

SUPPLIED AS

- ✦ Amoxicillin-clavulanic acid is now available for intravenous use at UHN in the following formulations:
 - 1000mg/200mg vial (5:1)
 - 2000mg/200mg vial (10:1)
- ✦ Vial sizes are not interchangeable.
- ✦ When reconstituted in sterile water, solutions are only stable for 15 minutes at room temperature. For this reason, it is not supplied pre-mixed by pharmacy given its short stability after reconstitution, and therefore requires RN admixing. Stability may also limit outpatient treatment depending on frequency of administration.

SPECTRUM OF ACTIVITY

- ✦ **Gram-positive organisms:** Many, including *Enterococcus faecalis*, *Streptococcal spp.*, and methicillin-susceptible *Staphylococcus aureus* (MSSA)
 - **Exception NO activity** against methicillin-resistant *Staphylococcus aureus* (MRSA), and most *Enterococcus faecium* (check local unit antibiogram)
- ✦ **Gram-negative organisms:** Many, including *E.coli*, *Proteus spp.*, *Klebsiella spp.*, *Haemophilus spp.*, *Moraxella spp.*
 - **Exception: NO activity** against *Pseudomonas spp.*, extended spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae*, SPICE organisms (AmpC producing organisms) or *Stenotrophomonas spp.*
- ✦ **Anaerobic organisms:** Most, including *Bacteroides spp.*

INDICATION AND DOSAGE

- ✦ Polymicrobial infections where anaerobic and/or enterococcal coverage is warranted, and pseudomonas aeruginosa is an unlikely pathogen. Consideration for use should include circumstances where IV administration is preferred for the particular foci of infection, or required due to impaired oral tolerability/absorption.. Indications may include:
 - Empiric treatment of pyelonephritis when *E. faecalis* coverage is warranted.
 - Community acquired intra-abdominal infections (an alternative to cephalosporin +/- metronidazole when *E. faecalis* activity is warranted)
 - Bone and joint infections
 - Skin and soft tissue infections where anaerobic coverage is warranted (e.g., diabetic foot infections where *Pseudomonas spp.* is unlikely to be a pathogen of concern)
 - Severe head and neck (ENT) infections
 - Obstetric/Gynecological infections where anaerobic coverage is warranted.
- ✦ Dosing to be ordered based on amoxicillin component:
 - For most infections: 1000mg/200mg IV Q8h (5:1) or 2000mg/200mg IV q12h (10:1)
 - For severe infections where augmented renal clearance or tissue penetration are of concern, the dose may be increased up to 2g IV q12h-8h (using the 10:1 formulation). Data for higher dosing is limited to pharmacokinetic and small clinical studies.⁶⁻¹¹
 - Dose adjustment is required for patients with severe renal insufficiency:
 - CrCl> 30 mL/min: No change in dosage
 - 10-30 mL/min: 1000 mg/200 mg followed by 500 mg/100 mg every 12 hours
 - < 10 mL/min: 1000 mg/200 mg followed by 500 mg/100 mg every 24 hours
 - Hemodialysis: Initial dose of 1000 mg/200 mg followed by 500 mg/100 mg 24 hourly, plus a dose of 500 mg/100 mg at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased)
- ✦ **Note:** Patients may be transitioned to oral amoxicillin-clavulanate when eligible

CONTRAINDICATIONS/PRECAUTIONS

- ✦ Amoxicillin and clavulanic acid should not be used in:
 - Patients with confirmed anaphylactic reactions to penicillin antibiotics
 - Patients with a previous history of amoxicillin-clavulanic acid associated jaundice/hepatic dysfunction. Re-challenge with amoxicillin/clavulanic acid results in recurrence and should be avoided
- ✦ Consider sodium and potassium content for patients with renal dysfunction, on a reduced sodium diet or who have electrolyte imbalances.

ADVERSE DRUG REACTIONS

Adverse effect profile for IV amoxicillin/clavulanic acid is similar to the oral formulation, with diarrhea being most commonly reported.

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Version 1.0

Reviewed by:

SH – UHN Antimicrobial Subcommittee

19 September 2022

UHN Pharmacy & Therapeutics (P&T):

5 December 2022

Sinai Health Pharmacy & Therapeutics (P&T)

Approved by:

UHN Medical Advisory Committee (MAC)

5 January 2023

Sinai Health Medical Advisory Committee (MAC)

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