



# BETA-LACTAM DRUG CHALLENGE Guidance Document

The [Beta-Lactam Allergy Risk Assessment Pathway](#) and the [Cross Reactivity Side-Chain Chart](#) should be utilized first when assessing a beta-lactam allergy label. This supplemental guidance document is intended to support clinicians **if a beta-lactam drug challenge is being considered** in a clinically stable patient with a low-risk beta-lactam allergy label. Guidance provided is not all inclusive. Clinical reasoning and clinical judgment should be applied throughout this process. For more information on managing beta-lactam allergy patients, visit: [NM ADSP Allergy Resources](#).

## WHO to consider for a drug challenge with a beta-lactam

*Drug challenges are considered the reference standard for determining tolerance to a drug.  
Most drug challenges in the selected low-risk categories may be performed without Allergy consultation.  
Patient-provider shared decision-making is advised*

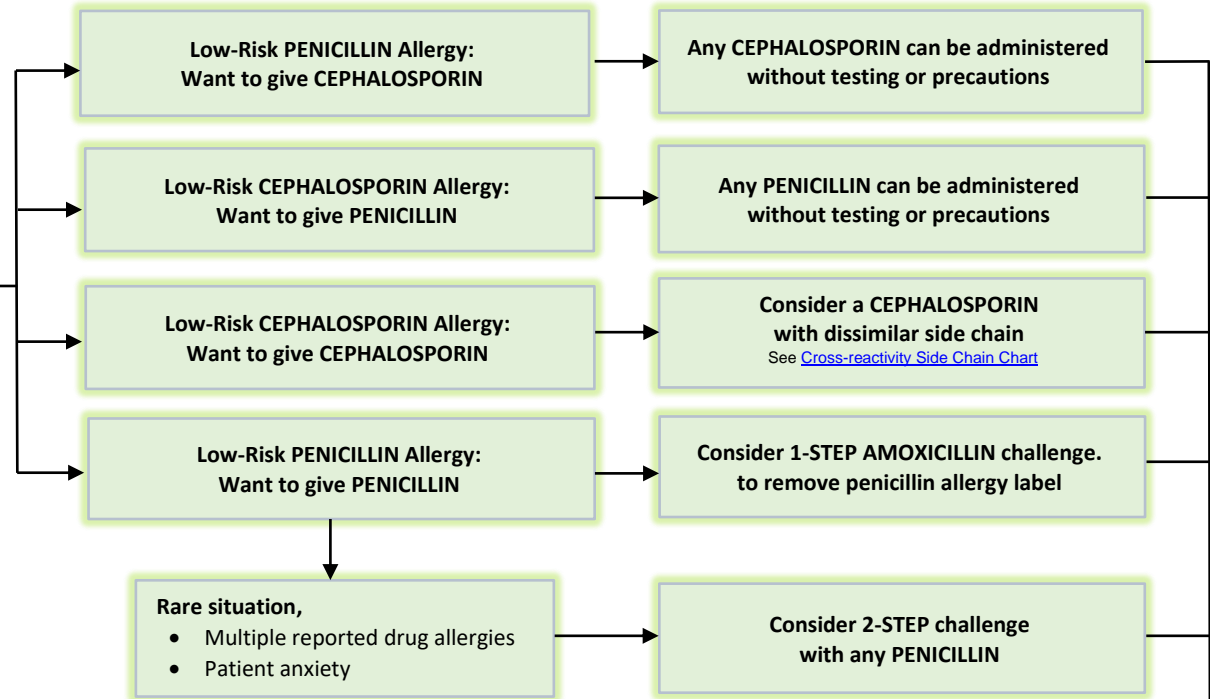
**LOW RISK**  
History of a **NONSEVERE (NONANAPHYLACTIC)** or **UNKNOWN PCN or CEPH** allergy  
**>5 years ago**

**Benign cutaneous rash**  
*Maculopapular exanthem or morbilliform cutaneous eruption occurring several hours to days after initial therapy without mucus membrane\* involvement, lasting several days*

**Mild remote urticarial rash**  
*Transient hives lasting < 24 hrs without systemic symptoms and no blistering or exfoliation of the skin or mucus membrane\* involvement*

**Unknown allergy**  
*Not aware of the allergy label or clinical signs or symptoms of a reaction*

\* Mucus membrane: the eyes, mouth, nose, genitourinary.



