

Metronidazole IV Shortage

Currently marketed formulations of metronidazole IV¹

DIN	Company	Product	Strength
00870420	BAXTER CORPORATION	METRONIDAZOLE 5 MG/ML INJECTION	5 MG / ML
00649074	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 (Do not use crushed tablets)	210 mg
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.

Therapeutic Alternatives^{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 IV OR cefuroxime 1.5 gm IV
Anaerobic infections (i.e., intra-abdominal, diverticulitis, cholangitis, abscess)	<ul style="list-style-type: none"> Consider oral metronidazole (e.g., 500 mg q12h) if feasible for patient. (Oral bioavailability is equivalent to IV) Piperacillin/tazobactam IV 4.5 gm q8h or 3.375 gm q6h 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 (efficacy of IV metronidazole is uncertain) Oral vancomycin 125 mg QID (IV vancomycin is not effective) Tigecycline 100 mg IV loading dose, then 50 mg IV BID (limited evidence)⁸
Amoebic 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

Prepared by K. Jensen. Reviewed by C. Bell, Y. Shevchuk, Z. Dumont, S. Gulka and A. Wells.
15 Oct 2014

References:

- Health Canada. Drug Product Database Online Query. Ottawa, ON: Health Canada; [cited 7 Oct 2014]. Available from: <http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>
- Metronidazole monograph. In: The Ottawa Hospital Parenteral Drug Therapy Manual, 33rd edition, 2012
- Metronidazole. In: DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; Available by subscription at <http://www.micromedexsolutions.com>. Accessed October, 2014.
- Farinde A. Shortage of IV metronidazole antibiotic prompts indication-specific alternatives. Formulary Watch. Available at http://formularyjournal.modernmedicine.com/search/solr_search/metronidazole. Accessed 7 Oct 2014.
- Metronidazole. Trissel's stability of compounded formulations. In STAT!Ref (Online service); Teton Data Systems (Firm) 2012.
- Blondel-Hill E, Fryters S. Bugs and drugs. Edmonton: Alberta Health Services; 2012.
- Sanford Guide of Antimicrobial Therapy, 42nd edition, 2012.
- Herpers B, Vlaminckx B, Burkhardt O, et. al. Intravenous tigecycline as adjunctive or alternative therapy for severe refractory clostridium difficile infection. Clin Infect Dis 2009;48:1732.
- Leder K, Weller P. Extraintestinal Entamoeba histolytica amebiasis. In UptoDate online. Available at www.uptodate.com by subscription. Accessed 7 Oct 2014