Allergic Cross-reactivity Among Beta-lactam Antibiotics: An Update

Introduction

Beta-lactams are first-line treatments for a number of common infections. Patients allergic to penicillins are often treated as also being allergic to cephalosporins. Historical data have suggested that up to 10% of patients allergic to penicillins are also allergic to cephalosporins.\(^1,2\) In addition, cross-reactivity with penicillins and carbapenems has been cited at nearly 50%, with little scientific data to back up the claim. It’s easy to see why penicillin-allergic patients might be prescribed a second-line therapy that is less effective, more expensive, more toxic, or has a broader spectrum of activity than necessary.\(^3\) More recent data suggest that the true incidence of allergic cross-reactivity between the penicillins and other beta-lactam antibiotics is much lower than originally reported.\(^3,4\) This is important for a number of reasons, including the fact that some non beta-lactam alternative therapies, such as macrolides for otitis media, are no longer preferred options due to high bacterial resistance rates.\(^5\) This document reviews the types of penicillin allergies, assesses current data on true cross-reactivity between penicillins and other beta-lactams, and provides treatment considerations.

Types of Penicillin Allergies

Approximately 10% of the population will report a history of an allergy to penicillin. However, up to 90% of these individuals will be able to tolerate treatment with a penicillin and further, will not have a positive skin test. The designation of “penicillin allergy” is not necessary for these individuals.\(^3,6\)

Several types of allergic reactions to penicillins are described in the medical literature.\(^7,8\) One method of classifying penicillin allergies is as follows:

- immediate/accelerated (type I reactions);
- late (type II, III, and IV reactions);
- other (idiopathic reactions).

Immediate/accelerated reactions typically occur within one hour (immediate) or one to 72 hours (accelerated) after administration of a penicillin. These reactions are mediated by penicillin-specific IgE antibodies. Clinical signs of an immediate or accelerated reaction include anaphylaxis, a drop in blood pressure, swelling of the larynx, wheezing, angioedema, and hives or an itchy rash.

Late reactions tend to occur more than 72 hours after exposure to a penicillin. As previously mentioned, these are sometimes referred to as type II, III, and IV reactions. Type II reactions are mediated by IgG antibodies and complement. Clinical signs include increased red blood cell and platelet clearance by the lymphoreticular system. Type III reactions are mediated by IgG and IgM immune complexes. Clinical signs include serum sickness and tissue injury. Type IV reactions are mediated through an unknown mechanism. A clinical sign is contact dermatitis.

Idiopathic reactions also tend to occur after 72 hours of exposure to a penicillin. Idiopathic reactions are mediated through unknown mechanisms. Clinical signs include a maculopapular or morbilliform rash which can progress to Stevens-Johnson syndrome.

An example of an idiopathic reaction is the rash that can occur following administration of drugs such as ampicillin and amoxicillin in patients with an Epstein-Barr virus (EBV) infection. The risk appears to be highest in patients who receive ampicillin.\(^9\) This rash typically occurs seven to 14 days after beginning antibiotic therapy. It is described as a red, itchy, maculopapular rash, involving primarily the upper extremities and trunk. The rash can be accompanied by fever, swelling of the lips and eyelids, diarrhea, and joint pain. Patients who develop this rash are likely to be able to tolerate penicillins in the future.\(^3,9,10\)
**Diagnosis of a Penicillin Allergy**

Prior to treating a patient who reports a penicillin allergy, a thorough history of the patient’s allergy should be obtained. Examples of questions the patient should be asked include the following:\(^{3,8}\)

- How old were you when the reaction occurred?
- Please describe the reaction.
- When did the reaction occur? After the first dose? After the tenth dose?
- How was the penicillin administered? Orally? Intravenously?
- Were you taking any other medications at the same time?
- When the penicillin was stopped, what happened?
- Have you since taken a penicillin, cephalosporin, carbapenem, or monobactam?

Only immediate or accelerated penicillin allergies (IgE-mediated) can be diagnosed with penicillin skin testing. Results from studies suggest that just 10% to 20% of patients who report a penicillin allergy will have a positive penicillin skin test.\(^{8,11}\) However, patients with a negative penicillin skin test can still be allergic to penicillins. In most of these cases, the allergy is a late or idiopathic type reaction.

