metronidazole

BRAND NAME: Flagyl

DRUG CLASS AND MECHANISM: Metronidazole is a nitroimidazole anti-infective medication used mainly in the treatment of infections caused by susceptible organisms, particularly anaerobic bacteria, protozoa and certain parasites. Anaerobic bacteria are single–celled, living organisms that thrive in environments in which there is little oxygen (anaerobic environments) and can cause disease in the abdomen (bacterial peritonitis), liver (liver abscess), and pelvis (abscess of the ovaries and the Fallopian tubes). Giardia lamblia and ameba are intestinal parasites that can cause abdominal pain and diarrhea in infected individuals. Trichomonas is a vaginal parasite that causes inflammation of the vagina (vaginitis). Metronidazole selectively blocks some of the functions within the bacterial cells and the parasites resulting in their death.

PRESCRIPTION: Yes

GENERIC AVAILABLE: Yes

PREPARATIONS: Tablets: 250 and 500 mg. Tablets, extended release: 750 mg. Capsule: 375 mg. Cream: 0.75% and 1%. Lotion: 0.75%. Gel: 0.75% and 1%. Injection: 5 mg/ml

STORAGE: Metronidazole should be stored at room temperature and protected from light.

PRESCRIBED FOR: Metronidazole is used to treat parasitic infections including Giardia infections of the small intestine, amebic liver abscess and amebic dysentery (infection of the colon causing bloody diarrhea), bacterial vaginosis, trichomonas vaginal infections, and carriers of trichomonas (both sexual partners) who do not have symptoms of infection. Metronidazole is also used alone or in combination with other antibiotics in treating abscesses in the liver, pelvis, abdomen and brain caused by susceptible anaerobic bacteria.

Metronidazole is also used in treating infection of the colon caused by a bacterium called *C. difficile*. (Many commonly–used antibiotics can alter the type of bacteria that inhabit the colon. *C. difficile* is an anaerobic bacterium that can infect the colon when the normal types of bacteria in the colon are inhibited by common antibiotics. This leads to inflammation of the colon (pseudomembranous colitis) with severe diarrhea and abdominal pain.) Metronidazole also is used in combination with other drugs to treat Helicobacter pylori (*H. pylori*) that causes stomach or intestinal ulcers. Metronidazole topical gel is used for treating acne rosacea, and the vaginal gel is used for treating bacterial vaginosis.

- Vaginitis due to *Trichomonas vaginalis* (protozoal) infection in both symptomatic patients as well as their asymptomatic sexual contacts; and due to bacterial *Gardnerella* or *Mycoplasma hominis* infection in symptomatic patients
- Pelvic inflammatory disease in conjunction with other antibiotics such as ofloxacin, levofloxacin, or ceftriaxone
- Protozoal infections due to *Entamoeba histolytica* (Amoebic dysentery or Hepatic abscesses), and *Giardia lamblia* (Giardiasis) should be treated alone or in conjunction with iodoquinol or diloxanide furoate
- Anaerobic bacterial infections such as *Bacteroides fragilis, spp*, *Fusobacterium spp*, *Clostridium spp*, *Peptostreptococcus spp*, *Prevotella spp*, or any other anaerobes in intraabdominal abscess, peritonitis, empyema, pneumonia, aspiration pneumonia, lung abscess, diabetic foot ulcer, meningitis and brain abscess, bone and joint infections, septicemia, endometritis, tubo-ovarian abscess, or endocarditis
- Pseudomembranous colitis due to *Clostridium difficile*
- *Helicobacter pylori* eradication therapy, as part of a multi-drug regimen in peptic ulcer disease
- Prophylaxis for those undergoing potentially contaminated colorectal surgery and may be combined with neomycin
- Acute gingivitis and other dental infections (TGA approved, non-Food and Drug Administration (FDA) approved)

- Crohn's disease with colonic or perianal involvement (non-FDA approved)

Topical metronidazole is indicated for the treatment of rosacea, and in the treatment of malodorous fungating wounds.[

DOSING: Metronidazole may be taken orally with or without food. In the hospital, metronidazole can be administered intravenously to treat serious infections. The liver is primarily responsible for eliminating metronidazole from the body, and doses may need to be reduced in patients with liver disease and abnormal liver function.

Various metronidazole regimens are used. Some examples are listed below.

