[Template:Drugbox](/wiki/Template:Drugbox" \o "Template:Drugbox) **Metronidazole** (**MNZ**), marketed under the brand name **Flagyl** among others, is an [antibiotic](/wiki/Antibiotic) and [antiprotozoal medication](/wiki/Antiprotozoal_medication).<ref name=AHFS2015/> It is used either alone or with other antibiotics to treat [pelvic inflammatory disease](/wiki/Pelvic_inflammatory_disease), [endocarditis](/wiki/Endocarditis), and [bacterial vaginosis](/wiki/Bacterial_vaginosis). It is effective for [dracunculiasis](/wiki/Dracunculiasis), [giardiasis](/wiki/Giardiasis), [trichomoniasis](/wiki/Trichomoniasis), and [amebiasis](/wiki/Amebiasis).<ref name=AHFS2015/> It is the drug of choice for a first episode of mild-to-moderate [*Clostridium difficile* colitis](/wiki/Clostridium_difficile_colitis).[[1]](#cite_note-1) Metronidazole is available by mouth, as a cream, and intravenously.<ref name=AHFS2015>[Template:Cite web](/wiki/Template:Cite_web)</ref>

Common side effects include [nausea](/wiki/Nausea), a metallic taste, loss of appetite, and headaches. Occasionally [seizures](/wiki/Seizure) or allergies to the medication may occur. Metronidazole should not be used in early pregnancy but appears to be safe later in pregnancy. It should not be used when [breastfeeding](/wiki/Breastfeeding).<ref name=AHFS2015/>

Metronidazole began to be commercially used in 1960 in France.[[2]](#cite_note-2) It is on the [World Health Organization's List of Essential Medicines](/wiki/World_Health_Organization's_List_of_Essential_Medicines), the most important medications needed in a basic [health system](/wiki/Health_system).<ref name=WHOEssen>[Template:Cite web](/wiki/Template:Cite_web)</ref> It is available in most areas of the world.[[3]](#cite_note-3) The pills are not very expensive being between 0.01 and 0.10 USD each.[[4]](#cite_note-4)[[5]](#cite_note-5) In the United States it is about 26 USD for ten days of treatment.<ref name=AHFS2015/>

## Contents

* 1 Medical uses[[edit](/index.php?title=(none)&action=edit&section=1)]
  + 1.1 Bacterial vaginosis[[edit](/index.php?title=(none)&action=edit&section=2)]
  + 1.2 Trichomoniasis[[edit](/index.php?title=(none)&action=edit&section=3)]
  + 1.3 Giardiasis[[edit](/index.php?title=(none)&action=edit&section=4)]
  + 1.4 ''C. difficile'' colitis[[edit](/index.php?title=(none)&action=edit&section=5)]
  + 1.5 ''E. histolytica''[[edit](/index.php?title=(none)&action=edit&section=6)]
  + 1.6 Preterm births[[edit](/index.php?title=(none)&action=edit&section=7)]
* 2 Adverse effects[[edit](/index.php?title=(none)&action=edit&section=8)]
  + 2.1 Stevens–Johnson syndrome[[edit](/index.php?title=(none)&action=edit&section=10)]
* 3 Drug interactions[[edit](/index.php?title=(none)&action=edit&section=11)]
  + 3.1 Alcohol[[edit](/index.php?title=(none)&action=edit&section=12)]
  + 3.2 Other drug interactions[[edit](/index.php?title=(none)&action=edit&section=13)]
* 4 Mechanism of action[[edit](/index.php?title=(none)&action=edit&section=14)]
* 5 Synthesis[[edit](/index.php?title=(none)&action=edit&section=15)]
* 6 Veterinary use[[edit](/index.php?title=(none)&action=edit&section=16)]
* 7 References[[edit](/index.php?title=(none)&action=edit&section=17)]
* 8 External links[[edit](/index.php?title=(none)&action=edit&section=18)]