Skin testing is the best method for diagnosing an IgE-mediated penicillin allergy. Skin testing is usually performed by an allergist. It typically involves placement of positive (histamine) and negative (saline) controls, and then an epidermal or intracutaneous prick test. If the penicillin prick test is negative, an intradermal skin test is done. Anaphylaxis can occur with skin testing. Therefore, providers performing penicillin skin testing must be prepared to quickly treat patients who have anaphylactic reactions. Other tests, such as patch testing, radioallergosorbent tests, and enzyme-linked immunoassay, are less reliable.\(^{3}\)

Current recommendations for penicillin skin testing are to administer both the major determinant (benzylpenicilloyl-polysilysine [Pre-Pen]) of penicillin allergy, and the minor determinant (e.g., penicillin G).\(^{3,7}\) The terms major and minor determinant refer to the amount of drug that is metabolized to that component.\(^{12}\) Allergic reactions are linked to the minor determinant in a large majority of cases.\(^{11}\)

Unfortunately, minor determinant skin testing is not standardized and can vary from place to place.

**Cephalosporin Cross-reactivity**

Studies performed in the 1960s and 1970s suggested that the rate of cross-reactivity between penicillins and cephalosporins was as high as 50%.\(^{13}\) However, early cephalosporins may have been contaminated with trace amounts of penicillins,\(^{6}\) and the rate of cross-reactivity has traditionally been cited as 8% to 10%. Note that people with a penicillin allergy, compared to those without a penicillin allergy, are three times more likely to have an adverse effect to an unrelated drug.\(^{4}\)

Current data suggest that the rate of cross-reactivity between penicillins and cephalosporins is probably less than 1% (approximately 0.1% of patients without skin test-confirmed penicillin allergy, 0.1% for those with mild reactions to penicillin, and 2% for patients who are penicillin skin test positive). This cross-reactivity is likely determined by the sharing of identical R-group side chains and not the beta-lactam structure itself.\(^{3,4,8}\)

In general, the rate of allergic cross-reactivity is highest between penicillins and first-generation cephalosporins. The risk for cross-reactivity may reach almost 40% between penicillins and cephalosporins with identical R-group side chains.\(^{6}\) Penicillins and cephalosporins with which have the same R-group side chains include the following:\(^{3,6}\)

- amoxicillin, cefadroxil, cefprozil
- ampicillin, cefaclor, cephalexin

**Carbapenem and Monobactam Cross-reactivity**

Cross-reactivity between penicillins and carbapenems (i.e., imipenem, meropenem, ertapenem, or doripenem) has been reported. In early studies, the cross reactivity of penicillin and imipenem was cited at 47%,\(^{14}\) but more recent studies estimate the likelihood of cross-reactivity to be close to 1%.\(^{15}\) The large difference in reaction rates is thought to be because of a small patient population and methods of taking allergy histories in the early studies.\(^{12}\)

Meropenem cross-reactivity is estimated at 0.9% in studies, although conservative statistical estimates cite a rate of 5.2% or less.\(^{16,17}\)

More . . .
There are no studies of ertapenem or doripenem cross-reactivity in patients with a penicillin allergy. Cross-reactivity between penicillins and aztreonam, a monobactam, does not generally occur. However, aztreonam and ceftazidime have the same R-group side chain. Therefore the potential for cross-reactivity to aztreonam exists in patients allergic specifically to ceftazidime. In addition, aztreonam should be used cautiously in cystic fibrosis patients reporting hypersensitivities to beta-lactam antibiotics.

**Treatment Recommendations**

Ideally, all patients who report symptoms consistent with an IgE-mediated reaction to penicillins would be evaluated by an allergist or immunologist. This could help reduce the unnecessary use of more broad-spectrum antibiotics. In the absence of skin testing, the risks and benefits of different treatment options must be weighed.

