

Penicillin Allergy – Clinician Guide

Importance of Documenting an Accurate Allergy History¹⁻²

- About 10 percent of people in the United States report an allergy to penicillin, but at least 95 percent of them can safely tolerate beta-lactam antibiotics such as penicillins and cephalosporins.²
- Inaccurate penicillin allergy documentation can lead to use of second-line antibiotics that may be less effective or more toxic.³⁻⁵
- Take an allergy history to (1) clarify the type of allergic reaction, (2) assess whether the patient can receive penicillin or related antibiotics, and (3) determine the need for referral to an allergist for further evaluation.

Of the 10% of the population with allergies

- 95% can safely tolerate beta-lactam antibiotics - penicillins and cephalosporins
- 5% need second-line antibiotics



Questions To Ask When Obtaining an Allergy History⁵

- Do you/your child have any allergies to any antibiotics? Which antibiotics?
- What was the reaction? How soon after taking the antibiotic did the reaction occur?

Reaction to Penicillin	Documentation	Next Steps
Swelling of the throat, tongue, lips, or eyes; wheezing or trouble breathing; or low blood pressure.	Anaphylaxis	Do not rechallenge with penicillins without an allergy consult. OK to administer cephalosporins.
Rash with raised, itchy bumps +/- white centers, appearing within approximately 6 hours after an antibiotic was started.	Hives	Do not rechallenge with penicillins without an allergy consult. OK to administer cephalosporins.
Rash that was peeling or blistering.	Stevens-Johnson–like syndrome	Do not rechallenge with beta-lactams without allergy consult.
Rash that appeared at least 2 days after the antibiotic started.	Non-urticarial rash	Rechallenge; if possible, use a different beta-lactam agent.
Side effects such as nausea, vomiting, diarrhea, headaches, dizziness, or fatigue.	Do not document allergy; remove allergy label	Rechallenge and manage symptoms.

3. Have you/your child taken the antibiotic since, or seen an allergist or had a penicillin skin test?

- If the patient has taken the same antibiotic without a subsequent reaction, do not document an allergy.
- If the patient has had a negative skin test for penicillin, the patient can be given a beta-lactam. Note that the patient may still develop a non-urticarial rash if that was the original reaction.
- Patients with past Stevens-Johnson syndrome, toxic epidermal necrolysis, or DRESS (drug rash with eosinophilia and systemic symptoms) should not be given the triggering antibiotic (or antibiotic class) again without a discussion with an allergist.²
- If the patient has taken the same antibiotic without a subsequent reaction or an allergist has concluded that the patient no longer has an allergy, inform the patient that they no longer have the allergy. Inform patients with a negative skin test for penicillin that they can be given beta-lactam antibiotics.
- Remove allergy labels in the electronic health record (delabeling) if the patient does not have the allergy.

4. Have you/your child been able to take other antibiotics? Which ones?

- Review the medical record and ask about experiences with other beta-lactam antibiotics such as amoxicillin, amoxicillin-clavulanate (Augmentin®), cephalexin (Keflex®), cefadroxil (Duricef®), cefuroxime (Ceftin, Zinacef®), cefdinir (Omnicef), cefpodoxime (Vantin®), cefixime (Suprax®), ceftriaxone (Rocephin®), or ceftazolin (Ancef). Consider using both generic and brand names for antibiotics.*
- If the patient has tolerated taking other beta-lactams previously, in most cases he/she can take them again. Document antibiotics he/she tolerated previously in the chart.

5. How long ago did you/your child have the reaction?

- If the reaction occurred more than 5 years ago, the patient may no longer have an allergy because even true penicillin allergies can go away over time. Consider consulting with an allergist for skin testing.²

**Note: Brand names may be registered trademarks and are named as examples and not for endorsement.*

References

1. Khan DA, Banerji A, Blumenthal KG, et al. Drug allergy: A 2022 practice parameter update. *J Allergy Clin Immunol*. 2022 Dec;150(6):1333-93. Epub 2022 Sep 17. PMID: 36122788.
2. Centers for Disease Control and Prevention. Clinical features of penicillin allergy. August 25, 2025. <https://www.cdc.gov/antibiotic-use/hcp/clinical-signs/index.html>. Accessed March 17, 2026.
3. MacFadden DR, LaDelfa A, Leen J, et al. Impact of reported beta-lactam allergy on inpatient outcomes: A multicenter prospective cohort study. *Clin Infect Dis*. 2016 Oct 1;63(7):904-10. Epub 2016 Jul 11. PMID: 27402820.
4. Blumenthal KG, Ryan EE, Li Y, et al. The impact of a reported penicillin allergy on surgical site infection risk. *Clin Infect Dis*. 2018 Jan 18;66(3):329-36. PMID: 29361015.
5. Blumenthal KG, Peter JG, Trubiano JA, et al. Antibiotic allergy. *Lancet*. 2019 Jan 12;393(10167):183-98. Epub 2018 Dec 14. PMID: 30558872.

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