### 1-STEP Give Full PO or IV dose

Observe with vitals/exam check  
30-minutes after start of oral dose  
60-minutes after start of IV infusion

### 2-STEP Step 1 → Give 10% PO or IV dose Step 2 → Give 90% PO or IV dose

Observe with vitals/exam check  
Dose-1: 30-minutes after start of oral dose  
60-minutes after start of IV infusion  
Dose-2: 30-minutes after start of oral dose  
60-minutes after start of IV infusion

*See page 2 for order set process, emergency medications, and administration tips*

### Terminate drug challenge if:

- Flushing, vomiting, cough, abdominal cramping, itching, fever, mouth or eye soreness
- Rash, hives (urticaria), angioedema, wheezing, hypoxia, hypotension, anaphylaxis

### Update allergy documentation in EPIC Inform primary team/pharmacist Discuss with patient and/or care-giver

- Indicate tolerance or intolerance to drug challenge.  
*Ex. Tolerated ceftriaxone drug challenge on 7.17.24*
- **DELABEL** allergy if tolerance to the culprit beta-lactam is confirmed.  
*Ex. Patient is no longer allergic. Tolerated amoxicillin drug challenge on 11.20.24*

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## Contraindications to drug challenges

Severe cutaneous adverse drug reactions  
SJS/TEN, DRESS, AGEP  
Drug-induced neutrophilic dermatosis  
Sweet's syndrome  
Drug-induced autoimmune diseases  
Bullous pemphigoid  
Pemphigus vulgaris  
Linear IgA bullous disease  
Drug induced lupus  
Other cutaneous drug reactions  
Generalized bullous FDE  
Exfoliative dermatitis

Severe drug anaphylaxis  
Organ-specific drug reactions  
Cytopenias (anemia, neutropenia, leukopenia, thrombocytopenia)  
Drug induced liver injury  
Nephritis  
Pneumonitis  
Meningitis  
Pancreatitis  
Drug-induced vasculitis  
Leukocytoclastic vasculitis  
Eosinophilic granulomatosis with polyangiitis  
Angiotensin-converting enzyme inhibitor angioedema

SJS: Stevens-Johnson syndrome (SJS); TEN: toxic epidermal necrolysis; DRESS: drug reaction with eosinophilia and systemic symptoms, AGEP: acute generalized exanthematus pustulosis; FDE: Fixed drug eruption

### A. Order-set process

#### 1. Beta-lactam challenge orders in EPIC

**Antibiotics/Anti-infective ORAL Beta-Lactam Drug Challenge Panels**

**Antibiotics/Anti-infective IVPB Beta-Lactam Drug Challenge Panels**

2. The following emergency medications will be ordered and made available with each beta-lactam drug challenge. Medications are available in site-specific locations (eg. unit Omnicells). **If any of the following medications are required, immediately stop beta-lactam drug challenge and call Rapid Response, if available.**
  - a. DiphenhydrAMINE (BENADRYL) injection; Dose: 50 mg IV Push ONCE
  - b. EPINEPHrine (ADRENALIN/EpiPEN) 1 mg/mL (1:1,000) injection; Dose: 0.3 mg IM ONCE
  - c. MethyLPREDNISolone sodium succinate (SOLU-MEDROL) injection; Dose: 125 mg IV Push ONCE
3. Systemic symptoms: diphenhydramine, epinephrine, and methylprednisolone are to be used in combination if symptoms of anaphylaxis, such as full body hives, flushing or angioedema with shortness of breath, wheezing, chest pain, hypotension, or severe nausea, vomiting, diarrhea are present.
4. Mild symptoms: diphenhydramine may be used alone for new onset runny nose, itching, congestion, mild nausea/discomfort, or a few scattered hives.

## B. Administration

1. According to this document, guidance of beta-lactam drug challenges may be performed in clinically stable patients with a low-risk beta-lactam allergy label in a healthcare setting. ICU admission is not required.
2. Receive from pharmacy or site-specific locations (eg. Omnicells)
  - a. 1-step → full therapeutic dose of the beta-lactam challenge agent.
  - b. 2-step → 10% dose and remaining 90% dose of the beta-lactam challenge agent.
  - c. Bedside emergency medicines should be ordered and made available in case of reaction.
3. IV and PO drug challenge administration
  - a. Each exam check should include examination of vitals, oral-pharyngeal, respiratory and skin exam at baseline and after each dose.
    - i. Observe: 30-minutes after start of oral dose or 60-minutes after start of IV infusion.
  - b. Instruct patient to alert nurse or push the call button with any questions or concerns during the drug challenge process.
  - c. Ordering provider should be available during administration of drug challenge.
  - d. Terminate the drug challenge and contact the ordering provider if patient poses any concerns or if any of the following are encountered: flushing, vomiting, cough, abdominal cramping, itching, fever, mouth or eye soreness, rash, hives (urticaria), angioedema, wheezing, hypoxia, hypotension, anaphylaxis.
    - i. If available, call rapid response team immediately if emergency medications are required.
  - e. If observation steps and vitals are normal, then the drug challenge is tolerated and the patient can safely receive the full dose of the drug at regularly scheduled intervals as ordered.
  - f. Notify primary team and pharmacist of results.
  - g. Update allergy documentation in EPIC, indicating tolerance or intolerance to the beta-lactam drug challenge.
    - i. Ex. *Tolerated ceftriaxone drug challenge on 7.17.24.*
  - h. Delabel allergy if tolerance to the culprit beta-lactam is confirmed with drug challenge.
    - i. Ex. *Patient is no longer allergic to amoxicillin. Tolerated amoxicillin drug challenge on 11.20.24.*

