

# β-Lactam Drug Allergy

## Evaluation of β-Lactam Drug Allergy Labels – Inpatient Setting

### Disclaimer

This clinical pathway is intended to provide general guidance and should not replace clinical judgment. It is meant to assist licensed practitioners and other health care providers in clinical decision-making by describing a range of generally acceptable approaches to the diagnosis and management of a particular condition. A particular patient's circumstances should always be taken into account when a practitioner is deciding on a course of management. This clinical pathway is current as of the date of publication and will be reviewed periodically to align with any updated best practices or evidence; however, new development may not be represented in the published version. The treating practitioner assumes all risks associated with care decisions. Phoenix Children's accepts no liability for the content of this clinical pathway or the outcomes a patient might experience where a practitioner consulted the content of this clinical pathway.

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## Pathway Flow Diagram/Algorithm

**Table 1. Drug Allergy Evaluation/Risk Stratification Tool**

Reaction history	Yes or No
Hypotension	
Blistering rash	
Evidence of internal organ involvement (liver, kidney failure)	

Any answer yes = moderate/high risk

- If the antibiotic with prior reaction is the drug of choice while inpatient, consult allergy
- If the antibiotic with prior reaction is not drug of choice inpatient, refer to allergy outpatient for drug allergy Testing

**Table 2. Dosing of antibiotics for 2-step direct challenges**

Adapted from Accarino et al. J Allergy Clin Immunol Pract 2025;13:1018-1026.e1

Antibiotic	Patient weight	Challenge route	1 <sup>st</sup> -step dose	Observation timing	2 <sup>nd</sup> -step dose	Observation timing
Penicillins: amoxicillin, penicillin V,	All	Oral	50 mg amoxicillin	15 min	200 mg amoxicillin	60 min
Amoxicillin-clavulanate acid	All	Oral	50 mg amoxicillin component	15 min	200 mg amoxicillin component	60 min
Cephalexin	All	Oral	25 mg	15 min	225 mg	60 min
Cefdinir	<30kg	Oral	25 mg	15 min	100 mg	60 min
Cefdinir	≥30kg	Oral	25 mg	15 min	225 mg	60 min

**Table 3. Sign and Symptom that may arise During a Drug Challenge Recommendations for intervention**

Sign or symptom	Recommended Action
Anxiety	Examine and reassure; provide distraction activities
Throat itching	Visually examine throat and obtain vital signs. Absence of visual changes reassure patient no visible changes. Offer water; reassess in 15 minutes

Nausea, vomiting, abdominal discomfort	Examine the patient and obtain vital signs. Absence of other signs/symptoms, reassure the patient. Mild gastrointestinal symptoms can be an anticipated adverse effect of antibiotics
Itching without a visible rash	Examine the patient. During baseline evaluation determine if patient has dermatographism* or other rashes. Absence of visible changes reassure the patient; reassess in 15 min.
Urticaria alone	Document timeframe of development of symptoms in relation to ingestion of drug dose. Urticaria within 1 hour of drug ingestion may be due to the drug. Urticaria within 1-4 hours of dose possibly due to drug. If more than 4 hours has passed since ingestion of drug and development of urticaria, less likely drug caused the urticaria.  Treat urticaria with cetirizine and refer to allergy/immunology for follow up and clarification of drug allergy
Anaphylaxis (at least 2 system involvement) <ul style="list-style-type: none"> <li>• Diffuse hives/angioedema</li> <li>• Shortness of breath, wheezing, coughing, increased supplemental oxygen requirement</li> <li>• Shock</li> <li>• Weak pulse</li> <li>• Change in mental status</li> <li>• Nausea, vomiting, diarrhea</li> </ul>	Treat per Phoenix Children's Anaphylaxis Pathway, see inpatient section <ul style="list-style-type: none"> <li>• Epinephrine IM</li> <li>• If symptoms persist or worsen after 5 minutes, administer second dose epinephrine IM</li> </ul> Contact primary team  Symptomatic drug challenge, refer to allergy/immunology for outpatient follow up

\*dermatographism: raised, red whealts (wheals), often itchy after light pressure or scratching

