-moderate risk of *C. difficile* infection]
- **Genito-urinary:** candida vaginitis
- **CNS:** high dose of ampicillin may increase risk of seizure, prudence required in dosing if renal insufficiency

MAJOR DRUG INTERACTIONS

- Allopurinol → increased frequency of rash
- Methotrexate high-dose (>500 mg/m²) → risk of methotrexate toxicity (very rare)

DRUG 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