## RECIPES FOR 2-STEP ORAL BETA-LACTAM DRUG CHALLENGE DOSES

Antimicrobials Oral suspension/solution	STOCK SOLUTION	Stock Concentration (mg/mL)	10% total dose Syringe 1	90% total dose Syringe 2
Penicillin VK	500 mg (10 mL)	50	50 mg per 1 mL	450 mg per 9 mL
Amoxicillin	500 mg (10 mL)	50	50 mg per 1 mL	450 mg per 9 mL
Amoxicillin-clavulanate (250-62.5 mg/5 mL, 4:1)	500 mg (10 mL)	50	50 mg per 1 mL	450 mg per 9 mL
Amoxicillin-clavulanate (200-28.5 mg/5 mL, 7:1)	875 mg (21.88 mL)	40	87.5 mg per 2.18 mL	787.5 mg per 19.7 mL
Amoxicillin-clavulanate (400-57 mg/5 mL, 7:1)	875 mg (10.94 mL)	80	87.5 mg per 1.09 mL	787.5 mg per 9.85 mL
Cephalexin (1 <sup>st</sup> gen) (Keflex)	500 mg (10 mL)	50	50 mg per 1 mL	450 mg per 9 mL
Cefadroxil (1 <sup>st</sup> gen) (Duricef)	500 mg (10 mL)	50	50 mg per 1 mL	450 mg per 9 mL
Cefuroxime (2 <sup>nd</sup> gen)* (Ceftin)	500 mg (50 mL)	10	50 mg per 5 mL	450 mg per 45 mL
Cefpodoxime (3 <sup>rd</sup> gen) (Vantin)	100 (5 mL)	20	10 mg per 0.5 mL	90 mg per 4.5 mL

\*Compounded suspension – contact ADSP for alternative challenge options, if needed.

## RECIPES FOR 2-STEP IV BETA-LACTAM DRUG CHALLENGE DOSES

IV Antimicrobials	STOCK BAG (empty vial/flex, TV bag)		Diluent	Final Conc. Stock Bag	10% total dose Bag 1	90% total dose Bag 2
Ampicillin	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Amp-sulbactam	1500 mg	TV 100 mL	NS	15 mg per mL	150 mg per 100 mL	1350 mg per 100 mL
Cefazolin	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Cefepime	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Cefiderocol	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Cefoxitin	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Ceftaroline	600 mg	TV 100 mL	NS	6 mg per mL	60 mg per 100 mL	540 mg per 100 mL
Ceftazidime	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Ceftolozane/tazo	1500 mg	TV 100 mL	NS	15 mg per mL	150 mg per 100 mL	1350 mg per 100 mL
Ceftriaxone	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Cefuroxime	1500 mg	TV 100 mL	NS	15 mg per mL	150 mg per 100 mL	1350 mg per 100 mL
Ertapenem	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Meropenem	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Nafcillin	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
Oxacillin	1000 mg	TV 100 mL	NS	10 mg per mL	100 mg per 100 mL	900 mg per 100 mL
PCN G-K	1 Million Units (Mu)	TV 100 mL	NS	0.01 Mu per mL	0.1 Mu per 100 mL	0.90 Mu per 100 mL
PCN G-sodium	1 Million Units (Mu)	TV 100 mL	NS	0.01 Mu per mL	0.1 Mu per 100 mL	0.90 Mu per 100 mL
Pip-tazobactam	4.5 gram	TV 100 mL	NS	0.045 g per mL	0.45 g per 100 mL	4.05 g per 100 mL

TV = Total Volume; NS = Normal Saline (0.9% Sodium Chloride)