In general, patients who report symptoms consistent with an immediate or accelerated reaction (type I) to penicillin (or are skin test positive to penicillin) should not receive any penicillin, unless they undergo desensitization (also called induction of drug tolerance). Usually desensitization is a last resort if a penicillin is the treatment of choice for an infection and no acceptable nonpenicillin alternatives are available. Desensitization involves incremental doses of an oral penicillin every 15 minutes for a total of nearly four hours before a full dose (oral or IV) is given. An example of a penicillin desensitization protocol is available in *Morbidity and Mortality Weekly Report* found at [http://www.cdc.gov/std/treatment/2006/penicillin-allergy.htm](http://www.cdc.gov/std/treatment/2006/penicillin-allergy.htm#skintesting).

Individuals with vague or distant histories of penicillin allergy may be candidates for receiving penicillins via graded challenge, although it is important to note that up to one-third of these individuals will have a positive skin test. (Graded challenge does not modify an individual’s immune response, it is simply a more cautious way of administering the drug.) Penicillin allergies are likely to wane over time. For example, about 80% of patients who report symptoms of an IgE-mediated allergic reaction to a penicillin ten years ago will not presently have a positive skin test.

Those who report immediate or accelerated reactions to semisynthetic penicillins such as amoxicillin or ampicillin may be able to tolerate other penicillins. Skin testing with penicillin may be helpful to determine this.

Historically, data suggested that patients who reported an immediate or accelerated reaction to a penicillin (or are skin test positive to penicillin) should not receive a cephalosporin. However with certain precautions (see below), some second, third, and fourth generation agents may be able to be safely administered to patients with an immediate or accelerated reaction to a penicillin. (The manufacturer of the fifth generation cephalosporin, ceftaroline, advises caution in beta-lactam allergic patients until more data are available on the potential for cross-reactivity.) Since side chain similarity appears to be important in allergic cross-reactivity between the penicillins and cephalosporins, those with an immediate or accelerated reaction to amoxicillin should not receive cefadroxil or cefprozil without desensitization and those with an immediate or accelerated reaction to ampicillin should not receive cefaclor or cephelexin without desensitization.

Administration of a cephalosporin to a patient who reports an immediate or accelerated penicillin allergy (or is skin test positive to penicillin) should be done cautiously. There is not good evidence that cephalosporin skin testing will predict IgE-mediated reactions to cephalosporins. Providers may opt for rapid desensitization to the cephalosporin, or for a graded challenge. For graded challenge with oral cephalosporins, 10% of the first dose is administered, followed one hour later by the full dose, under observation, in the absence of a reaction. For graded challenge with intravenous cephalosporins, 1% of the full dose is administered, then 10% of the full dose, then the full dose, separated by one hour each, under observation, in the absence of a reaction.

**Carbapenems** can be used in patients who report an immediate or accelerated type reaction with a penicillin (or are skin test positive to penicillin), after optional skin testing and a graded challenge.

For example, if a patient needs to be skin tested with imipenem, a concentration of 0.5 mg/mL of imipenem-cilastatin should be used.

More...
If the skin test is negative, some studies have used a graded challenge: 1% of the dose in the first hour, 10% of the dose in the second hour, and a full imipenem-cilastatin dose in the third hour if no reaction has occurred.15

Skin testing for meropenem should be performed with a concentration of 1 mg/mL. Then, one of two equally safe graded challenge regimens can be chosen: 1% of the dose in the first hour, then 10% of the dose in the second hour, and the full dose in the third hour if no reaction occurs in the first or second hour; or 10% of the dose in the first hour, and the full dose in the second hour if no reaction occurs in the first hour.16

In some cases, it may be preferable to use an antibiotic from a different drug class (a non beta-lactam) for patients with penicillin allergy. However, the latest treatment guidelines for infections such as sinusitis and acute otitis media recommend against the routine use of some alternatives such as macrolides due to an increase in resistance. For more information, see our PL Detail-Document, Should Macrolides Be Used for Respiratory Tract Infections?

Treatments for patients reporting a cephalosporin allergy may also be chosen based on R-group side-chain similarities. Patients with an immediate or accelerated allergy to a cephalosporin should not receive a cephalosporin with the same R-group side chain without desensitization to that drug.3 For example, a patient with an IgE-mediated reaction to cefuroxime should not receive cefoxitin.3 Likewise, a patient with an IgE-mediated reaction to ceftriaxone should not receive cefotaxime or cefpodoxime.3 A cephalosporin with a different side chain may be able to be used safely. However, consideration should be given to the use of either rapid desensitization or graded challenge, depending on the severity of the reaction.3,4

Patients who report an immediate or accelerated allergy to cefazidime should not receive aztreonam, since these drugs have identical R-group side chains.3 As previously mentioned, aztreonam should be used cautiously in cystic fibrosis patients reporting hypersensitivities to beta-lactam antibiotics.12,19

If a patient has a documented immediate or accelerated reaction to a carbapenem, use of another agent from that particular class should be avoided until more data are available.

