EFLARON®

Metronidazole BP tablets

Metronidazole Benzoate BP suspensions

Composition:

Each tablet contains: 200 mg, 250mg, 400mg, or 500mg of Metronidazole BP

Each 5ml spoonful of suspension contains: Metronidazole BP 125mg or 200mg (as Benzoate) BP

Pharmacology:

Metronidazole is a 5-nitroimidazole derivative with activity against anaerobic bacteria and protozoa. It also has a radiosensitising effect on hypoxic tumour cells. Its mechanism of action is thought to involve interference with DNA by a metabolite in which the nitro group of metronidazole has been reduced. Metronidazole is active against several protozoa including *Balantidium coli*, *Blastocystis hominis*, *Entamoeba histolytica*, *Giardia intestinalis* (*Giardia lamblia*), and *Trichomonas vaginalis*. Most obligate anaerobic bacteria, including *Bacteroides* and *Clostridium* spp., are sensitive *in vitro* to metronidazole. It is bactericidal. It also has activity against the facultative anaerobes *Gardnerella vaginalis* and *Helicobacter pylori* and against some spirochaetes. Metronidazole has well-established bactericidal activity against obligate anaerobic bacteria *in vitro*, including the Gram-negative organisms *Bacteroides fragilis* and other *Bacteroides* spp., *Fusobacterium* spp., and *Veillonella* spp., and the Gram-positive organisms *Clostridium difficile, Cl. perfringens,* and other *Clostridium* spp., *Eubacterium* spp., *Peptococcus* spp., and *Peptostreptococcus* spp.; *Propionibacterium* and *Actinomyces* spp. are often resistant. It also has activity against the facultative anaerobe *Gardnerella vaginalis*, although its bactericidal effect is reported to be much slower than against obligate anaerobes, against some strains of *Campylobacter* spp. including *C. fetus* subsp. *jejuni*, and against *Helicobacter pylori.* The oxidative metabolites of metronidazole also have antibacterial activity; the hydroxy metabolite has been reported to be consistently more active than metronidazole against strains of *G. vaginalis*.

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.

Peak steady-state plasma concentrations of about 25 micrograms/mL with trough concentrations of about 18 micrograms/mL have been reported in patients given an intravenous loading dose of 15 mg/kg followed by 7.5 mg/kg every 6 hours.

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 and rapidly enters the fetal circulation. No more than 20% is bound to plasma proteins. Metronidazole is metabolised in the liver by side-chain oxidation and glucuronide formation. The principal oxidative metabolites are 1-(2-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole (the hydroxy metabolite), which has antibacterial activity and is detected in plasma and urine, and 2-methyl-5-nitroimidazole-1-acetic acid (the acid metabolite), which has virtually no antibacterial activity and is often not detected in plasma, but is excreted in urine. Small amounts of reduced metabolites, acetamide and *N*-(2-hydroxyethyl) oxamic acid (HOA), have also been detected in urine and are probably formed by the intestinal flora. The elimination half-life of metronidazole is about 8 hours; that of the hydroxy metabolite is slightly 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. The majority of a dose of metronidazole is excreted in the urine, mainly as metabolites; a small amount appears in the faeces.

Indications:

Anaerobic infections: gynaecological and intra-abdominal infections, infections of the CNS, pulmonary infections, septicaemia, endocarditis, infections caused by susceptible anaerobic bacteria: Bacteroides species, including *B. fragilis* group (*B. distosonis*, *B. ovatus, B. thetaiotaomicron, B. vulgatus*), Clostridium species, Eubacterium species, Peptococcus species, Peptostreptococcus species. Ulcerative gingivitis Infections caused by Trichomonas in both sexes. Amoebiasis Lambliasis and *Helicobacter pylori* eradication.

Dosage and Administration:

Anaerobic infections

Treatment of anaerobic infections (usually treated for 7 days and for 10 days in antibiotic – associated colitis), by mouth either 800mg initially then 400mg every 8 hours or 500mg every 8 hours.

