

Metronidazole IV Shortage

Currently marketed formulations of metronidazole IV¹

DIN	Company	Product	Strength
<u>00870420</u>	BAXTER CORPORATION	METRONIDAZOLE 5 MG/ML INJECTION	5 MG / ML
<u>00649074</u>	HOSPIRA HEALTHCARE CORPORATION	METRONIDAZOLE INJECTION USP	5 MG / ML

Health Canada-approved indications for IV metronidazole²:

- Treatment of infections due to susceptible anaerobic bacteria
- Prevention of post-operative anaerobic sepsis in patients undergoing colorectal surgery
- Treatment of amebic liver abscess
- Treatment of *clostridium difficile*-associated diarrhea when oral route is not possible.

Alternative metronidazole formulations:

- **Oral metronidazole is 100 % bioavailable.³ Reserve stock of IV metronidazole for situations in which there is a compelling indication for the injectable formulation e.g., patients who are strictly NPO and no effective alternative available.⁴ Step down to oral metronidazole as soon as possible.⁴**
- Rectal suppositories – no pre-manufactured product available in Canada.¹ Can be compounded but variable bioavailability (59 – 94%).³
- Compounded parenteral metronidazole⁵
 - Prepare in clean air environment using aseptic procedure. If nonsterile components, use appropriate sterilization process.
 - Stability data available for the following formulation (210 mg/100 ml):

Metronidazole powder		210 mg
(Do not use crushed tablets)		
Dextrose		5.25 g
Sterile water for injection	qs	100 mL

- Dissolve the metronidazole and dextrose in about 90 mL of sterile water for injection that has been heated to about 60°C.
- Mix until the powders are dissolved.
- Cool solution, bring to 100 ml with sterile water for injection.
- Filter through suitable 0.2-µm sterilizing filter.
- Package in sterile tight, light-resistant containers.
- If no sterility test performed, beyond-use date of 24 hours at room temperature or three days stored under refrigeration.

- If official USP sterility test complete for each batch of drug, a beyond-use date of six months at room temperature is suggested based on the expiration date of similar commercially manufactured products; however no stability studies have been performed on compounded product.

Alternative drugs^{4,6,7}:

Indication	Drug
Surgical prophylaxis	<u>Colorectal</u> <ul style="list-style-type: none"> • Cefoxitin 1 to 2 gm IV OR ertapenem 1 gm IV <u>Gastric / biliary</u> <ul style="list-style-type: none"> • Cefazolin 1 gm IV OR cefoxitin 2 gm OR cefuroxime 1.5 gm IV
Anaerobic infections (ie, intra-abdominal, diverticulitis, cholangitis, abscess)	<ul style="list-style-type: none"> • Consider oral metronidazole (e.g., 500 mg q 12 h) if feasible for patient. (Oral bioavailability is equivalent to IV) • Piperacillin/tazobactam IV 4.5 gm q 8 h or 3.375 gm q 6 h • Moxifloxacin 400 mg IV q 24h
<i>Clostridium difficile</i> – associated diarrhea	<ul style="list-style-type: none"> • Oral metronidazole if possible - 500 mg TID. (IV metronidazole of uncertain efficacy) • Oral vancomycin 125 mg QID (IV vancomycin is not effective) • Tigecycline 100 mg IV loading dose, then 50 mg IV BID (limited evidence)⁸
Amebic liver abscess	<ul style="list-style-type: none"> • IV therapy provides no significant advantage as long as the patient can take oral medications and has no absorption problems in small bowel⁹ • Recommended dose of metronidazole 500 to 750 mg TID • No therapeutic alternative for metronidazole for this indication

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