**Conclusion**

The incidence of allergic cross-reactivity among beta-lactam antibiotics appears to be less than historically thought. Ideally, all patients who report symptoms consistent with an IgE-mediated reaction to penicillins would be evaluated by an allergist or immunologist. This could help reduce the unnecessary use of more broad spectrum antibiotics.3,4,6,7

A patient’s allergy history should be carefully obtained and the decision about which antibiotic class to administer should be based on this information. Under certain conditions, patients with an IgE-mediated penicillin allergy may be able to safely receive a cephaplosporin, particularly second, third, and fourth generation cephalosporins.3,6

The carbapenems and aztreonam pose little risk to patients with a true type I penicillin allergy in most cases, although skin testing and graded challenge is recommended prior to treatment with carbapenems.3

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**Project Leader in preparation of this PL Detail-Document:** Stacy A. Hester, R.Ph., BCPS, Assistant Editor

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## Comparison of Cephalosporins

Cephalosporin antibiotics have been around for decades, yet remain a relatively prolific class of antibiotics. New agents continue to be developed and marketed. The most recent was ceftaroline (Teflaro-U.S.), a “fifth generation” agent that has activity against methicillin-resistant S. aureus (MRSA). Cephalosporins continue to find a place as preferred therapy for inpatients (e.g., cefazolin for surgical prophylaxis, cefotaxime or ceftriaxone for bacterial meningitis, cefepime for neutropenic fever) and less frequently for outpatients (e.g., cephalexin for non-MRSA skin infections). However, there are a number of cases where the use of cephalosporins has fallen out of favor (e.g., cefuroxime for community-acquired pneumonia, cefaclor for any indication) due to bacterial resistance. The following chart reviews bacterial activity for the different generations of cephalosporins, routes of administration, conditions that require dose adjustments, and whether or not each individual agent is approved for use in children. We also have a chart of pediatric oral antibiotic liquids that includes dosing and product specifics (U.S. subscribers; Canadian subscribers). Information about cross-reactivity among beta-lactam antibiotics is also available.

<table>
<thead>
<tr>
<th>Generation</th>
<th>Organisms Covered&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>Comments&lt;sup&gt;1,2&lt;/sup&gt;</th>
</tr>
</thead>
</table>
| **First Generation** | • Primarily cover gram positive organisms: methicillin-sensitive S. aureus, group A strep  
• Some gram negative coverage: *E. coli*, *Klebsiella* species, *P. mirabilis*  
• Poor anaerobic coverage | • Increased risk of cross-reactivity in penicillin-allergic patients in comparison with other cephalosporins |
| **Second Generation** | • Maintain gram positive coverage similar to first generation agents. Cefuroxime and cefprozil cover *S. pneumoniae*.  
• Enhanced coverage of gram negative organisms: *H. influenza*, *M. catarrhalis*, *Neisseria* species  
• Some anaerobic coverage. Cefoxitin and cefotetan cover *B. fragilis*. | • Second-generation agents include both cephalosporins (cefaclor, cefprozil, cefuroxime) and cephamycins (cefotetan, cefoxitin). Cephamycins do not have adequate gram positive coverage to treat respiratory infections. Cefuroxime, etc. does not have adequate anaerobic coverage to be used for abdominal infections. |
| **Third Generation** | • Maintain varying degrees of gram positive coverage, except for ceftazidime. Cefotaxime and ceftiraxone have increased potency against penicillin-resistant pneumococci compared with first- and second-generation agents.  
• Enhanced coverage of gram negative organisms compared to first- and second-generation agents: Enterobacteriaceae (e.g., *Citrobacter*, *Enterobacter*, *Salmonella*, *Serratia* species), *E. coli*, *Klebsiella* species, *P. mirabilis*, etc. However, *Enterobacter* is often resistant.  
• Ceftazidime covers *P. aeruginosa*.  
• Some anaerobic coverage. No agents cover *B. fragilis*. | • Inactivated by AmpC beta-lactamases, extended-spectrum beta-lactamases (ESBLs), and carbapenemases (KPCs).  
• Ceftazidime, which has a different spectrum activity than other third-generation cephalosporins, is structurally similar to aztreonam. |
### Generation Organisms Covered