**Table 4. Nursing and Provider Responsibilities**

Nursing responsibilities	Provider Responsibilities
<ul style="list-style-type: none"> <li>• Ensure consent form is signed, parent/guardian/legally authorized representative at bedside with patient</li> <li>• Ensure IM epinephrine and cetirizine (oral) are accessible (per unit protocol) *do not need to be at the bedside</li> <li>• Perform assessment and obtain baseline vital signs</li> <li>• Give initial oral dose of antibiotic as ordered</li> </ul>	<ul style="list-style-type: none"> <li>• Obtain consent for drug challenge (standard PC consent form to be used)(see Table 5)</li> <li>• Educate patient/family on what symptoms to notify healthcare team about <ul style="list-style-type: none"> <li>○ New rashes or skin changes</li> <li>○ Difficulty breathing or new cough</li> <li>○ Dizziness</li> <li>○ Change in behavior</li> <li>○ Vomiting</li> </ul> </li> </ul>

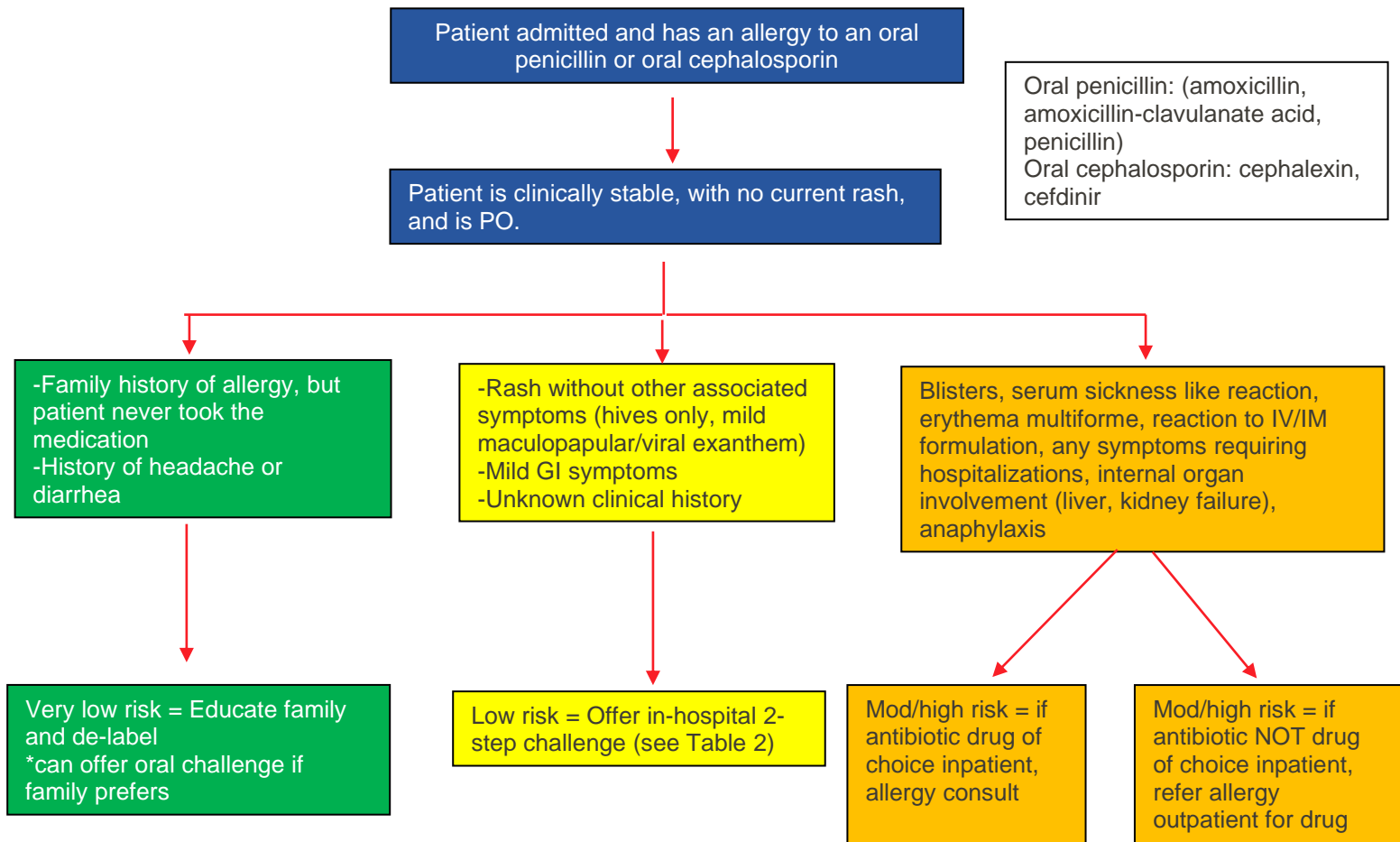
<ul style="list-style-type: none"> <li>• 15 minutes after first dose: repeat assessment, administer second dose of antibiotic</li> <li>• Perform final assessment 60 minutes after second dose of antibiotic given</li> <li>• If signs/symptoms develop: refer to table 3 for guidance</li> <li>• Patient remains asymptomatic, notify provider challenge is complete and patient developed no symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• Notify nurse of challenge recommendation to determine best time to perform (daytime, not prior to procedure, won't delay discharge)</li> <li>• Order direct challenge via inpatient drug challenge order set</li> <li>• If symptoms develop during challenge, document in EMR under allergy tab and in discharge summary; refer to allergy outpatient</li> <li>• If asymptomatic challenge:             <ul style="list-style-type: none"> <li>○ Remove allergy label via allergy tab: patient passed direct challenge to [abx] with no reaction on [date]</li> <li>○ Update discharge summary to include "patient had direct challenge to [abx] with no reaction on [date]. Allergy label to [abx] removed from chart. Patient and family educated that they may take this medication when clinically indicated"</li> <li>○ Discuss with patient and family safe to use this medication in the future when indicated</li> </ul> </li> </ul>
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**Table 5. Discussion Points for consenting before a Drug Challenge**

