

Appendix A: β -lactam Rechallenge Risk Assessment Tables and Cross-Reactivity Chart

Table 1. PENICILLIN Allergy and Beta-lactam Rechallenge

Re-challenge	Allergy Risk		Severe non-IgE
	Low Risk ¹	High Risk ² (Anaphylaxis)	
Penicillin	Evaluate eligibility for Amoxicillin PO Challenge to de-label allergy*	Do not rechallenge	Do not rechallenge: SJS/TEN, DRESS, serum sickness, hemolytic anemia, acute interstitial nephritis or drug induced liver failure*
Cephalosporin	May rechallenge with structurally dissimilar side chain (see chart)		
Carbapenem	May safely rechallenge		
Aztreonam	May safely rechallenge		

*Refer to Policy 43008 for additional considerations

Table 2. CEPHALOSPORIN Allergy and Beta-lactam Rechallenge

Re-challenge	Allergy Risk		Severe non-IgE
	Low Risk ¹	High Risk ² (Anaphylaxis)	
Penicillin	May rechallenge with structurally dissimilar side chain (see chart)		Do not rechallenge: SJS/TEN, DRESS, serum sickness, hemolytic anemia, acute interstitial nephritis or drug induced liver failure*
Cephalosporin	May rechallenge with structurally dissimilar side chain (see chart)	Do not rechallenge	
Carbapenem	May safely rechallenge		
Aztreonam	May rechallenge with structurally dissimilar side chain (see chart)		

*Refer to Policy 43008 for additional considerations

1. Low Risk Definition:

- Remote (>10 years) unknown reaction
- Patient denies allergy but it is on record
- Self-limited rash or pruritus
- Urticaria (hives) with no other symptoms (>5 years since reaction)
- Tolerated structurally dissimilar cephalosporins in the past

2. High Risk Definition: Features of anaphylaxis, including but not limited to: respiratory symptoms, angioedema/swelling, and/or cardiovascular symptoms (syncope/passing out, arrhythmia)

*The above recommendations are based on available literature and national guidelines.
These are not intended to replace physician clinical judgement based on patient-specific factors.*

Appendix A: β -lactam Rechallenge Risk Assessment Tables and Cross-Reactivity Chart

The β -lactam Cross-Reactivity Chart below should be used in conjunction with the risk assessment tables on page 1.

Abx Allergy \rightarrow	Penicillin	Amoxicillin	Nafcillin	Piperacillin	Cephalexin*	Cefazolin	Cefoxitin	Cefuroxime	Cefdinir	Cefpodoxime	Ceftriaxone	Ceftazidime	Cefepime	Ceftolozane	Ceftaroline	Cefiderocol	Carbapenem	Aztreonam
Abx Ordered \downarrow	Penicillin	Amoxicillin	Nafcillin	Piperacillin	Cephalexin*	Cefazolin	Cefoxitin	Cefuroxime	Cefdinir	Cefpodoxime	Ceftriaxone	Ceftazidime	Cefepime	Ceftolozane	Ceftaroline	Cefiderocol	Carbapenem	Aztreonam
Penicillin	Black	Red	Red	Red	Red	White	White	White	White	White	White	White	White	White	White	White	White	White
Amoxicillin	Red	Black	Red	Red	Red	White	White	White	White	White	White	White	White	White	White	White	White	White
Nafcillin	Red	Red	Black	Red	White	White	White	White	White	White	White	White	White	White	White	White	White	White
Piperacillin	Red	Red	Red	Black	Red	White	White	White	White	White	White	White	White	White	White	White	White	White
Cephalexin*	Red	Red	White	Red	Black	White	White	White	White	White	White	White	White	White	White	White	White	White
Cefazolin	White	White	White	White	White	Black	White	White	White	White	White	White	White	White	White	White	White	White
Cefoxitin	White	White	White	White	White	White	Black	Red	White	White	White	White	White	White	White	White	White	White
Cefuroxime	White	White	White	White	White	White	Red	Black	White	Red	Red	Red	Red	Red	White	White	White	White
Cefdinir	White	White	White	White	White	White	White	White	Black	White	White	White	White	White	White	White	White	White
Cefpodoxime	White	White	White	White	White	White	White	Red	White	Black	Red	Red	Red	Red	White	White	White	White
Ceftriaxone	White	White	White	White	White	White	White	Red	White	Red	Black	Red	Red	Red	White	White	White	White
Ceftazidime	White	White	White	White	White	White	White	Red	White	Red	Red	Black	Red	Red	White	Red	White	Red
Cefepime	White	White	White	White	White	White	White	Red	White	Red	Red	Red	Black	Red	White	White	White	White
Ceftolozane	White	White	White	White	White	White	White	Red	White	Red	Red	Red	Red	Black	White	White	White	White
Ceftaroline	White	White	White	White	White	White	White	White	White	White	White	White	White	White	Black	White	White	White
Cefiderocol	White	White	White	White	White	White	White	White	White	White	White	Red	White	White	White	Black	White	Red
Carbapenem	White	White	White	White	White	White	White	White	White	White	White	White	White	White	White	White	Black	White
Aztreonam	White	White	White	White	White	White	White	White	White	White	White	White	Red	White	White	Red	White	Black

*Note: cefaclor, cefadroxil, cefprozil, and cephalexin share identical side chains.

- Structurally dissimilar side chain
- Structurally similar or identical side chain
- Same drug

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