



GUIDELINE

Beta-lactam Allergy Guideline

Scope (Staff):	Medical, Nursing, Pharmacy
Scope (Area):	Perth Children's Hospital (PCH)

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

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 (> 1 hr after initial exposure) without mucosal or systemic involvement (without respiratory distress and/or cardiovascular compromise).
- **High risk:** an immediate rash (< 1 hr 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 empiric guidelines AND:
 - **If ≥ 1 year since reaction:** consider oral challenge for PCH inpatients if stable in discussion with Immunology
 - **If < 1 year since reaction:** Immunology outpatient referral to explore allergy / de-labelling

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

- **High risk:** Immunology referral, alternate antibiotic as per ChAMP empiric guidelines.
 - For high risk patients a non-Beta-lactam antibiotic is generally 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 if alternative options are limited.

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.

Figure 1: Antibiotics grouped by similar side chain⁹.

	PENICILLIN G	PENICILLIN VK	AMPICILLIN	AMOXICILLIN	SEMI-SYNTHETIC ANTI-STAPH PEN	PIPERACILLIN-TAZOBACTAM	CEFADROXIL	CEFAZOLIN	CEFALEXIN	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 ANTI-STAPH PEN					■																			
PIPERACILLIN-TAZOBACTAM						■																		
CEPHALOSPORIN 1st GENERATION																								
CEFADROXIL			R1*	R1*			■	R1*	R1*	R1*														
CEFPROZIL			R1*	R1*			R1*	R1*	R1*	■														
CEFAZOLIN			R1*	R1*			R1*	■	R1*	R1*														
CEFALEXIN			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

▲ *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

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



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

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



Related CAHS internal policies, procedures and guidelines

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

[Antibiotic Challenge](#)

References and related external legislation, policies, and guidelines (if required)

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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.
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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.
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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.

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 <h2 style="margin: 0;">Healthy kids, healthy communities</h2> <div style="display: flex; justify-content: space-around; margin: 0;"> Compassion Excellence Collaboration Accountability Equity Respect </div> <p style="margin: 0; font-size: small;">Neonatology Community Health Mental Health Perth Children’s Hospital</p>			