<p>Benefits of a Drug Challenge</p>	<ul style="list-style-type: none"> <li>• The benefits of a drug challenge is that we will know for sure if your child is able to tolerate the antibiotic. This can allow for treatment with the preferred antibiotic, sparing higher costs from the use of alternative antibiotics that may be less effective.</li> <li>• We are learning that many of the rashes or symptoms children develop when taking antibiotics are actually due to the illness or the combination of the illness, medication, and immune response. When they take the antibiotic in the future, they are able to take it without the symptoms happening again.</li> <li>• At Phoenix Children's, over 97% of children who completed antibiotic challenges do not have any symptoms. The children that did have symptoms reported a mild delayed rash.</li> </ul>
<p>Risks of a Drug Challenge</p>	<ul style="list-style-type: none"> <li>• There is a small chance you could develop symptoms during the drug challenge. Some of these symptoms may be related to the medication and others may not be.</li> <li>• Your health care team will be monitoring for any symptoms during the drug challenge and ready to treat as needed. Completing this in a medically supervised setting is the ideal place to be.</li> </ul>

Alternatives to a Drug Challenge	<ul style="list-style-type: none"><li>• If a drug challenge is not performed, alternative antibiotics may be available. However, these alternatives may have less ideal efficacy, safety and cost.</li></ul>
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**Penicillin/Cephalosporin Allergy De-Labeling Pathway**



## Scope

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Definition – Immediate drug allergy reactions typically present within 1 to 6 hours of drug exposure.<sup>[1]</sup> The signs and symptoms of immediate drug reactions include angioedema, bronchospasm, urticaria, and anaphylaxis.<sup>[1]</sup> Delayed reactions can include diffuse morbilliform eruptions and severe cutaneous adverse reactions that involved both cutaneous and systemic symptoms. Antibiotics are the most frequent drug allergy label and their presence can prevent use of first line antibiotic therapies, increased rates of surgical site infections, and other complications. The majority of drug allergy labels are unconfirmed and >95% of patients can tolerate the medications when re-exposed.

β-lactam drug allergy labels include drug allergy labels to penicillin and cephalosporin antibiotics.

Categories of risk include: (1) very low risk: Family history allergy, never took medication, headache, diarrhea; (2) low risk: Rash without other associated symptoms (hives only, mild maculopapular/viral exanthem), mild GI symptoms, unknown clinical history; and (3) od/high risk: Blisters, serum sickness like reaction, erythema multiforme, reaction to IV/IM formulation, any symptoms requiring hospitalizations, internal organ involvement (liver, kidney failure), anaphylaxis.

Inclusion criteria for this pathway includes adults, children, and infants with drug allergy labels to oral penicillin and oral cephalosporin antibiotics who are clinically stable. Exclusion criteria for this pathway includes patients who do not have drug allergy labels to penicillin and oral cephalosporin antibiotics (IM/IV penicillins and cephalosporins), unstable/critically ill/worsening clinical condition, current rash, and/or NPO status.

