



GUIDELINE	
Beta-lactam Allergy Guideline	
Scope (Staff):	Medical, Nursing, Pharmacy
Scope (Area):	Perth Children’s Hospital (PCH)

This document should be read in conjunction with this [DISCLAIMER](#)

Aim

To help guide antibiotic selection in children with allergies, a risk stratification approach has been adopted based on the current available evidence.

Background

Beta-lactams are the most commonly used antibiotics and include penicillins (e.g. amoxicillin, piperacillin, benzylpenicillin), cephalosporins (e.g. cefalexin, ceftriaxone) and carbapenems (e.g. meropenem). Similarly Beta-lactam allergies are the most frequently reported antibiotic reactions in children.

Recent data support that the majority of patients who are ‘labelled’ with a Beta-lactam allergy can in fact tolerate the antibiotic in question without the need for skin testing.^{1,2} Moreover, the use of alternative antibiotics for patients labelled with allergy leads to poorer clinical outcomes, prolonged hospitalisation, increased costs and increased adverse effects.³⁻⁶

The risk stratification system used in this guideline is a safe but simplified approach to a very complex issue. An individualised approach may be required in certain settings.

Risk Classification

Beta-lactam allergies can be classified into high risk and low risk based on the likelihood of subsequent reaction upon exposure.^{7,8}

- **No risk:** no previous reaction; non-immune mediated intolerances (e.g. nausea, diarrhoea); family history of Beta-lactam allergy.
- **Low risk:** a delayed rash (>1hr after initial exposure) without mucosal or systemic involvement (without respiratory distress and/or cardiovascular compromise).
- **High risk:** an immediate rash (<1hr after exposure); anaphylaxis; severe cutaneous adverse reaction {e.g. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) and Stevens – Johnson syndrome (SJS) / Toxic Epidermal Necrolysis (TEN)} or other severe systemic reaction.

Management

The Children's Antimicrobial Management Programme (ChAMP) guidelines stratify recommendations based on Beta-lactam allergy and risk classification.

Low risk: alternate antibiotic as per ChAMP* AND

- **>1yr since reaction:** consider oral challenge for PCH inpatients if stable[#]
- **<1yr since reaction:** immunology outpatient referral to explore allergy / de-labelling

- **High risk:** immunology referral, alternate antibiotic as per ChAMP**

**Refer to individual guidelines for specific antibiotic recommendations*

#Immunology inpatient consult required for all oral challenges

The majority of true Beta-lactam allergies are mediated by reactivity to the side chains present on the beta-lactam ring. Antibiotics with similar side chains in both the penicillin and cephalosporin classes carry a higher risk of cross reaction (Figure 1). There is a very low risk of cross reaction (<2%) if a beta-lactam with a different side chain is administered.

**For high risk patients a non-Beta-lactam antibiotic is recommended. Refer to individual guidelines for specific antibiotic recommendations. In selected patients with a history of high-risk allergy, a Beta-lactam from another subclass (e.g. a cephalosporin or carbapenem) may be considered in discussion with immunology.

Oral Challenge

At present inpatient oral challenges are reserved for low-risk patients admitted to PCH in discussion with immunology – for other patients labelled with Beta-lactam allergy complete an outpatient referral to PCH immunology.

Please refer to: [Antibiotic Challenge \(Immunology\) Protocol](#)

Figure 1: Antibiotics grouped by similar side chain⁹.

	PENICILLIN G	PENICILLIN VK	AMPICILLIN	AMOXICILLIN	SEMI-SYNTHETIC ANTISTAPH PEN	PIPERACILLIN-TAZOBACTAM	CEFADROXIL	CEFAZOLIN	CEPHALEXIN	CEPROZIL	CEPHALOTHIN ^a	CEFOXITIN ^a	CEFOTETAN	CEFAMANDOLE	CEFUROXIME	CEFEPIME	CEFTRIAXONE	CEFOTAXIME	CEFTAZIDIME	CEFDINIR	CEFIXIME	CEFTAROLINE	CEFTOBIPROLE	CEFTOZOLANE-TAZOBACTAM
PENICILLIN G	■	R1*									▲	▲												
PENICILLIN VK	R1*	■																						
AMPICILLIN			■	R1*			R1*	R1*	R1*	R1*														
AMOXICILLIN			R1*	■			R1*	R1*	R1*	R1*														
SEMI-SYNTHETIC ANTISTAPH PEN					■																			
PIPERACILLIN-TAZOBACTAM						■																		
CEPHALOSPORIN 1st GENERATION																								
CEFADROXIL			R1*	R1*			■	R1*	R1*	R1*														
CEPROZIL			R1*	R1*			R1*	R1*	R1*	■														
CEFAZOLIN			R1*	R1*			R1*	■	R1*	R1*														
CEPHALEXIN			R1*	R1*			R1*	R1*	■	R1*														
CEPHALOTHIN	▲										■	R1*										R2		
CEPHALOSPORIN 2nd GENERATION																								
CEFOXITIN	▲										R1*	■			R2									
CEFOTETAN													■	R2										
CEFAMANDOLE													■	R2	■									
CEFUROXIME												R2			■	R1°	R1°	R1°	R1°					
CEPHALOSPORIN 3rd/4th/5th GENERATION																								
CEFEPIME															■	R1*	R1*							
CEFTRIAXONE															R1*	■	R1*							
CEFOTAXIME																■	R1*							
CEFTAZIDIME																		■						
CEFDINIR																				■	R1*			
CEFIXIME																					■	R1*		
CEFTAROLINE																						■	R1*	R1*
CEFTOBIPROLE																						■	R1*	R1*
CEFTOZOLANE-TAZOBACTAM																						■	R1*	R1*
MONOBACTAM																								
AZTREONAM																						■	R1*	

