

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.

Generation	Organisms Covered ^{1,2}	Comments ^{1,2}
First Generation	- Primarily cover gram positive organisms: methicillin-sensitive <i>S. aureus</i>, group A strep - Some gram negative coverage: <i>E. coli</i>, <i>Klebsiella</i> species, <i>P. mirabilis</i> - 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 <i>S. pneumoniae</i>. - Enhanced coverage of gram negative organisms: <i>H. influenza</i>, <i>M. catarrhalis</i>, <i>Neisseria</i> species - Some anaerobic coverage. Cefoxitin and cefotetan cover <i>B. fragilis</i>.	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 ceftriaxone 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., <i>Citrobacter</i>, <i>Enterobacter</i>, <i>Salmonella</i>, <i>Serratia</i> species), <i>E. coli</i>, <i>Klebsiella</i> species, <i>P. mirabilis</i>, etc. However, <i>Enterobacter</i> is often resistant. - Ceftazidime covers <i>P. aeruginosa</i>. - Some anaerobic coverage. No agents cover <i>B. fragilis</i>.	- 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.

More . . .

Generation	Organisms Covered ^{1,2}	Comments ^{1,2}
Fourth Generation	- Broad coverage of gram positive and gram negative organisms. Coverage of <i>Pseudomonas</i> similar to ceftazidime. Coverage of <i>S. pneumonia</i> similar to ceftriaxone. - Some anaerobic coverage. No coverage of <i>B. fragilis</i>.	- No oral agents currently available - Less susceptible to inactivation by AmpC beta-lactamases than second- or third-generation agents, so better against <i>Citrobacter</i> and <i>Enterobacter</i>.
Fifth Generation (MRSA-active)	- Enhanced coverage of gram positive organisms: MRSA, <i>S. pneumonia</i>, and <i>E. faecalis</i> - Similar gram negative coverage to third- and fourth-generation agents. Ceftaroline does not cover <i>Pseudomonas</i>. - Limited anaerobic activity.	No oral agents currently available

Drug	Route ^a	Approved in Children? ^b	Renal Dose Adjustment?	Hepatic Dose Adjustment?	Generic Available?	Comments
First Generation Agents						
Cefadroxil (<i>Duricef</i>)	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
Cefazolin (<i>Ancef</i> , <i>Kefzol</i> -U.S.)	IM/IV	Y	Y (CrCl <55 mL/min)	N	Y	<i>Ancef</i> brand discontinued
Cephalexin (<i>Keflex</i>)	PO	Y	Y (Some sources recommend dose reduction with CrCL <40 to 50 mL/min.) ^{3,4}	N	Y	Available as powder for oral suspension, soluble tablet (<i>Panixine Disperdose</i>-U.S. only), and capsule

Drug	Route ^a	Approved in Children? ^b	Renal Dose Adjustment?	Hepatic Dose Adjustment?	Generic Available?	Comments
Second Generation Agents						
Cefaclor (<i>Ceclor</i>)	PO	Y (≥1 month [U.S.])	N	N	Y	•Brand products discontinued in the U.S. •Available as powder for oral suspension, extended-release tablets (U.S. only), and capsules
Cefotetan - U.S. only (<i>Cefotan</i>)	IV	N	Y (CrCl ≤30 mL/min)	N	Y	•Brand products discontinued
Cefoxitin (<i>Mefoxin</i>)	IM/IV	Y (≥3months [U.S.])	Y (CrCl ≤50 mL/min)	N	Y	•Brand products not available in Canada
Cefprozil (<i>Cefzil</i>)	PO	Y (≥6 months)	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
Cefuroxime (<i>Ceftin</i> [oral], <i>Zinacef</i> [injectable])	PO/IM/IV	Y (≥3 months [oral]) (>3 months [Injectable; U.S.])	Y (CrCl ≤20 mL/min [for injectable]; no data for oral route)	N	Y	•<i>Zinacef</i> 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)

Drug	Route ^a	Approved in Children? ^b	Renal Dose Adjustment?	Hepatic Dose Adjustment?	Generic Available?	Comments
Third Generation Agents						
Cefdinir -U.S. only (<i>Omnicef</i>)	PO	Y (≥6 months)	Y (CrCl <30 mL/min)	N	Y	•Brand product is discontinued •Available as powder for oral suspension and capsules
Cefditoren pivoxil -U.S. only (<i>Spectracef</i>)	PO	N (≥12 years)	Y (CrCl <50 mL/min)	N	Y	•Available as tablets
Cefixime (<i>Suprax</i>)	PO	Y (≥6 months)	Y (CrCl <40 mL/min [Canada]; <60 mL/min [U.S.])	N	N	•Available as powder for oral suspension and tablets
Cefotaxime (<i>Claforan</i>)	IM/IV	Y	Y (CrCl <20 mL/min)	N	Y	•None
Cefpodoxime proxetil -U.S. only (<i>Vantin</i>)	PO	Y (≥2 months)	Y (CrCl <30mL/min)	N	Y	•Available as granules for oral suspension and tablets
Ceftazidime (<i>Fortaz</i>)	IM/IV	Y	Y (CrCl ≤50 mL/min [Canada]; <50 mL/min [U.S.])	N	Y	•None
Ceftibuten -U.S. only (<i>Cedax</i>)	PO	Y (≥6 months)	Y (CrCl <50 mL/min)	N	N	•Available as powder for oral suspension and capsules
Ceftriaxone (<i>Rocephin</i>)	IM/IV	Y (>28 days)	N	N	Y	•Brand product discontinued in Canada
Fourth Generation						
Cefipime (<i>Maxipime</i>)	IM/IV	Y (≥2 months)	Y (CrCl ≤50 mL/min [Canada]; ≤60 mL/min [U.S.])	N	Y	•None

Drug	Route ^a	Approved in Children? ^b	Renal Dose Adjustment?	Hepatic Dose Adjustment?	Generic Available?	Comments
Fifth Generation (MRSA-active)						
Ceftaroline- U.S. only (<i>Teflaro</i>)	IV	N	Y (CrCl ≤50 mL/min)	N	N	•None

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), *Ceftin* (January 2010), cefdinir (Teva; June 2009), *Spectracef* (2011), *Suprax* (October 2008), *Claforan* (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), *Ceftin* (November 2010), cefuroxime (Pharmaceutical Partners of Canada; January 2008), *Suprax* (November 2010), *Claforan* (November 2010), *Fortaz* (November 2010), Ceftriaxone (Novopharm; February 2012), *Maxipime* (September 2008).

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