Monographs for Commonly Administered Intravenous Medications in Home and Community Care

Metronidazole

Drug Class[1]	Antibiotic – Nitroimidazole	
Spectrum[1,2]	**Refer to product monograph for complete spectrum** *Bacteroides* species, *Fusobacterium, Porphyromonas, Prevotella, Clostridium* species, *Peptostreptococcus* species, *Veillonella* species, *Blastocystis hominis, Entamoeba histolytica, Giardia lamblia, Trichomonas vaginalis*	
Cross Sensitivities / Allergies[1]	Hypersensitivity to Metronidazole and other nitroimidazole derivatives (e.g., Tinidazole)	
Indications[1,3]	• Abdominal infections • Diabetic foot • Osteomyelitis	• *C. Difficile* diarrhea (IV for resistant cases) • Amebic liver abscess • Other conditions based on culture and sensitivity results
Outpatient Considerations[1]	• Must be able to access laboratory monitoring (either at outpatient laboratory or by arranging in-home lab) if using an interacting oral medication requiring therapeutic drug monitoring (see Selected Clinically Significant Drug Interactions). • For patients receiving Metronidazole IV for the first time, the first dose should be given in the hospital or other setting where the patient can be monitored for 2 hours. Rarely a profound neurological toxicity can occur. Should not be administered to patients with active neurological disorders. • Oral metronidazole may be considered after 3-5 days of intravenous therapy, depending on indication, gastrointestinal absorption and clinical status.	
Prescribing Considerations and Dosage in Adults[1,3,4]	Usual adult dose: 500 mg IV every 8-12 hours Once daily dosing of 1 to 1.5 g IV has been shown to be as effective for *B. fragilis* (intra-abdominal/ diabetic foot infections) as multiple daily dosing. Maximum daily dose is 4 g. Caution when used in patients with severe liver disease. Doses adjustment may be required—consult the pharmacist or prescriber. Metronidazole should not be used in patients with active neurological disorders, or those with a history of hypothyroidism, hypoadrenalism, or blood dyscrasias.[1]	
Administration	• Dispensed in an ambulatory cassette/multi-dose bag intended for an infusion pump, programmed to deliver total daily dose via preprogrammed boluses over 24 hours.	

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	• If ordered only twice daily, nurse may administer dose via gravity or pole pump. • Prior to connecting the patient to therapy, double check the pump programming against the order. Recheck after each order change. • Contact pharmacy infusion provider for specific questions pertaining to administration.	
Stability / Compatibilities[1,3]	*Compatible with:* • 0.9% Sodium Chloride (NS) • Dextrose 5% in Water (D5W) • Ringer's Lactate	Follow the stability as specified by the infusion provider (as it is based on the dilution). Ensure appropriate storage conditions as specified are being met.
Monitoring parameters[1]	**Laboratory:** • Baseline liver function tests if there is a concern that liver disease is present • See Selected Clinically Significant Drug Interactions section below for additional monitoring as needed	**Clinical by Nurse:** • If ataxia (uncontrollable body movements) occurs during infusion, discontinue immediately and contact prescriber. • Assess for gastrointestinal tolerance to therapy in the first 2 days. • If course of therapy exceeds 2 weeks, observe for and report any signs of peripheral neuropathy (e.g. numbness, paresthesias in extremities). Very rarely seizures may occur. • Monitor for edema or congestive heart failure exacerbation as each 500 mg dose contains 322 mg sodium • Review home medications and compare against the selected drug interactions listed below. Report to prescriber if patient is using an interacting drug and obtain further orders. For more comprehensive drug interaction screening, contact the patient's community pharmacist(s).
Selected Clinically Significant Drug interactions[1,2]	**Warfarin** – adding metronidazole can increase the effect of warfarin, putting the patient at risk of bleeding. International Normalized Ratio (INR) should be checked more frequently after initiating metronidazole (at least weekly) until stable. When metronidazole treatment is finished, INR should be checked more frequently with dosage adjustments until stable thereafter. **Phenytoin** – levels may be toxic during course of metronidazole. Suggest monitoring phenytoin level (+/- albumin level) every 5 to 7 days and adjusting dose if needed. **Lithium** – metronidazole reduces clearance of lithium, potentially causing lithium	

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	toxicity and kidney damage. Dose of lithium may need to be reduced. Monitor lithium levels and serum creatinine every 3 days during treatment and after completing the metronidazole course until stable lithium levels are attained. **Busulfan** – concomitant use can cause toxic levels of busulfan. Avoid combination if possible. **Tacrolimus** – concomitant use may increase tacrolimus levels. Monitoring tacrolimus levels is recommended during treatment, particularly during the first 2 weeks and after discontinuation.[5] **Cyclosporin –** concomitant use of metronidazole may increase cyclosporin levels. Cyclosporin levels and serum creatinine should be closely monitored during treatment. **5-Fluorouracil (5-FU)** – metronidazole may reduce the clearance of 5-FU during treatment. **Alcohol –** consumption of alcoholic beverages should be avoided during metronidazole therapy as a severe flushing reaction, retching, vomiting and headache may occur. The reaction is similar to that generated by disulfiram, a medication administered to discourage alcoholics from drinking.
Patient Education	*Advise patient to report to their doctor or nurse if they have:* • Ankle swelling or increased blood pressure, especially if they are on a sodium reduced diet. Intravenous metronidazole contains sodium and it may be necessary to add it to daily diet calculations. • Any signs of bleeding (if taking an anticoagulant). Advise patients to avoid alcohol during the treatment and up to 48 hours after course completion as it may produce a disulfiram-like reaction (manifesting as flushing, rapid heartbeat, low blood pressure, sweating, retching, vomiting or throbbing headache.[1,6] Patients may also notice a darkening of their urine. This is not harmful.[1] Patients may also notice a metallic taste in their mouth. If bothersome, ice chips, sugarless gum, or saliva substitute may be helpful.[7]
Other	For information on pregnancy and nursing please contact the Motherisk Helpline found at http://www.motherisk.org/women/contactUs.jsp

References:

1. Metronidazole product monograph. Saint-Laurent (QC): Hospira Healthcare Corporation; 2014 May 1 [cited 2016 Mar 3]. Obtained through Health Canada Drug Product Database; search term "metronidazole" as active ingredient, available from: http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp
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3. Metronidazole [monograph]. In: Bedard M, Gergoure N, Massicotte A, Editors. Parenteral Drug Therapy Manual. Ottawa (ON); 2015
4. Wang S, Cunha BA, Hamid NS, Amato BM, Feuerman M, Malone B. Metronidazole single versus multiple daily dosing in serious intraabdominal/pelvic and diabetic foot infections. J Chemother. 2007;19(4):410-6.
5. Page II RL, Klem PM, Rogers C. Potential elevation of tacrolimus trough concentrations with concomitant metronidazole therapy. Ann Pharmacother. 2005 Jun;39(6):1109-13.
6. When can I drink alcohol after finishing metronidazole? National Health Services (NHS) Choices. 2015 [cited 2016 Mar 16]. Available from: http://www.nhs.uk/chq/pages/864.aspx
7. Metronidazole (oral route). Mayo Clinic. 2016 [accessed 2016 Apr 2]. Available from: http://www.mayoclinic.org/drugs-supplements/metronidazole-oral-route/precautions/drg-20064745

Disclaimer: This monograph is intended to be used as a reference to support healthcare professionals in the home and community setting. It supplements, but does not replace: clinical judgement, the information provided by the product manufacturers, and the need to consult with the prescriber.

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