Legend

^a *In vitro* data proposed cross-reactivity between cefoxitin and cephalothin based upon shared but not shared R1

Exactly the same drug



R1 – Identical R1 side chain



R1* – Almost Identical R1 side chain



R2 - Identical R2 and non-identical R1 with some cross-reactivity



R1° Non-identical R1 with some clinical cross-reactivity



Shared class specific ring but no shared side chain structure



No shared class specific ring, only shared beta-lactam ring



No shared cross reactivity with beta-lactam ring



Related internal policies, procedures and guidelines


[Allergic Reactions and Anaphylaxis – Management for Planned Allergy Challenges \(Immunology\)](#)

[Antibiotic Challenge](#)

References

1. Vezir E, Dibek Misirlioglu E, Civelek E, Capanoglu M, Guvenir H, Ginis T, Toyran M, Kocabas CN. Direct oral provocation tests in non-immediate mild cutaneous reactions related to beta-lactam antibiotics. *Pediatric Allergy and Immunology*. 2016 Feb;27(1):50-4.
2. Mustafa SS, Conn K, Ramsey A. Comparing direct challenge to penicillin skin testing for the outpatient evaluation of penicillin allergy: A randomized, controlled trial. *The Journal of Allergy and Clinical Immunology: In Practice*. 2019 Jun 3.
3. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. *The Lancet*. 2018 Dec 14.
4. Huang KH, Cluzet V, Hamilton K, Fadugba O. The impact of reported beta-lactam allergy in hospitalized patients with hematologic malignancies requiring antibiotics. *Clinical Infectious Diseases*. 2018 Jan 16;67(1):27-33.
5. Charneski L, Deshpande G, Smith SW. Impact of an antimicrobial allergy label in the medical record on clinical outcomes in hospitalized patients. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2011 Aug;31(8):742-7.
6. Abrams EM, Atkinson AR, Wong T, Ben-Shoshan M. The importance of delabeling β -lactam allergy in children. *The Journal of pediatrics*. 2019 Jan 1;204:291-7.
7. Siew LQ, Li PH, Watts TJ, Thomas I, Ue KL, Caballero MR, Rutkowski K, Till SJ, Pillai P, Haque R. Identifying low-risk beta-lactam allergy patients in a UK tertiary centre. *The Journal of Allergy and Clinical Immunology: In Practice*. 2019 Mar 25.
8. Stevenson B, Trevenen M, Klinken E, Smith W, Yuson C, Katelaris C, et al. Multicenter Australian Study to Determine Criteria for Low- and High-Risk Penicillin Testing in Outpatients. *The journal of allergy and clinical immunology in practice*. 2019.
9. Trubiano JA, Stone CA, Grayson ML, Urbancic K, Slavin MA, Thursky KA, Phillips EJ. The 3 Cs of antibiotic allergy—classification, cross-reactivity, and collaboration. *The Journal of Allergy and Clinical Immunology: In Practice*. 2017 Nov 1;5(6):1532-42.

This document can be made available in alternative formats on request for a person with a disability.

File Path:	W:\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\ChAMP				
Document Owner:	Infectious Diseases Head of Department				
Reviewer / Team:	Children's Antimicrobial Management Program				
Date First Issued:	March 2020	Last Reviewed:	New	Review Date:	March 2023
Approved by:	Medication Safety Committee			Date:	March 2020
Endorsed by:	Drug and Therapeutics Committee			Date:	March 2020
Standards Applicable:	NSQHS Standards: 				
Printed or personally saved electronic copies of this document are considered uncontrolled					