

Metronidazole Fact Sheet for Prescribers

Key messages – Use less metronidazole and usually give it by mouth

- Metronidazole is often given empirically for anaerobic cover in combination with another antibiotic that already covers anaerobes such as co-amoxiclav, piperacillin-tazobactam, clindamycin, meropenem and tigecycline
 - This is associated with a risk of side-effects and usually does no good.
- Metronidazole should usually be given by mouth if practical to do so
 - Giving it intravenously is associated with a risk of infection and is usually no better than the oral route.

Information regarding use in acute hospitals in Ireland

- Metronidazole is the third most commonly prescribed antimicrobial in Irish hospitals¹
- Over two thirds of prescriptions were for intravenous metronidazole.
- Almost half of prescriptions were in combination with a second antibiotic with anaerobic activity.

Patient safety considerations with metronidazole

- **Adverse effects**, some are common and can be very disturbing for the patient.
 - Most common side effects are: dry mouth, metallic taste, "furry" tongue, nausea (approximately 12% of patients), vomiting and myalgia.
 - Mild, reversible leukopenia can occur with long term or intensive therapy.
 - Peripheral neuropathy can occur with long-term or repeated use.
 - Appearance of abnormal neurological signs requires prompt evaluation.
 - Can be irreversible and even fatal.
 - Risk is greater when treatment exceeds 4 weeks or >42g total dose.
 - Patients for whom metronidazole is deemed necessary above these duration/dosage cut-offs should receive appropriate counselling on the increased risk of peripheral neuropathy.
 - CNS effects (e.g. headache, aseptic meningitis, encephalopathy).
- Overall, metronidazole has few **drug-drug interactions**. Of particular note are 3 severe interactions:
 - Alcohol: a disulfiram-like reaction (flushing, vomiting, tachycardia) occurs when taken with alcohol. Patients should be advised to avoid alcohol during and within 48 hours of therapy. Also applies to alcohol containing medicines.
 - Lithium: close monitoring required as lithium levels may increase. Advise patients to report lithium adverse effects (tremor, dysarthria, ataxia, confusion).
 - Warfarin: anticoagulant effects of warfarin are increased by metronidazole. Bleeding has been seen in some cases. Monitor INR if metronidazole is added or withdrawn in patients taking warfarin.
- 50% dose reduction required for **severe hepatic impairment**.
- See SmPC on www.hpra.ie for further information on cautions and interactions.

Is my patient on an antibiotic that already has anaerobic activity, therefore metronidazole may not be required?

Other agents with anaerobic activity include:

- penicillin/ β -lactamase-inhibitor combinations (co-amoxiclav or piperacillin/tazobactam)
- carbapenems (meropenem or ertapenem)
- clindamycin
- tigecycline

In what infections is its use justified?

Metronidazole is an important drug for the management of infections caused by anaerobic organisms (including Gram-negative bacteria, Gram-positive bacteria, and protozoa).

There are some common infections for which metronidazole is a first line choice and it is used as monotherapy:

- Bacterial vaginosis
- *Clostridioides difficile* infections (mild/moderate)

There are some common infections for which metronidazole is used in addition to other antibiotics:

- PID with ceftriaxone and doxycycline
- *H. pylori* combination drug therapies

In infections where resistant anaerobic bacteria are suspected/confirmed then metronidazole may be required in addition to an agent also with anaerobic activity. Seek infection specialist advice if necessary.

If metronidazole is indicated for my patient what formulation should I prescribe?

- Metronidazole has excellent oral bioavailability - it is readily and almost completely absorbed after oral doses.
- It's important to remember that in most instances if patient is nil by mouth tablets can be taken with a sip of water.
- Only if patient is strictly nil by mouth, has no oral access such as unconscious, vomiting, high outputs from NG/PEG that the intravenous route should be considered.
- Using an intravenous medication when not required exposes a patient to the unnecessary risk of line-associated infections. Note that even in a patient with an intravenous catheter for other reasons the risk of infection is likely to be reduced if the catheter is accessed as little as possible.

This is available on the Hospital-Related page on www.antibioticprescribing.ie

References

1. Annual Hospital Antimicrobial Point Prevalence Survey in Ireland 2019. <https://www.hpsc.ie/a-z/microbiology/antimicrobialresistance/europeansurveillanceofantimicrobialconsumptionesac/surveillancereports/PPS%20poster%20ISCM%20FINAL%2013.03.pdf>
2. <https://www.pharmaceutical-journal.com/news-and-analysis/opinion/correspondence/metronidazole-high-dose-and-long-duration-risks-peripheral-neuropathy/20205255.article?firstPass=false>