## Medical uses[[edit](/index.php?title=(none)&action=edit&section=1)]

Metronidazole is primarily used to treat: [bacterial vaginosis](/wiki/Bacterial_vaginosis), [pelvic inflammatory disease](/wiki/Pelvic_inflammatory_disease) (along with other antibacterials like [ceftriaxone](/wiki/Ceftriaxone)), [pseudomembranous colitis](/wiki/Pseudomembranous_colitis), [aspiration pneumonia](/wiki/Aspiration_pneumonia), [rosacea](/wiki/Rosacea) (topical), fungating wounds (topical), intra-abdominal infections, [lung abscess](/wiki/Lung_abscess), [periodontitis](/wiki/Periodontitis), [amoebiasis](/wiki/Amoebiasis), oral infections, [giardiasis](/wiki/Giardiasis), [trichomoniasis](/wiki/Trichomoniasis), and infections caused by susceptible anaerobic organisms such as [*Bacteroides*](/wiki/Bacteroides)*,* [*Fusobacterium*](/wiki/Fusobacterium)*,* [*Clostridium*](/wiki/Clostridium)*,* [*Peptostreptococcus*](/wiki/Peptostreptococcus), and [*Prevotella*](/wiki/Prevotella) species.<ref name = AMH/> It is also often used to eradicate [*Helicobacter pylori*](/wiki/Helicobacter_pylori) along with other drugs and to prevent infection in people recovering from surgery.<ref name = AMH/> It is on the [World Health Organization's List of Essential Medicines](/wiki/World_Health_Organization's_List_of_Essential_Medicines), a list of the most important medication needed in a basic [health system](/wiki/Health_system).<ref name=WHOEssen/>

### Bacterial vaginosis[[edit](/index.php?title=(none)&action=edit&section=2)]

Drugs of choice for the treatment of bacterial vaginosis include metronidazole and [clindamycin](/wiki/Clindamycin). The treatment of choice for bacterial vaginosis in nonpregnant women include metronidazole oral twice daily for seven days, or metronidazole gel intravaginally once daily for five days, or clindamycin intravaginally at bedtime for seven days. For pregnant women, the treatment of choice is metronidazole oral three times a day for seven days. Data does not report routine treatment of male sexual partners.[[6]](#cite_note-6)

### Trichomoniasis[[edit](/index.php?title=(none)&action=edit&section=3)]

The 5-[nitroimidazole](/wiki/Nitroimidazole) drugs (metronidazole and [tinidazole](/wiki/Tinidazole)) are the mainstay of treatment for infection with [*Trichomonas vaginalis*](/wiki/Trichomonas_vaginalis). Treatment for both the infected patient and the patient's sexual partner is recommended, even if asymptomatic. Therapy other than 5-nitroimidazole drugs is also an option, but cure rates are much lower.[[7]](#cite_note-7)

### Giardiasis[[edit](/index.php?title=(none)&action=edit&section=4)]

Oral metronidazole is a treatment option for [giardiasis](/wiki/Giardiasis), however the increasing incidence of nitroimidazole resistance is leading to the increased use of other compound classes.[Template:Mcn](/wiki/Template:Mcn)

### ''C. difficile'' colitis[[edit](/index.php?title=(none)&action=edit&section=5)]

Initial antibiotic therapy for less-severe *Clostridium difficile* colitis ([pseudomembranous colitis](/wiki/Pseudomembranous_colitis)) consists of oral metronidazole or oral vancomycin. Several randomized controlled trials have demonstrated equivalent efficacy of oral metronidazole and oral vancomycin in treating this colitis.[[8]](#cite_note-8)[[9]](#cite_note-9)[[10]](#cite_note-10) However, oral vancomycin is shown to be more effective in treating patients with severe *C. difficile* colitis.[[8]](#cite_note-8)

### ''E. histolytica''[[edit](/index.php?title=(none)&action=edit&section=6)]

Invasive [colitis](/wiki/Colitis) and extraintestinal disease including liver abscesses, pleuropulmonary infections, and brain abscesses can result from infection with [*Entamoeba histolytica*](/wiki/Entamoeba_histolytica). Metronidazole is widely used in patients with these infections.[Template:Mcn](/wiki/Template:Mcn)

### Preterm births[[edit](/index.php?title=(none)&action=edit&section=7)]

Metronidazole has also been used in women to prevent [preterm birth](/wiki/Preterm_birth) associated with [bacterial vaginosis](/wiki/Bacterial_vaginosis), amongst other risk factors including the presence of cervicovaginal fetal fibronectin (fFN). Metronidazole was ineffective in preventing preterm delivery in high-risk pregnant women (selected by history and a positive fFN test) and, conversely, the incidence of preterm delivery was found to be higher in women treated with metronidazole.[[11]](#cite_note-11)