Children: 7.5mg / kg every 8 hours.

Preventive treatment: adults and children more than 12 years old: (100ml) administered in slow intravenous drip infusion immediately before, or during operation; the same dose is repeated every 8 hours until oral treatment is possible (200mg to 400mg) 3 times daily. The treatment (intravenous and oral together) should not last more than a week.

Children less than 12 years old: 7.5mg/kg body weight (=1.5ml/kg) administered in slow intravenous drip infusion following the same schedule as in adults. Orally, a dosage of 3.7 to 7.5 mg/kg body weight is administered 3 times daily. The complete treatment lasts 7 days.

Trichomoniasis

Both partners should be treated simultaneously. Metronidazole is given by mouth 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. If treatment needs to be repeated, an interval of 4 to 6 weeks between courses has been recommended.

Children with trichomoniasis may be given a 7-day course of metronidazole by mouth as follows: 1 to 3 years, 50 mg three times daily; 3 to 7 years, 100 mg twice daily, and 7 to 10 years, 100 mg three times daily. An alternative children's dose is 15 mg/kg daily in divided doses for 7 days.

Amoebiasis

Metronidazole is given in doses of 400 to 800 mg three times daily by mouth for 5 to 10 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 has been used. An alternative adult dose is 1.5 to 2.5 g as a single daily dose for 2 or 3 days.

Lambliasis:
Adults: 800mg daily, divided into two doses for a period of 5 days.
Children: 35mg to 50mg/kg body weight divided into two doses for a period of 5 days
Leg ulcers and pressure sores
400mg every 8 hours for 7 days by mouth.
Bacterial vaginosis
400 – 500mg twice daily for 5 - 7 days or 2g as a single dose by mouth.
Pelvic inflammatory disease
400 mg twice daily for 14 days
Acute ulcerative gingivitis
Adults: 200 - 250mg daily every 8 hours for 3 days
Children 1 – 3 years: 50mg daily every 8 hours for 3 days, 3 – 7 years 100mg every 12 hours and 7-10 years 100mg every 8 hours.
Acute oral infections
Adults: 200mg daily every 8 hours for 3 - 7 days
*Children 1 – 3 years:*50mg daily every 8 hours for 3 - 7 days,3 – 7 years 100mg every 12 hours and 7-10 years 100mg every 8 hours.
Surgical prophylaxis
Adults: 400 - 500mg daily every 2 hours before surgery; upto 3 further doses of 400 - 500 mg may be given every 8 hours for high – risk procedures.
Children : 7.5mg / kg 2 hours before surgery; upto 3 further doses of 7.5 mg / kg may be given every 8 hours for high – risk procedures
Side effects:
Nausea, gastrointestinal pain, diarrhea, metallic taste may occur. With protracted intravenous use, transient neutropenia as well as peripheral neuropathy, headache, sleepiness, dizziness, ataxia and par aesthesia may occur.
Contraindications:
Hypersensitivity to metronidazole or other nitro- imidazole derivatives.
The first trimester of pregnancy.
If CNS disorders occur (ataxia, paraesthesia), treatment should be discontinued immediately. Concomitant administration of disulfiram is contraindicated too.
Caution:
When warfarin or other anticoagulants are administered concomitantly, the dose should be adequately reduced. Patients should abstain from alcoholic beverages during treatment. Metronidazole is excreted with human milk and penetrates the placental barrier. The use of metronidazole during pregnancy and lactation is not recommended.
Presentation:
HDPE jars with 1000 tablets of 200mg / 250mg
HDPE jars with 500 tablets of 400mg/500mg.
Blister pack of 10 X 10's tablets
60ml and 100ml bottles
Distribution category:
Prescription Only Medicine (POM)
Storage conditions:
Store in a dry place, below 30°C. Protect from light.
Keep all medicines out of reach of children.
Manufactured by:

DAWA	**DAWA Limited,** **Plot No. 7879/8, Baba Dogo Road, Ruaraka** **P. O. Box 16633 – 00620, Nairobi, Kenya.**

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