PACKAGE LEAFLET: Information for the patient

METRONIDAZOL

Tablets – 250 mg

Solution for infusion – 0.5%

(Metronidazole)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT METRONIDAZOL IS AND WHAT IT IS USED FOR

Metronidazole, a synthetic derivative of nitroimidazole, acts against gram-positive and gram-negative anaerobic microorganisms (*Bacteroides* species, including the *B.fragilis* bacterial group, *Clostridium* species, *Eubacterium* species, *Peptococcus* species, *Peptostreptococcus* species and against protozoan (*Trichomonas vaginalis, Entamoeba histolytica,* and *Giardia lamblia*). The mechanism of action of metronidazole is not yet clear. It is thought that metronidazole inhibits the synthesis of DNA. It has bactericidal action.

Metronidazol is used in:

- the treatment of infections caused by anaerobic microorganisms and infections from protozoa;
- prevention of postoperative infections caused by anaerobic bacteria, especially bacteroides and anaerobic streptococci species;
- the treatment of septicemia, bacteremia, peritonitis, brain abscess, necrotizing pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis and postoperative infections wounds when from them are isolated sensitive anaerobic pathogen microorganisms; urogenital trichomoniasis in females (trichomonial vaginitis) and in males; bacterial vaginosis (also known as non-specific vaginitis), or anaerobic vaginosis or *Gardnerella* vaginitis;
- acute ulcerative gingivitis; leg ulcers, infected by anaerobic microorganisms;
- acute dental infections (e.g. acute pericoronitis and acute apical infections);
- all forms of amoebiasis (intestinal and extraintestinal disease) and those of asymptomatic cyst holders;
- giardiasis;
- treatment of *Helicobacter pylori,* in combination with other medicines.

Your doctor may have given you Metronidazol for another purpose. Ask your doctor if you want to know why you were given Metronidazol.

2. BEFORE YOU TAKE METRONIDAZOL

Do not take Metronidazol if you suffer from hypersensitivity to metronidazole or to any of the other nitroimidazole derivatives.

Take special care with Metronidazol

You should not consume alcoholic beverages during treatment with metronidazole and for at least 48 hours after the end of treatment because there is a risk of disulfiram-like reaction.
Metronidazol should be used with caution in active diseases of the central nervous system, except for brain abscess, in patients that are having kidney dialysis and those that have blood disorders.
Also care should be taken in patients with impaired liver function, during pregnancy and breastfeeding.
Cases of severe liver toxicity / acute liver failure, including cases with a fatal outcome, in

patients with Cockayne syndrome have been reported with products containing metronidazole. If you are affected by Cockayne syndrome, your doctor should also monitor your liver function frequently while you are being treated with metronidazole and afterwards.
Tell your doctor immediately and stop taking metronidazole if you develop:

- stomach pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine, putty or mastic coloured stools or itching.

Special patient monitoring is advised if the treatment continues for more than 10 days.

Additional precautions for the solution for infusion:
Special caution is required in patients who are on a controlled sodium diet.

Taking other medicines
Concomitant treatment with other medicines may affect or be affected by Metronidazol.
Please contact your doctor or pharmacist if you are taking or have recently taken other medicines, including those obtained without a prescription. Do not forget to inform your doctor for the treatment with Metronidazol if you take any other medicine during treatment.

- When given with alcohol, metronidazole may provoke a disulfiram-like reaction in some patients.
- During concomitant use of disulfiram with metronidazole, acute psychosis or confusion were observed.
- It is reported a metabolism or excretion impairment of many drugs including: warfarin, phenytoin, lithium, busulphan and fluorouracil causing an increased incidence of side effects.
- It is thought that phenytoin may accelerate the metabolism of metronidazole.
- Metronidazole plasma concentrations are reduced from phenobarbital, causing a reduction in the efficacy of metronidazole.
- Cimetidine increases the plasma concentrations of metronidazole and may increase the risk of neurological side effects as a result of treatment with metronidazole.
- Omeprazole may reduce plasma concentrations of metronidazole in gastric fluid. This can be significant in the treatment of *Helicobacter pylori* infections.

Taking Metronidazol with food and drinks

Metronidazol should not be taken together with alcoholic beverages because there is a risk of a disulfiram-like reaction.

Pregnancy

Tell your doctor or pharmacist if you are pregnant or are planning to have a baby.
Metronidazole is mutagenic in bacteria and carcinogenic in rodents. It readily crosses the placenta achieving similar concentrations with the rest of the body. For this reason its use in pregnancy is contraindicated.
Meta-analyses of studies involving the use of metronidazole in the first trimester of pregnancy concluded that there did not appear to be an increased risk of teratogenicity. However, the risks and benefits of treatment with metronidazole should be weighed carefully, especially in the first trimester of pregnancy.

Breastfeeding

Metronidazole is excreted into breast milk giving it a bitter taste which may impair baby's feeding. It is recommended to stop breastfeeding for 12 to 24 hours when the mother is treated with a single-dose of Metronidazol, while no specific recommendations are given for long-term treatment.

Driving and using machines

While taking Metronidazol you may experience: dizziness, drowsiness, confusion, seizures, and visual disturbances. If this happens, do not drive or use any machinery or tools.

Important information about some of the excipients of Metronidazol

Metronidazol tablets contain lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
Metronidazol solution for infusion contains sodium. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE METRONIDAZOL

Always take Metronidazol as your doctor has told you. Check with your doctor or pharmacist if you are not sure. If you notice that Metronidazol effects are too strong or too weak, talk to your doctor or pharmacist.