## Adverse effects[[edit](/index.php?title=(none)&action=edit&section=8)]

Common [adverse drug reactions](/wiki/Adverse_drug_reaction) (≥1% of those treated with the drug) associated with systemic metronidazole therapy include: [nausea](/wiki/Nausea), [diarrhea](/wiki/Diarrhea), weight loss, abdominal pain, vomiting, headache, dizziness, and metallic taste in the mouth. [Intravenous](/wiki/Intravenous) administration is commonly associated with [thrombophlebitis](/wiki/Thrombophlebitis). Infrequent adverse effects include: [hypersensitivity](/wiki/Hypersensitivity) reactions (rash, itch, flushing, fever), headache, dizziness, [vomiting](/wiki/Vomiting), [glossitis](/wiki/Glossitis), [stomatitis](/wiki/Stomatitis), dark urine, and [paraesthesia](/wiki/Paraesthesia).[[12]](#cite_note-12) High doses and long-term systemic treatment with metronidazole are associated with the development of [leucopenia](/wiki/Leucopenia), [neutropenia](/wiki/Neutropenia), increased risk of [peripheral neuropathy](/wiki/Peripheral_neuropathy), and [central nervous system](/wiki/Central_nervous_system) toxicity.<ref name=AMH/> Common adverse drug reaction associated with topical metronidazole therapy include local redness, dryness and skin irritation; and eye watering (if applied near eyes).<ref name=AMH/> Metronidazole has been associated with cancer in animal studies.[[13]](#cite_note-13)[[19]](#cite_note-19)Metronidazole is listed as a possible carcinogen according to the [WHO](/wiki/World_Health_Organization) [International Agency for Research on Cancer](/wiki/International_Agency_for_Research_on_Cancer).[[20]](#cite_note-20) A study in those with [Crohn's disease](/wiki/Crohn's_disease) also found chromosomal abnormalities in circulating lymphocytes in people treated with metronidazole.<ref name = TGA>[Template:Cite web](/wiki/Template:Cite_web)</ref>

Due to its potential carcinogenic properties, metronidazole is banned in the [European Union](/wiki/European_Union) and the United States for veterinary use in the feed of animals and is banned for use in any food animals in the USA.[[21]](#cite_note-21)[[22]](#cite_note-22)

### Stevens–Johnson syndrome[[edit](/index.php?title=(none)&action=edit&section=10)]

Metronidazole alone rarely causes [Stevens–Johnson syndrome](/wiki/Stevens–Johnson_syndrome), but is reported to occur at high rates when combined with [mebendazole](/wiki/Mebendazole).<ref name=Chen>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

## Drug interactions[[edit](/index.php?title=(none)&action=edit&section=11)]

### Alcohol[[edit](/index.php?title=(none)&action=edit&section=12)]

Consuming [alcohol](/wiki/Ethanol) while taking metronidazole has long been thought to have a [disulfiram](/wiki/Disulfiram)-like reaction with effects that can include [nausea](/wiki/Nausea), [vomiting](/wiki/Vomiting), [flushing](/wiki/Flushing_(physiology)) of the skin, [tachycardia](/wiki/Tachycardia), and [shortness of breath](/wiki/Shortness_of_breath).[[23]](#cite_note-23) Consumption of alcohol is typically advised against by patients during systemic metronidazole therapy and for at least 48 hours after completion of treatment.[[12]](#cite_note-12) However, some studies call into question the mechanism of the interaction of alcohol and metronidazole,[[24]](#cite_note-24)[[25]](#cite_note-25)[[26]](#cite_note-26)and a possible [central toxic serotonin reaction](/wiki/Serotonin_toxicity) for the alcohol intolerance is suggested.[[14]](#cite_note-14) Metronidazole is also generally thought to inhibit the liver metabolism of [propylene glycol](/wiki/Propylene_glycol) (found in some foods, medicines, and in many [electronic cigarette e-liquids](/wiki/Electronic_cigarette_e-liquids)), thus propylene glycol may potentially have similar interaction effects with metronidazole.[Template:Citation needed](/wiki/Template:Citation_needed)

### Other drug interactions[[edit](/index.php?title=(none)&action=edit&section=13)]

It also inhibits [CYP2C9](/wiki/CYP2C9) and [CYP3A4](/wiki/CYP3A4), so may interact with medications metabolised by these enzymes (e.g. [lomitapide](/wiki/Lomitapide), [warfarin](/wiki/Warfarin)).<ref name = MSR/>

