Alberta Health Services Pharmacy Services

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Antimicrobial Stewardship Backgrounder

Ceftriaxone—What is the Dose?

BOTTOM LINE: Indication-appropriate dosing of ceftriaxone is important to maximize treatment success, reduce unnecessary antibiotic exposure, and optimize treatment costs.

	Usual Ceftriaxone Dose	Ceftriaxone Dose in Obesity**
• Pneumonia • Pyelonephritis	1 g daily	More than 100 kg – 2 g daily
• Peritonitis / intra-abdominal infections	1 or 2 g daily	More than 100 kg – 2 g daily
• Endocarditis caused by susceptible *Streptococcus spp.* or Gram negative organisms (e.g. HACEK*, *Enterobacteriaceae*) • Culture-negative endocarditis	2 g daily	More than 150 kg – Consider 2 g every 12 hours
• CNS infections (e.g. meningitis) • Endophthalmitis • Enterococcal endocarditis synergy	2 g every 12 hours	
• Outpatient empiric therapy of mild to moderate nonpurulent skin/soft tissue infections (SSTI) when neither oral agents nor cefazolin +/- probenecid*** can be used	2 g daily	More than 150 kg – Consider 2 g every 12 hours

* HACEK: *Haemophilus parainfluenzae*, *Aggregatibacter*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella*
** Suggested doses are based on pharmacokinetic considerations, not clinical data.
*** Please refer to Antimicrobial Stewardship Backgrounder: Cefazolin + Probenecid for Outpatient Treatment of Uncomplicated SSTIs (https://www.albertahealthservices.ca/assets/info/hp/as/if-hp-asb-2016-04-issue-11.pdf).

Background:

- Ceftriaxone is commonly used for community-acquired pneumonia (CAP), bacteremia, pyelonephritis, intra-abdominal infections, and central nervous system (CNS) infections, and, in the outpatient setting, for skin & soft tissue infections (SSTI).

Ceftriaxone has:	**RELIABLE** activity against:	**NO** activity against:
Gram Positives	*Streptococcus* spp.	*Enterococcus* spp., *Listeria* spp., methicillin-resistant S. *aureus* (MRSA)
Gram Negatives	HACEK, *Enterobacteriaceae* (*E. coli, Klebsiella* (except *K. aerogenes*) spp., *Proteus mirabilis*, *Salmonella* spp., *Shigella* spp.), *Moraxella catarrhalis*, *Neisseria* spp., *Haemophilus influenzae*	*Pseudomonas* spp., extended-spectrum β-lactamase (ESBL) producers, AmpC β-lactamase producers*, *Acinetobacter* spp.
Anaerobes and Atypicals	*Cutibacterium* (formerly *Propionibacterium*) *acnes*	Most anaerobes (esp. *B. fragilis*) and atypicals (*Legionella* spp., *Mycoplasma* spp., *Chlamydophila* spp.)

* *Serratia*, *Providencia*, *Citrobacter freundii* complex, *Enterobacter*, *Klebsiella aerogenes*, *Hafnia*, *Morganella*

Efficacy:

- At 1 g daily, the resultant serum concentration is high enough throughout the 24-hour period to inhibit growth of most pathogens responsible for CAP[1], pyelonephritis[2,3], and spontaneous bacterial peritonitis[4], but may not be sufficient to treat methicillin-susceptible *Staphylococcus aureus* (MSSA) infections.
- Ceftriaxone is NOT first line therapy for severe MSSA infections or bacteremia due to poorer outcomes, including increased mortality.[5-7] Cefazolin or cloxacillin are considered first-line.
    - Ceftriaxone 2 g daily has been shown to have some use in osteoarticular MSSA infections and may be an option in very select circumstances when daily dosing is required.[8]

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- Ceftriaxone 2 g daily is most commonly used in outpatient treatment of SSTI (which is largely due to *Streptococcus* and *Staphylococcus* spp.) with good clinical outcomes. However, antimicrobials with a narrower spectrum of activity, such as cefazolin, to which these pathogens are more susceptible, are more appropriate.[9]
- To achieve appropriate CNS concentrations, 2 g every 12 hours is needed.[10]
- There are no published clinical data for ceftriaxone dosing in obesity. However, use of higher doses in patients over 100 kg may be considered based on pharmacokinetic evidence for other cephalosporins.[11,12]

Safety/Sustainability:

- The use of 1 g instead of 2 g of ceftriaxone when appropriate represents a **40% cost saving**.
- Higher doses of ceftriaxone have been associated with an increased risk of hepatotoxicity.[13]
- Ceftriaxone does not require dose adjustment in renal dysfunction.

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