The tablets should be swallowed with a glass of water (200 – 250 ml water).

Dosage is as follows:

In anaerobic infections (usually treatment lasts for 7 days),

by mouth: at the beginning 750 mg, then 500 mg, every 8 hours;

by intravenous infusion: 500 mg, every 8 hours.

Children, through any route: 7.5 mg / kg of body weight, every 8 hours.

In ulcus cruris and decubitus: *by mouth*, 500 mg, every 8 hours for 7 days.

In bacterial vaginosis: *by mouth*, 500 mg, twice daily, for 7 days or 2 g as a single dose.

In acute ulcerative gingivitis: *by mouth*, 250 mg, every 8 hours for 3 days.

Children 1 - 3 years: 50 mg, every 8 hours for 3 days;

3 - 7 years: 100 mg every 12 hours;

7 - 10 years: 125 mg, every 8 hours.

In acute dental infections: by mouth: 250 mg, every 8 hours for 3 - 7 days.

In surgical prophylaxis: *by mouth*, 500 mg, every 8 hours, which begins before surgery and then in the postoperative period should be continued with intravenous infusion until oral therapy can be initiated.

Children: 7.5 mg / kg of body weight, every 8 hours.

In treatment of *Helicobacter pylori:* according to medical prescription, in combination with other medicines.

By intravenous infusion: 500 mg before surgery and then continued every 8 hours until oral therapy can be initiated.

Children: 7.5 mg / kg of body weight, every 8 hours.

In trichomoniasis: *by mouth*, 250 mg, every 8 hours for 7 days or 500 mg, every 12 hours for 7 days or 750 mg in the morning and 1.25 g in the evening, before bedtime, for 2 days or 2 g, as a single dose. When the infection is repeated, the sexual partner should also be treated with the same dosage regimen.

Children 1 - 3 years: 50 mg, every 8 hours for 7 days;

3 - 7 years; 100 mg every 12 hours;

7 - 10 years: 100 mg, every 8 hours.

In invasive intestinal amoebiasis, by mouth: 750 mg, every 8 hours, for 5 days;

Children 1 - 3 years: 250 mg, every 8 hours;

3 - 7 years: 250 mg every 6 hours;

7 - 10 years: 500 mg, every 8 hours.

In extraintestinal amoebiasis (including liver abscesses) and asymptomatic holders of amebic cysts: 500 - 750 mg, every 8 hours for 5-10 days.

Children 1 - 3 years: 125 – 250 mg, every 8 hours;

3 - 7 years: 125 – 250 mg, every 6 hours;

7 - 10 years: 250 – 500 mg, every 8 hours.

In giardiasis: 2 g per day for 3 days.

Children 1 - 3 years: 500 mg per day;

3 - 7 years: 500 - 750 mg per day;

7 - 10 years: 1 g per day.

If you take more Metronidazol than you should

If you take more Metronidazol than you should, or if the children take it accidentally, please contact your doctor, the hospital or any medical care site to seek advice on the risk and the appropriate measures.

The symptoms described by overdose of a single dose up to 12 g metronidazole are: vomiting, ataxia and mild disorientation.

Treatment: there is no specific antidote for metronidazole. In cases of an acute overdose, it should be continued with a symptomatic treatment (gastric lavage, activated charcoal, hemodialysis).

If you forget to take Metronidazol

If you forget to take one dose (or more), take the next dose in its usual time.

Do not take a double dose (or higher) to make up a forgotten dose(s).

If you have further questions on the use of this medicinal product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Metronidazol can cause side effects, although not everybody gets them. Metronidazole is well tolerated in the recommended doses. Tell your doctor about the following side effects that may occur:

- mild gastrointestinal disorders (nausea, vomiting, abdominal pain, metallic taste, dry mouth, or rarely diarrhoea);
- hypersensitivity reactions (angioedema, eczema, urticaria, severe skin reactions) are rare;
- neurological adverse reactions (headache, dizziness, drowsiness, ataxia, seizures, encephalopathy, peripheral neuropathy, cerebellar syndrome, confusion, nerve disorders, psychotic disorders, hallucinations, depression);
- darkening of urine;
- visual disturbances;
- hearing impairment, ringing in the ears (tinnitus);
- inflammation of the mucous membranes (mucositis);
- transitional neutropenia;
- appetite decreased;
- pancreatitis, hepatic disorders, which may appear in very rare cases;
- pancytopenia, agranulocytosis, thrombocytopenia and leucopenia;
- muscles pain, asthenia;
- aseptic meningitis.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

When any of the above-mentioned side effects appears, the treatment with Metronidazol should be discontinued and you should consult your doctor or pharmacist.

5. HOW TO STORE METRONIDAZOL

Keep out of the sight and reach of children!

Do not use Metronidazol after the expiry date which is stated on the package.

Do not store above 25°C!

Keep in the original package to protect from light and humidity.

6. FURTHER INFORMATION

What Metronidazol 250 mg tablets contain

The active substance is metronidazole.

Each tablet contains 250 mg metronidazole.

The excipients are lactose monohydrate, microcrystalline cellulose, povidone, sodium starch glycolate, magnesium stearate, talc.

What Metronidazol 0.5% solution for infusion contains

The active substance is metronidazole.

1 ml solution for infusion contains 5 mg metronidazole.

The excipients are sodium hydrogenphosphate dibasic dihydrate, citric acid monohydrate, sodium chloride, water for injection.

Contents of the pack

Tablets: Box with 30 tablets.

Solution for infusion: 100 ml glass bottles or 100 ml plastic bags.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,

St. “Skënder Vila”,

Tirana, Albania.

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