Metronidazole

Flagyl®

125 mg per 5 mL Oral Suspension
Antiprotozoal (Nitroimidazole Derivative)

sanofi

Formulation:
Each 5 mL (1 teaspoonful) contains:
Metronidazole (as benzoate) ..... 125 mg
(equiv. to 201 mg Metronidazole)

Product Description:
Flagyl® is a white to off-white lemon flavored suspension with characteristic sweet fruit taste. Flagyl® is Metronidazole: 2-methyl-5-nitroimidazole; 1-ethanol;(2-hydroxyethyl)-2-methyl)-5-nitroimidazole;1-(bethylol)-2-methyl-5-nitro-3-azapyrole or $C_6H_9N_3O_3$with molecular weight of 171.16.

Pharmacodynamics:
Specific bactericidal activity against important obligate anaerobes.

Pharmacokinetics:
Metronidazole is readily and almost completely absorbed after oral doses. Peak plasma concentrations of about 6 and 12 micrograms/mL are achieved, usually within 1 to 2 hours, after single doses of 250 and 500 mg respectively. Some accumulation occurs and consequently there are higher concentrations when multiple doses are given. Absorption may be delayed, but is not reduced overall by food. Metronidazole benzoate given by mouth is hydrolysed in the gastrointestinal tract to release metronidazole, which in turn is then absorbed.

Metronidazole is widely distributed. It appears in most body tissues, and fluids including bile, bone, breast milk, cerebral abscesses, CSF. Liver and liver abscesses, saliva, seminal fluid, and vaginal secretions, and achieves concentrations similar to those in plasma. It also crosses the placenta rapidly and enters fetal circulation. Not more than 20% is bound to plasma proteins.

The elimination half-life of metronidazole is about 8 hours that of hydroxy metabolite is sligthly longer. The half-life of metronidazole is reported to be longer in neonates and in patients with severe hepatic impairment, that of the hydroxy metabolite is prolonged in patients with substantial renal impairment.

Indications:
For the treatment of anaerobic protozoal infections such as amoebiasis (intestinal and extraintestinal), giardiasis, trichomoniasis, balantidiasis, blastocystiasis and dientamoebiasis; for the treatment of bacterial infections, including *Bacteroides fragilis* and *Clostridium tetanus.*

Dosage and Administration:
Trichomoniasis:
Adults: Given orally either as a single 2 g dose, as a 2-day course of 800 mg in the morning and 1.2 g in the evening, or as a 7-day course of 600 mg to 1 g daily in two or three divided doses.
Anaerobic infections: Given orally in an initial dose of 800 mg followed by 400 mg every 8 hours, usually for about 7 days.
Amoebiasis:
Adults: Given in oral doses of 400 to 800 mg three times daily for 5 days to 10 days. An alternative adult dose is 1.5 to 2.5 g as a single daily dose for 2 or 3 days.
Children: Aged 1 to 3 years may be given one-quarter, those aged 3 to 7 years one-third, and those aged 7 to 10 years one-half the total adult daily dose; alternatively 35 to 50 mg/kg daily in divided doses.
Giardiasis:
Adults: Usual oral dose is 2 g once daily for 3 successive days, or 400 mg three times daily for 5 days, or 500 mg twice daily for 7 to 10 days
Children: Alternative schedule for children is 15 mg/kg daily in divided doses.
Or as prescribed by the physician.

Contraindications:
Patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives. Patients with history or evidence of blood dyscrasia. In patients with trichomoniasis, metronidazole is contraindicated during the first trimester of pregnancy.

Precautions:
Patients should be monitored for neurological signs. Candida overgrowth, may occur, interacts with alcohol and warfarin. As much as possible, its use should be avoided during pregnancy.

Warning: Metronidazole has been shown to be carcinogenic in mice and possibly carcinogenic in rats. Unnecessary use of the drug should be avoided.

Pregnancy and Lactation:
Metronidazole should not be given in the first trimester of pregnancy as it crosses the placenta and enters fetal circulation rapidly. Metronidazole is secreted in breast milk. In view of its tumorigenic and mutagenic potential, breastfeeding is not recommended.

Drug Interactions:
When given with alcohol, metronidazole may provoke a disulfiram-like reaction in some patients. Acute psychoses or confusion have been associated with the use of metronidazole and disulfiram together.

Metronidazole is reported to impair the metabolism or excretion of several drugs including warfarin and phenytoin, lithium, ciclosporin, and fluorouracil, with the consequent potential for an increased incidence of adverse effects. There is some evidence that phenytoin might accelerate metabolism of metronidazole. Plasma concentrations of metronidazole are decreased by Phenobarbitals, with a consequent reduction in the effectiveness of metronidazole. Cimetidine has increased plasma concentration of metronidazole and might increase the risk of neurological adverse effects.

Adverse Drug Reactions:
The adverse drug reactions of metronidazole are generally dose-related. The most common are gastrointestinal disturbances, especially nausea and an unpleasant metallic taste. Vomiting and diarrhea or constipation may also occur. A furred tongue, glossitis and stomatitis may be associated with an overgrowth of Candida. There have been rare reports of antibiotic-associated colitis with metronidazole, although it is also used in the treatment of this condition.

Weakness, dizziness, ataxia, headache, drowsiness, insomnia and changes in mood or mental state such as depression or confusion have also been reported. Peripheral neuropathy, usually presenting as numbness or tingling in the extremities, and epileptiform seizures have been associated with high doses of metronidazole or prolonged treatment.

Temporary moderate leucopenia and thrombocytopenia may occur in some patients receiving metronidazole. Skin rashes, urticaria and pruritus occur occasionally and multiforme, angioedema and anaphylaxis have been reported rarely. Other adverse effects include urethral discomfort and darkening of the urine. Raised liver enzyme values, cholestatic hepatitis, and jaundice have occasionally been reported. Thrombophlebitis may follow the intravenous administration of metronidazole.

Studies have shown metronidazole to be mutagenic in bacteria and carcinogenic in some animals.

Overdose and Treatment:
Single oral doses of metronidazole, up to 12 g, have been reported in suicide attempts and accidental overdoses. Symptoms reported include nausea, vomiting, and ataxia. Oral metronidazole has been studied as a radiation sensitizer in the treatment of malignant tumors. Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after 5 to 7 days of doses of 6 to 10.4 g every other day.

Treatment: There is no specific antidote for metronidazole overdose; therefore, management of the patient should consist of symptomatic and supportive therapy.

Storage Condition:
Store at temperatures not exceeding 30ºC.

Availability:
Amber Glass Bottle x 60mL (Box of 1's)

Caution:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

ADR Reporting Statement:
For suspected adverse drug reaction, report to the **FDA: www.fda.gov.ph.**
If you experience any side effects with the use of this product, you are advised to seek medical attention.

You are also encouraged to report any side effects to Sanofi Philippines Pharmacovigilance Unit at **PV.Philippines@sanofi.com.**
By reporting side effects, you can help provide more information on the safety of this product.

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Manufactured by:
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