## Mechanism of action[[edit](/index.php?title=(none)&action=edit&section=14)]

Metronidazole is of the [nitroimidazole](/wiki/Nitroimidazole) class. It inhibits nucleic acid synthesis by disrupting the DNA of microbial cells.<ref name = MSR/> This function only occurs when metronidazole is partially reduced, and because this reduction usually happens only in anaerobic cells, it has relatively little effect upon human cells or [aerobic bacteria](/wiki/Aerobic_bacteria).[[27]](#cite_note-27)

## Synthesis[[edit](/index.php?title=(none)&action=edit&section=15)]

[2-Methylimidazole](/wiki/2-Methylimidazole) (**1**) may be prepared via the [Debus-Radziszewski imidazole synthesis](/wiki/Debus-Radziszewski_imidazole_synthesis), or from [ethylenediamine](/wiki/Ethylenediamine) and [acetic acid](/wiki/Acetic_acid), followed by treatment with [lime](/wiki/Calcium_oxide), then [Raney nickel](/wiki/Raney_nickel). 2-Methylimidazole is nitrated to give 2-methyl-4(5)-nitroimidazole (**2**), which is in turn [alkylated](/wiki/Alkylation) with [ethylene oxide](/wiki/Ethylene_oxide) or [2-chloroethanol](/wiki/2-chloroethanol) to give metronidazole (**3**):[[28]](#cite_note-28)[[29]](#cite_note-29)[[30]](#cite_note-30)

[600px](/wiki/File:Synthesis_of_metronidazole.png)

## Veterinary use[[edit](/index.php?title=(none)&action=edit&section=16)]

Metronidazole is not labeled for animal use, but is widely used to treat infections of [*Giardia*](/wiki/Giardia) in dogs, cats, and other companion animals, although it does not reliably clear infection with this organism and is being supplanted by [fenbendazole](/wiki/Fenbendazole) for this purpose in dogs and cats.[[31]](#cite_note-31) It is also used for the management of chronic inflammatory bowel disease in cats and dogs.[[32]](#cite_note-32) Another common usage is the treatment of systemic and/or gastrointestinal clostridial infections in horses. Metronidazole is used in the aquarium hobby to treat ornamental fish and as a broad-spectrum treatment for bacterial and protozoan infections in reptiles and amphibians. In general, the veterinary community may use metronidazole for any potentially susceptible anaerobic infection. The U.S. [Food and Drug Administration](/wiki/Food_and_Drug_Administration) suggests it only be used when necessary because it has been shown to be carcinogenic in mice and rats, as well as the microbes for which it is prescribed, and resistance can develop.[[33]](#cite_note-33)[[34]](#cite_note-34)

## References[[edit](/index.php?title=(none)&action=edit&section=17)]

[Template:Reflist](/wiki/Template:Reflist)

## External links[[edit](/index.php?title=(none)&action=edit&section=18)]

* [Template:Cite web](/wiki/Template:Cite_web)
* [Template:Cite web](/wiki/Template:Cite_web)
* [Template:Cite web](/wiki/Template:Cite_web)
* [Template:Cite web](/wiki/Template:Cite_web)

[Template:Stomatological preparations](/wiki/Template:Stomatological_preparations) [Template:Antibiotics and chemotherapeutics for dermatological use](/wiki/Template:Antibiotics_and_chemotherapeutics_for_dermatological_use) [Template:Gynecological anti-infectives and antiseptics](/wiki/Template:Gynecological_anti-infectives_and_antiseptics) [Template:Nucleic acid inhibitors](/wiki/Template:Nucleic_acid_inhibitors) [Template:Agents against amoebiasis and other protozoal diseases](/wiki/Template:Agents_against_amoebiasis_and_other_protozoal_diseases) [Template:Excavata antiparasitics](/wiki/Template:Excavata_antiparasitics) [Template:Agents against amoebozoa](/wiki/Template:Agents_against_amoebozoa)

[Category:Nitroimidazole antibiotics](/wiki/Category:Nitroimidazole_antibiotics) [Category:Antiprotozoal agents](/wiki/Category:Antiprotozoal_agents) [Category:Pfizer products](/wiki/Category:Pfizer_products) [Category:World Health Organization essential medicines](/wiki/Category:World_Health_Organization_essential_medicines) [Category:IARC Group 2B carcinogens](/wiki/Category:IARC_Group_2B_carcinogens) [Category:Sanofi](/wiki/Category:Sanofi) [Category:RTT](/wiki/Category:RTT)