



Beta-lactam Cross-reactivity: One-page Clinical Reference

Start with the reaction phenotype. Then compare the exact culprit and candidate by R1 side-chain relationship - not cephalosporin generation alone.

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Version 0.2 | July 21, 2026

1. Identify the reaction phenotype

Confirm culprit, timing, symptoms, treatment, and later tolerated beta-lactams.

NON-ALLERGIC EFFECT

Nausea, diarrhea, headache, yeast infection, or family history only.

Action: Reconcile the label; these do not establish immune cross-sensitivity.

REMOTE / BENIGN / UNKNOWN

Remote childhood rash, vague history, or nonurticarial rash without systemic features.

Action: Use a validated history pathway; many patients qualify for direct challenge or routine use under local policy.

IMMEDIATE / IgE-TYPE

Urticaria, angioedema, bronchospasm, hypotension, or anaphylaxis.

Action: Confirm culprit and timing; use current allergy guidance and a dissimilar agent or supervised evaluation as appropriate.

SEVERE DELAYED / ORGAN-SPECIFIC

SJS/TEN, DRESS, AGEF, serum sickness, cytopenia, interstitial nephritis, or hepatitis.

Action: STOP. Do not clear with this chart. Obtain allergy, ID, or specialist guidance.

2. Check the exact drug relationship

A side-chain relationship changes the question; it does not diagnose, exclude, or de-label an allergy.

AMINO CLUSTER - CLOSEST PAIRS

Amoxicillin <-> cefadroxil / cefprozil
Ampicillin <-> cefaclor / cephalexin

Highest clinically important penicillin-cephalosporin R1 similarity cluster.

METHOXYIMINO CEPHALOSPORINS

Cefuroxime | cefotaxime | ceftriaxone
Cefepime | cefpodoxime

Related R1 features; assess a prior cephalosporin reaction by exact culprit and side chain.

CEFTAZIDIME <-> AZTREONAM

Ceftazidime | aztreonam

Shared R1 side chain. This is the key exception to aztreonam's otherwise minimal beta-lactam cross-reactivity.

CEFAZOLIN

Cefazolin

Unique R1 among commonly used beta-lactams. Penicillin allergy alone does not predict cefazolin allergy; do not apply this shortcut to severe delayed reactions or known cefazolin allergy.

CARBAPENEMS

Ertapenem | imipenem/cilastatin | meropenem

Low observed cross-reactivity with proven penicillin allergy (0.87% pooled estimate in Romano 2019).

DISSIMILAR CEPHALOSPORIN

Use the exact candidate drug and R1 structure

Risk follows R1 similarity more than generation. Pooled risk in proven penicillin allergy was 2.11% for low-similarity cephalosporins versus 16.45% for identical-side-chain aminocephalosporins.

Do not use this chart alone for severe delayed reactions, desensitization, skin testing, challenge, or allergy de-labeling.

Sources: 2022 Drug Allergy Practice Parameter; Romano et al., J Allergy Clin Immunol Pract 2019; Chaudhry et al., Pharmacy (Basel) 2019; CSACI position statement 2020.

Confirm the exact product, current institutional pathway, reaction history, and subsequent tolerance. Full evidence and limitations: rxtray.com/resources/beta-lactam-cross-sensitivity

CLINICAL CROSS-REFERENCE