#### Fourth Generation
- Broad coverage of gram positive and gram negative organisms.
- Coverage of *Pseudomonas* similar to ceftazidime.
- Coverage of *S. pneumonia* similar to ceftriaxone.
- Some anaerobic coverage. No coverage of *B. fragilis*.

#### Fifth Generation (MRSA-active)
- Enhanced coverage of gram positive organisms: MRSA, *S. pneumonia*, and *E. faecalis*
- Similar gram negative coverage to third- and fourth-generation agents. Ceftaroline does not cover *Pseudomonas*.
- Limited anaerobic activity.

### Drug Route

|------|-------|-----------------------|------------------------|--------------------------|---------------------|----------|
| Cefadroxil (Duricef) | PO    | Y (≥6 weeks, depending on indication [Canada]) | Y (CrCL ≤50 mL/min) | N | Y | •Brand products discontinued  
•Available as powder for oral suspension, tablets, and capsules |
<p>| Cefazolin (Ancef, Kefzol-U.S.) | IM/IV | Y (CrCl &lt;55 mL/min) | N | Y | •Ancef brand discontinued |
| Cephalexin (Keflex) | PO    | Y (Some sources recommend dose reduction with CrCL &lt;40 to 50 mL/min.) | N | Y | •Available as powder for oral suspension, soluble tablet (<em>Panixe Disperdose</em>-U.S. only), and capsule |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Route&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Approved in Children?&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Renal Dose Adjustment?</th>
<th>Hepatic Dose Adjustment?</th>
<th>Generic Available?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second Generation Agents</strong></td>
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</table>
| Cefaclor (Ceclor) | PO                | Y                                 | N                      | N                        | Y                  | • Brand products discontinued in the U.S.  
• Available as powder for oral suspension, extended-release tablets (U.S. only), and capsules |
|                   | (≥1 month [U.S.]) |                                   |                        |                          |                    |                                                                                                   |
| Cefotetan-       | IV                | N                                 | Y (CrCl ≤30 mL/min)    | N                        | Y                  | • Brand products discontinued                                                                |
| U.S. only        |                   |                                   |                        |                          |                    |                                                                                                   |
| (Cefotan)        |                   |                                   |                        |                          |                    |                                                                                                   |
| Cefoxitin (Mefoxin) | IM/IV            | Y                                 | Y (CrCl ≤50 mL/min)    | N                        | Y                  | • Brand products not available in Canada                                                              |
|                   | (≥3 months [U.S.])|                                   |                        |                          |                    |                                                                                                   |
| Cefprozil (Cefzil) | PO                | Y                                 | Y (CrCl ≤30 mL/min [Canada]; <30 mL/min [U.S.]) | N                        | Y                  | • Brand product discontinued in the U.S.  
• Available as powder for oral suspension and tablets                                               |
|                   | (≥6 months)       |                                   |                        |                          |                    |                                                                                                   |
| Cefuroxime       | PO/IM/IV          | Y                                 | Y (CrCl ≤20 mL/min [for injectable]; no data for oral route) | N                        | Y                  | • *Zinacef* brand not available in Canada  
• Available oral formulations are powder for oral suspension and tablets  
• Dosing information for neonates is included in Canadian product labeling for injectable cefuroxime  
• Tablets not recommended for children <12 years (Canada)                                           |
<p>| (Ceftin [oral], |                   |                                   |                        |                          |                    |                                                                                                   |
| <em>Zinacef</em> [injectable]) |                   |                                   |                        |                          |                    |                                                                                                   |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Route&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Approved in Children?</th>
<th>Renal Dose Adjustment?</th>
<th>Hepatic Dose Adjustment?</th>
<th>Generic Available?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefdinir-U.S. only</td>
<td>PO</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>•Brand product is discontinued •Available as powder for oral suspension and capsules</td>
</tr>
<tr>
<td>(Omnicef)</td>
<td>(≥6 months)</td>
<td></td>
<td>(CrCl &lt;30 mL/min)</td>
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<tr>
<td>Cefditoren pivoxil-U.S.</td>
<td>PO</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>•Available as tablets</td>
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<tr>
<td>(Spectracef)</td>
<td>(≥12 years)</td>
<td></td>
<td>(CrCl &lt;50 mL/min)</td>
<td></td>
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<tr>
<td>Cefixime (Suprax)</td>
<td>PO</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>•Available as powder for oral suspension and tablets</td>
</tr>
<tr>
<td></td>
<td>(≥6 months)</td>
<td></td>
<td>(CrCl &lt;40 mL/min [Canada]; &lt;60 mL/min [U.S.])</td>
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<td></td>
<td></td>
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<tr>
<td>Cefotaxime (Claforan)</td>
<td>IM/IV</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>•None</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(CrCl &lt;20 mL/min)</td>
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<tr>
<td>Cefpodoxime proxetil-U.S.</td>
<td>PO</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>•Available as granules for oral suspension and tablets</td>
</tr>
<tr>
<td>(Vantin)</td>
<td>(≥2 months)</td>
<td></td>
<td>(CrCl &lt;30mL/min)</td>
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<tr>
<td>Ceftazidime (Fortaz)</td>
<td>IM/IV</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>•None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(CrCl ≤50 mL/min [Canada]; &lt;50 mL/min [U.S.])</td>
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<tr>
<td>Ceftibuten- U.S. only</td>
<td>PO</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>•Available as powder for oral suspension and capsules</td>
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<tr>
<td>(Cedax)</td>
<td>(≥6 months)</td>
<td></td>
<td>(CrCl &lt;50 mL/min)</td>
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<tr>
<td>Ceftiriaxone (Rocephin)</td>
<td>IM/IV</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>•Brand product discontinued in Canada</td>
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<tr>
<td></td>
<td>(&gt;28 days)</td>
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</table>