Amebic dysentery: 750 mg orally 3 times daily for 5–10 days

Amebic liver abscess: 500–750 mg orally three times daily for 5–10 days

Anaerobic infections: 7.5 mg/kg orally every 6 hours not to exceed 4 grams daily

Bacterial Vaginosis: 750 mg (extended release tablets) once daily for 7 days. One applicator–full of 0.75% vaginal gel, once or twice daily for 5 days.

Clostridium difficile infection: 250–500 mg orally 4 times daily or 500–750 orally 3 times daily

Giardia: 250 mg orally three times daily for 5 days

Helicobacter pylori: 800–1500 mg orally daily for several days in combination with other drugs.

Pelvic inflammatory disease (PID): 500 mg orally twice daily for 14 days in combination with other drugs.

Trichomoniasis: 2 g single dose or 1 g twice

Rosacea: apply topical gel 0.75–1% once daily

DRUG INTERACTIONS: Alcohol should be avoided because metronidazole and alcohol together can cause severe nausea, vomiting, cramps, flushing, and headache. Consuming ethanol (alcohol) while using metronidazole causes a disulfiram-like reaction with effects that can include nausea, vomiting, flushing of the skin, tachycardia (accelerated heart rate), shortness of breath, and even death. Consumption of alcohol should be avoided by patients during systemic metronidazole therapy and for at least 24 hours after completion of treatment. However, the mechanism of this reaction in the clinical setting has recently been questioned by some authors, and a possible central toxic seratonin reaction for the alcohol intolerance suggested.

Metronidazole can increase the blood thinning effects of warfarin (Coumadin) and increase the risk of bleeding probably by reducing the break down of warfarin.

Cimetidine (Tagamet) increases blood levels of metronidazole while cholestyramine reduces blood levels of metronidazole by reducing its absorption.

Metronidazole should not be combined with amprenavir for treating human immunodeficiency disease (infection with HIV) because amprenavir contains propylene glycol. Metronidazole blocks the breakdown of propylene glycol in the liver leading to accumulation of propylene glycol in blood. Accumulation of propylene glycol could cause seizures, increased heart rate, and lead to kidney failure.

Metronidazole increases the blood levels of carbamazepine, lithium and cyclosporine though unknown mechanisms. Serious reactions may occur if these drugs are taken with metronidazole.

Pregnancy: Metronidazole is not used in early pregnancy because of potential adverse effects on the fetus.

Nursing Mothers: Metronidazole is excreted in breast milk. Nursing mothers, because of potential adverse effects on the newborn, should not use metronidazole.

Side effects: Metronidazole is a valuable antibiotic and is generally well tolerated with appropriate use. Minor side effects include nausea, headaches, loss of appetite, a metallic taste, and rarely a rash. Serious side effects of metronidazole are rare. Serious side effects include seizures and damage of nerves resulting in numbness and tingling of extremities (peripheral neuropathy). Metronidazole should be stopped if these symptoms appear.

Prevention of preterm births

Metronidazole has also been used in women to prevent preterm birth associated with bacterial vaginosis, amongst other risk factors including the presence of cervicovaginal fetal fibronectin (fFN). A randomised controlled trial demonstrated that metronidazole was ineffective in preventing preterm delivery in high-risk pregnant women and, conversely, the incidence of preterm delivery was actually higher in women treated with metronidazole.

Lamont has argued that Metronidazole is not the right antibiotic to administer in these circumstances and was often administered too late to be of use. Clindamycin administered early in the second trimester to women who test positive for bacterial vaginosis seems to be more effective.

Adverse effects

Common adverse drug reactions (≥1% of patients) associated with systemic metronidazole therapy include: nausea, diarrhea, and/or metallic taste in the mouth. Intravenous administration is commonly associated with thrombophlebitis. Infrequent adverse effects include: hypersensitivity reactions (rash, itch, flushing, fever), headache, dizziness, vomiting, glossitis, stomatitis, dark urine, and/or paraesthesia.

High doses and/or long-term systemic treatment with metronidazole is associated with the development of black hairy tongue, leukopenia, neutropenia, increased risk of peripheral neuropathy and/or CNS toxicity.

Metronidazole is listed by the International Agency for Research on Cancer (IARC) as a potential human carcinogen. Although some of the testing methods have been questioned, it has been shown to cause cancer in experimental animals. Nevertheless, it appears to have a fairly low potential for cancer risk and under most circumstances the benefits of treatment outweigh the risk.

Common adverse drug reactions associated with topical metronidazole therapy include local redness, dryness, and/or skin irritation; and eye watering (if applied near eyes).