

VANDERBILT  UNIVERSITY
MEDICAL CENTER

Vanderbilt Adult Antimicrobial Stewardship Program

VASP β -Lactam Allergy Assessment for Hospitalized Patients

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Note: This guidance document is meant to provide general recommendations and does not supersede clinical decision making.

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B-Lactam Allergy Assessment for Hospitalized Patients

Patient with a β -lactam allergy in need of treatment or prophylaxis with a β -lactam

- Low Risk Allergy History**
- Urticaria only, > 5 years have passed
 - Self-limited cutaneous rash at any point
 - Remote childhood reaction with limited details
 - Family history of penicillin allergy only
 - Avoidant from fear of allergy only
 - Known tolerance of a penicillin since original reaction

If patient has previously tolerated desired β -lactam, may skip the following steps

Review patient's medication history to see if they have previously tolerated β -lactams

Amoxicillin challenge for penicillin allergic patients

Cephalosporin allergy

Passed amoxicillin challenge

Failed amoxicillin challenge or unable to perform

- Delabel patient allergy
- Use preferred β -lactam for indication

Use the table on the next page and locate the β -lactam(s) to which the patient is allergic

- Avoid β -lactams with a red box
- OK to select a β -lactam with a yellow or green box

Use the table on the next page and locate the β -lactam(s) to which the patient is allergic

- Avoid β -lactams with a red box
- OK to select a β -lactam with a yellow or green box

Failed challenge resulting in anaphylaxis—avoid all penicillins and all cephalosporins with a red or yellow box in the table below

- Moderate to High-Risk Allergy History**
- Anaphylaxis (with no allergy team-provided recommendations)
 - Disseminated hives, urticaria, flushing, pruritis
 - Angioedema, swelling of the face or throat
 - Shortness of breath, wheezing, coughing
 - Weak pulse
 - Loss of consciousness or confusion

Use the table on the next page and locate the β -lactam(s) to which the patient is allergic

- Avoid β -lactams with a red or yellow box unless documented tolerance since initial allergic reaction
- OK to select a β -lactam with a dark green box
- Consider inpatient allergy consult or outpatient allergy clinic appointment

Patients with an anaphylactic reaction should avoid all other medications in the same class unless cleared by allergy (including agents with a light green box).
Cefazolin is the exception in cases of anaphylaxis to another cephalosporin.

- Highest Risk Allergy History**
- Severe delayed symptoms at any time
 - Any severe cutaneous adverse reactions
 - Stevens-Johnson Syndrome (SJS)
 - Toxic epidermal necrolysis (TEN)
 - Drug reaction with systemic symptoms (DRES)
 - Acute generalized exanthematous pustulosis (AGEP)
 - Generalized bullous fixed drug reaction (GBFDE)
 - Drug induced liver injury (DILI)
 - Drug induced kidney injury (DIKI)
 - Immune-mediated cytopenias
 - Febrile skin rash without a better explanation

• Avoid all penicillins or cephalosporins unless previously approved by allergy
• Consider inpatient allergy consult or outpatient allergy clinic appointment
• Do **NOT** use the chart on the following page to evaluate for cross-reactivity; it is not designed for use with these types of reactions

- General comments:**
- Cefazolin is considered generally safe to administer to any patient unless the β -lactam allergy is specific to cefazolin itself. In the setting of anaphylaxis to cefazolin, a successful cephalexin challenge (with the appropriate precautions) would allow for safe use of all other cephalosporins.
 - Patients with a confirmed penicillin allergy by skin test should avoid other penicillins unless use approved by allergy.
 - Patients with anaphylaxis to a penicillin or a cephalosporin should avoid drugs within the same class unless approved by allergy.
 - Any allergic reaction to piperacillin-tazobactam may indicate a specific reaction to that drug with limited cross-reactivity to other penicillins.
 - Patient with an allergy labeled as a GI reaction should receive β -lactams as long as they are willing to try the medication.