## Pathway Goals

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The goal of this clinical pathway is to address beta-lactam drug allergy labels for patients who are currently admitted. With proper evaluation, this will lead to de-labeling of beta-lactam allergy labels. This is cost-effective and will improve antibiotic stewardship by providing access to treatment with first line antibiotic options.

## Key Clinical Recommendations with Evidence Based Supporting Material

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Approximately 10% of US patients report an allergy to penicillin-class antibiotics, making it one of the most frequently reported drug allergies.<sup>[1]</sup> Of those, over 90% can tolerate penicillin (PCN) upon confirmatory testing.<sup>[1]</sup> The prevalence of these unconfirmed penicillin allergy labels leads to negative health outcomes and higher costs from the use of alternative antibiotics that are often less effective and lead to higher antibiotic resistance.<sup>[1]</sup> Studies have shown PCN allergy labels are associated with increased rates of infection with MRSA, vancomycin-resistant enterococcus, C. Difficile and increased surgical site infections.<sup>[1]</sup>

Another β-lactam drug class, cephalosporins, allergy is documented in about 0.5-2.0% of patients within the U.S.; 0.5-3% of children report an allergy to cephalosporin.<sup>[2]</sup> Growing data suggests that cephalosporin allergies can be risk stratified similar to penicillin allergy labels, with direct oral challenges being a possible option for low risk histories.<sup>[3,4]</sup>

For pediatric patients, viral exanthems and side effects of antibiotics are often inappropriately attributed as allergic reactions and patients are labeled as having drug allergies.<sup>[2]</sup>

The AAAAI/ACAAI Joint Practice 2022 Practice Parameters recommend patients with antibiotic drug allergy labels are proactively evaluated.<sup>[1]</sup> There is growing data suggesting direct drug challenge is the best diagnostic tool for pediatric patients without history of anaphylaxis or severe cutaneous adverse reaction (SCAR).

## Medication Recommendations

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Direct challenge dosing recommendations are included in Table 2. If the patient has symptoms concerning for anaphylaxis, refer to the Phoenix Children's Anaphylaxis Pathway and administer epinephrine as outlined in the pathway and below. Adjunct therapies are included in the anaphylaxis clinical pathway.

## Admission Criteria

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Inclusion criteria is for admitted patients with drug allergy labels to oral penicillin and oral cephalosporin antibiotics who are clinically stable.

## Discharge Criteria

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Discharge criteria include:

- As clinically indicated based on reason for admission
- Clinical resolution of serious symptoms should they occur with drug challenge
- Allergy/immunology outpatient consultation follow up for patients/patient families who:
  - decline inpatient direct challenge
  - are moderate/high risk
  - develop symptoms with drug challenge
  - aren't able to receive a drug challenge for external/other reasons during their inpatient stay

## Patient and Family Education/Discharge Planning

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1. [Drug Allergy Symptoms, Diagnosis, Treatment](#)
2. [Penicillin Allergy - FAQ](#)
3. [Why Most Kids Can Safely Undergo Amoxicillin Challenges](#)
4. [How to Conduct an Inpatient Oral Amoxicillin Challenge](#)

## References

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1. Khan DA, Banerji A, Blumenthal KG, et al. Drug allergy: A 2022 practice parameter update. *J Allergy Clin Immunol*. 2022;150(6):1333-1393. doi:10.1016/j.jaci.2022.08.028
2. Accarino JJO, Chow TG, Ramsey A, et al. A Guide to Pediatric Antibiotic Allergy Testing: A Report From the US Drug Allergy Registry. *J Allergy Clin Immunol Pract*. 2025;13(5):1018-1026.e1. doi:10.1016/j.jaip.2024.12.036
3. Sillcox C, Gabrielli S, O'Keefe A, McCusker C, Abrams EM, Eiwegger T, et al. Assessing Pediatric Cephalosporin Allergic Reactions Through Direct Graded Oral Challenges. *J Allergy Clin Immunol Pract*. 2024;12(1):156-64.e4.
4. Koo G, Sundar A, Woodward KB, Stone CA, Norton AE. Do not wait to challenge children: Results of a standard operating procedure for low-risk antibiotic challenges. *Ann Allergy Asthma Immunol*. 2025;134(6):736-8.
5. Phoenix Children's Anaphylaxis Clinical Pathway

## Pathway Champions

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P&T – approved 10/22/2025

CEC – Approved 12/18/2025