**Fourth Generation**

<p>| Cefipime (Maxipime)       | IM/IV             | Y                     | Y                      | N                        | Y                   | •None                                                                                              |</p>
<table>
<thead>
<tr>
<th></th>
<th>(≥2 months)</th>
<th></th>
<th>(CrCl ≤50 mL/min [Canada]; ≤60 mL/min [U.S.])</th>
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<tr>
<td><strong>Fifth Generation (MRSA-active)</strong></td>
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<tr>
<td>Cefaroline- U.S. only (Teflaro)</td>
<td>IV</td>
<td>N</td>
<td>Y (CrCl ≤50 mL/min)</td>
<td>N</td>
<td>N</td>
<td>•None</td>
</tr>
</tbody>
</table>

a. Off-label routes such as intraperitoneal may be appropriate for some drugs.
b. Consult a neonatal dosing reference such as Neofax for information on use in premature neonates.

**U.S. product information used for preparation of the above chart:** cefadroxil (Ranbaxy; July 2007), cefazolin (Hospira; June 2011), Keflex (October 2010), cefaclor (Ranbaxy; May 2007), cefotetan (B. Braun; May 2011), Mefoxin (October 2006), cefprozil (Teva; September 2007), Zinacef (August 2010), Cefin (January 2010), cefdinir (Teva; June 2009), Spectracef (2011), Suprax (October 2008), Ceforan (July 2009), Vantin (April 2007), Fortaz (August 2010), Cedax (April 2010), Rocephin (November 2010), Maxipime (August 2010), Teflaro (May 2012).

**Canadian product monographs used for preparation of the above chart:** cefadroxil (Teva; March 2012), cefazolin (Hospira; May 2010), Keflex (May 2012), Ceclor (February 2012), cefoxitin (Hospira; August 2010), Cefzil (December 2010), Cefin (November 2010), cefuroxime (Pharmaceutical Partners of Canada; January 2008), Suprax (November 2010), Ceforan (November 2010), Fortaz (November 2010), Ceftriaxone (Novopharm; February 2012), Maxipime (September 2008).

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Project Leader in preparation of this PL Detail-
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Assistant Editor

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