B-Lactam Allergy Cross-Reactivity Table (Do NOT Use for Highest Risk Allergies)

| | | Penicillins | | | | | | | | Cephalosporins | | | | | | | | | | | | Mono | | | | | | |
|------------------------|-------------------------|--------------|--------------|------------|-------------|-----------|-----------|---------------|-------------------------|----------------|------------|-----------|-----------|-----------|-----------|----------|------------|-------------|------------|-------------|----------|-------------|----------|----------|-------------|------------------------|-------------|-----------|
| | | Penicillin G | Penicillin V | Ampicillin | Amoxicillin | Nafcillin | Oxacillin | Dicloxacillin | Piperacillin-tazobactam | Cefadroxil | Cephalexin | Cefazolin | Cefoxitin | Cefotetan | Cefprozil | Cefaclor | Cefuroxime | Ceftriaxone | Cefotaxime | Ceftazidime | Cefdinir | Cefpodoxime | Cefixime | Cefepime | Ceftaroline | Ceftolozane-tazobactam | Cefiderocol | Aztreonam |
| Penicillins | Penicillin G | Black | Red | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Penicillin V | Red | Black | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Ampicillin | Yellow | Yellow | Black | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Red | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Amoxicillin | Yellow | Yellow | Yellow | Black | Yellow | Yellow | Yellow | Yellow | Red | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Nafcillin | Yellow | Yellow | Yellow | Yellow | Black | Yellow | Yellow | Yellow | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Oxacillin | Yellow | Yellow | Yellow | Yellow | Yellow | Black | Yellow | Yellow | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Dicloxacillin | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Black | Yellow | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Piperacillin-tazobactam | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Black | Yellow | Yellow | Green | Green | Green | Green | Yellow | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Red | Green |
| Cephalosporins | Cefadroxil | Yellow | Yellow | Yellow | Red | Green | Green | Green | Green | Black | Yellow | Green | Green | Green | Green | Red | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cephalexin | Yellow | Yellow | Red | Yellow | Green | Green | Green | Green | Yellow | Black | Green | Green | Green | Green | Red | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cefazolin | Green | Green | Green | Green | Green | Green | Green | Green | Green | Black | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cefoxitin | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Black | Green | Green | Green | Green | Green | Red | Green | Yellow | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cefotetan | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Black | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cefprozil | Yellow | Yellow | Yellow | Red | Green | Green | Green | Yellow | Red | Yellow | Green | Green | Green | Green | Black | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cefaclor | Yellow | Yellow | Red | Yellow | Green | Green | Green | Yellow | Red | Yellow | Green | Green | Green | Green | Black | Yellow | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green |
| | Cefuroxime | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Red | Green | Green | Green | Black | Yellow | Yellow | Yellow | Green | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow |
| | Ceftriaxone | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Black | Red | Yellow | Yellow | Red | Yellow | Yellow | Yellow | Yellow | Yellow |
| | Cefotaxime | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Green | Green | Green | Yellow | Red | Black | Yellow | Yellow | Red | Yellow | Yellow | Yellow | Yellow | Yellow |
| | Ceftazidime | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Black | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Red |
| | Cefdinir | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Black | Yellow | Red | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow |
| | Cefpodoxime | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Red | Red | Yellow | Black | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow |
| | Cefixime | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Red | Yellow | Black | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow |
| | Cefepime | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Red | Red | Yellow | Red | Yellow | Black | Yellow | Yellow | Yellow | Yellow |
| Ceftaroline | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Yellow | Yellow | Green | Yellow | Yellow | Black | Yellow | Yellow | Yellow | |
| Ceftolozane-tazobactam | Green | Green | Green | Green | Green | Green | Green | Green | Red | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Yellow | Yellow | Green | Yellow | Yellow | Black | Yellow | Yellow | Yellow | |
| Cefiderocol | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Yellow | Red | Yellow | Yellow | Yellow | Yellow | Yellow | Black | Red | |
| Mono | Aztreonam | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | Yellow | Yellow | Red | Yellow | Yellow | Yellow | Yellow | Yellow | Yellow | Black | |

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Cross-Reactivity Table Key

- Green: safe to use with low and moderate-high risk allergies
- Yellow: safe to use with low-risk allergies
- Red: Do **NOT** use regardless of allergy severity

References

1. Collins CD, Scheidel C, Anam K, et al. Impact of an antibiotic side-chain-based cross-reactivity chart combined with enhanced allergy assessment processes for surgical prophylaxis antimicrobials in patients with β -lactam allergies. *Clin Infect Dis*. 2021;72(8):1404-1412. doi: 10.1093/cid/ciaa232.
2. Trubiano JA, Stone CA, Grayson ML. The 3 Cs of antibiotic allergy-classification, cross-reactivity, and collaboration. *J Allergy Clin Immunol Pract*. 2017;5(6):1532-1542. doi: 10.1016/j.jaip.2017.06.017.
3. Zagursky RJ and Pichichero ME. Cross-reactivity in β -lactam allergy. *J Allergy Clin Immunol Pract*. 2018;6(1):72-81. doi: 10.1016/j.jaip.2017.08.027.

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