

**Amoxicillin-clavulanate is now available IV****Inside this issue:**Amoxicillin-clavulanate spectrum of activity **1**Amoxicillin-clavulanate indications for use and dosing **2**

IV amoxicillin-clavulanate has recently become available in Canada and has been added to the Alberta Health Services (AHS) provincial formulary

- Amoxicillin-clavulanate is a broad spectrum antimicrobial that contains an aminopenicillin (amoxicillin) and a beta-lactamase inhibitor (clavulanate) making it effective against some beta-lactamase producing bacteria.
- Unlike piperacillin-tazobactam, IV amoxicillin-clavulanate has no activity against *Pseudomonas* spp and therefore exerts less selective pressure on this often multi-drug resistant organism. Amoxicillin-clavulanate should be used preferentially over piperacillin-tazobactam in community acquired polymicrobial infections where *Pseudomonas* spp are not involved.
- Amoxicillin-clavulanate IV is cost neutral compared to piperacillin-tazobactam at usual doses but is MORE expensive than ceftriaxone +/- metronidazole IV/PO.
- The IV formulation has short stability once prepared (4 hours refrigerated, 60 minutes room temperature) which means:
 - ◊ It may not be suitable for home parenteral therapy (it is also not on the Alberta Drug Benefit List)
 - ◊ Nursing preparation of amoxicillin-clavulanate will be required

Amoxicillin-clavulanate spectrum of activity includes:

- Gram positive organisms such as methicillin-susceptible *S. aureus* (MSSA), most *Streptococci* spp, *E. faecalis*, and *Listeria* spp
- Gram negative organisms such as *Moraxella catarrhalis*, *Proteus* spp, *Haemophilus* spp, *Klebsiella* spp, and *E. coli*
- Anaerobes (Gram positive and negative, including *Bacteroides* spp.)

#Extended spectrum β -lactamase producing organisms#
Acinetobacter spp., *Citrobacter* spp, *Enterobacter* spp,
H. alvei, *M. morgani*, *Providencia* spp, *S. marcescens*

Amoxicillin-clavulanate has NO activity against:

- Methicillin-resistant *S. aureus* (MRSA)
- Ampicillin-resistant *E. faecium*
- *P. aeruginosa*
- Enterobacterales spp with ESBL[#], AmpC[‡], or carbapenemase
- Atypical organisms (e.g. *Mycoplasma*, *Legionella*, *Chlamydia*)
- *Stenotrophomonas maltophilia*

DO NOT use amoxicillin-clavulanate if clinical history or cultures indicate that *P. aeruginosa* may be a causative organism.

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AHS Provincial Formulary Guidelines For IV Amoxicillin-Clavulanate Use¹:

IV amoxicillin-clavulanate is clinically indicated for the treatment of polymicrobial infections in individuals **unable to take oral amoxicillin-clavulanate**, including:

- Skin and soft tissue infections (e.g. animal bite or polymicrobial diabetic foot infections)
- Bone and joint infections including osteomyelitis
- Severe odontogenic infections
- Intra-abdominal infections
- Polymicrobial respiratory tract infections (e.g. aspiration pneumonia in individuals with risk factors for anaerobes)

Clinical scenarios where IV amoxicillin-clavulanate* can replace IV piperacillin-tazobactam:

Infectious syndrome	Rationale for IV Amoxicillin-Clavulanate Use
Intra-abdominal infections [IAIs] (e.g. peritonitis, abscess, diverticulitis, appendicitis, cholangitis). (not tertiary/hospital acquired)	Good coverage of gastrointestinal flora associated with IAIs ² . <i>P. aeruginosa</i> is not a usual pathogen in IAI unless tertiary/hospital acquired. <i>Reserve amoxicillin-clavulanate for polymicrobial infections not covered by ceftriaxone/metronidazole (e.g. including E. faecalis).</i>
Polymicrobial skin and soft tissue infections (SSTIs) such as diabetic foot infections/osteomyelitis where <i>Pseudomonas</i> spp are not involved.	Complicated SSTI: randomized controlled trial (RCT) data is available for the use of IV amoxicillin-clavulanate in complicated SSTIs ³ . Bone and joint infection: adequate bone penetration following a single dose in adults and clinical data in the pediatric population is available ^{4,5} .
Community acquired polymicrobial respiratory tract infections (CA-RTIs) such as aspiration pneumonia.	Multiple RCTs demonstrate clinical efficacy when compared to ceftriaxone, IV cefuroxime, or moxifloxacin for CA-RTIs ¹ . <i>Ceftriaxone (plus metronidazole if risk factors for anaerobes) remains first line. Reserve amoxicillin-clavulanate for polymicrobial infections not covered by these first line regimens.</i>
Severe odontogenic infections in patients unable to take oral antibiotics.	Oral amoxicillin-clavulanate is effective and well tolerated for odontogenic infections ⁷ . <i>If IV required, ceftriaxone plus metronidazole is preferred over IV amoxicillin-clavulanate since it provides appropriate spectrum at a lower cost. Reserve IV amoxicillin-clavulanate for those allergic/intolerant of metronidazole.</i>

***Amoxicillin-clavulanate IV vs. PO:** Patients can be easily transitioned to oral amoxicillin-clavulanate if they are clinically improving, have a functional gastrointestinal tract and can take PO medications, thereby facilitating hospital discharge.

Dosing

- The usual/most well studied dose is amoxicillin-clavulanate 1000mg-200mg (1.2g) IV q8h
- Other doses in the Canadian product monograph (2.2g IV q8h or q12h) are based primarily on pharmacokinetic data, rather than clinical, and may require further study before widespread use^{6,8}.
- RCTs for amoxicillin-clavulanate IV are available for SSTI (n=1), CA-RTIs (n=6), and IAIs (n=4), at the 1.2g IV q8h dose, except one RCT in adult CAP in which 2.2g IV q8h was used⁶.
- Recommended dosing in pediatrics and renal dysfunction (CrCl less than 30mL/min) is available in Bugs & Drugs⁹.

References:

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