PACKAGE LEAFLET: Information for the patient

MEZYL

Oral suspension – 125 mg / 5 ml

(Metronidazole benzoate)

Read all of 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Mezyl is and what it is used for
2. Before you take Mezyl
3. How to take Mezyl
4. Possible side effects
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1. WHAT MEZYL IS AND WHAT IT IS USED FOR

Mezyl contains the active ingredient metronidazole. Metronidazole, a synthetic derivative of nitroimidazole, is active against several anaerobic gram-positive and gram-negative microorganisms (*Bacteroides fragilis* and other *Bacteroides* spp., *Clostridium* spp., *Eubacterium* spp., *Peptococcus* spp., and *Peptostreptococcus* spp.) and several protozoa (*Trichomonas vaginalis, Entamoeba histolytica* and *Giardia lamblia).* The mechanism of action of metronidazole is not entirely clear, but it is thought to inhibit DNA synthesis. Metronidazole has a bactericidal action.

It is indicated in:

- treatment of infections caused by anaerobic microorganisms, and protozoan infections;
- the prevention of post-operative infections due to anaerobic bacteria, particularly species of *Bacteroides* and anaerobic *Streptococci;*
- treatment of septicaemia, bacteraemia, peritonitis, brain abscesses, necrotizing pneumonia, osteomyelitis, puerperal sepsis, pelvic abscesses, pelvic cellulitis and post-operative wound infections from which pathogenic anaerobes have been isolated, urogenital trichomoniasis in females (trichomonal vaginitis) and in males; bacterial vaginosis (known as nonspecific vaginitis), anaerobic vaginosis or *Gardnerella* vaginitis;
- acute ulcerative gingivitis; anaerobically-infected leg ulcers or pressure sores;
- acute dental infections (e.g. acute pericoronitis and acute apical infections);
- all forms of amoebiasis (intestinal and extra-intestinal disease) and symptomless cyst passers;
- giardiasis;
- eradication of *Helicobacter pylori*, in combination with other drugs.

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

2. BEFORE YOU TAKE MEZYL

Do not take Mezyl if you:

- suffer from hypersensitivity to metronidazole or to other derivatives of nitroimidazole or hypersensitivity to any of the ingredients of the product.

Take special care with Mezyl

Ask your doctor before taking Mezyl.

Peripheral neuropathy, transient epileptiform seizures, and leukopenia have sometimes been associated with prolonged or intensive treatment with metronidazole. These effects are reversible. Clinical and laboratory monitoring is advised in patients receiving metronidazole for more than 10 days. The patients should be monitored for adverse reactions, such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, convulsive seizures).

Cases of severe liver toxicity or acute liver failure, including cases with a fatal outcome, in patients with Cockayne syndrome have been reported with product 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.

Doses should be reduced in patients with severe hepatic impairment. It is suggested that the use of metronidazole should be avoided during pregnancy, and this caution applies especially to use during the first trimester and to the use of high-dose regimens.
It is advised not to drink alcoholic beverages while taking Mezyl. It should be used with caution in patients with active central nervous system disease, except in cerebral abscesses, due to the risk of neurological aggravation. Mezyl should be administered with caution to patients with hepatic encephalopathy. This drug may darken urine as a result of its metabolites.
Metronidazole is removed during haemodialysis and for this reason it should be administered after the procedure has been completed.
Doses above 12.5 ml Mezyl (equivalent to 312.5 mg metronidazole) contain more than 5 g sucrose. This should be taken into account in patients with diabetes mellitus.

Taking other medicines
Concomitant use with other drugs may affect or be affected by Mezyl. Please, tell your doctor or pharmacist if you are taking or have taken recently other drugs, including those without prescription. Remember to tell your doctor about the treatment with Mezyl, if you are given another drug during treatment.

- 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, phenytoin, lithium and fluorouracil, with the consequent potential for an increased incidence of adverse effects.
- There is some evidence that phenytoin might accelerate the metabolism of metronidazole by decreasing its plasmatic levels. A similar effect may be noticed with other drugs that induce microsomal hepatic enzymes.
- Plasma concentrations of metronidazole are decreased by phenobarbital, with a consequent reduction in the effectiveness of metronidazole.
- Cimetidine increases plasma concentrations of metronidazole and might increase the risk of neurological adverse effects, because of treatment with metronidazole.
- Plasma levels of busulfan may be increased by metronidazole which may lead to severe busulfan toxicity.
- An increase of ciclosporin serum levels is noticed. Serum ciclosporin and serum creatinine should be closely monitored when coadministration is necessary.
- Metronidazole enhances anticoagulant effect of coumarins.

Taking Mezyl with food and drinks

Metronidazole should not be taken with alcohol because it may provoke a disulfiram-like reaction. Avoid taking alcohol for at least 48 hours after stopping treatment.

Pregnancy

Tell your doctor or pharmacist if you are pregnant or are planning to have a baby. It is suggested to avoid taking Mezyl, if you are pregnant, think you may be pregnant, or are planning to become pregnant.

Metronidazole is mutagenic in bacteria and carcinogenic in rodents. It readily crosses the placenta achieving similar concentrations in the other parts of the organism. Use of metronidazole should be avoided during pregnancy, especially in the first trimester of pregnancy and use of high doses should be avoided, too. Risks and benefits of treatment with metronidazole should be weighed carefully in cases where administration of Mezyl during pregnancy is deemed necessary.

Before use of Mezyl, pregnant women should take into account the information in “Important information about some of the ingredients of Mezyl” regarding the content of ethanol (alcohol).

Breastfeeding

Tell your doctor or pharmacist if you are breastfeeding. It is suggested to avoid taking taking Mezyl if you are breastfeeding.

Mezyl is distributed into breast milk giving it a bitter taste which may impair feeding. It is recommended to discontinue the breastfeeding for 12 to 24 hours when single-dose therapy is used; no specific recommendations are given for long-term treatment.

Before use of Mezyl, breastfeeding women should take into account the information in “Important information about some of the ingredients of Mezyl” regarding the content of ethanol (alcohol).

Driving and using machines

Use of Mezyl may cause drowsiness, dizziness, confusion, hallucinations, convulsions or transient visual disorders. You should not drive or operate machinery if these symptoms occur.

Important information about some of the ingredients of Mezyl

Mezyl contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product. Doses above 12.5 ml Mezyl (equivalent to 312.5 mg metronidazol) contain more than 5 g sucrose. This should be taken into account in patients with diabetes mellitus.

Mezyl contains also methyl hydroxybenzoate and propyl hydroxybenzoate, which may cause allergic reactions (possibly delayed).

Mezyl contains approximately 1% of the volume ethanol (alcohol); this is equivalent to 40.278 mg ethanol 96% in 5 ml oral suspension.

The amount of alcohol in this medicine is not likely to have an effect in adults and adolescents, and its effects in children are not likely to be noticeable. It may have some effects in younger children, for example feeling sleepy.

The alcohol in this medicine may alter the effects of other medicines. Talk to your doctor or pharmacist if you are taking other medicines.

If you are pregnant or breastfeeding, talk to your doctor or pharmacist before taking this medicine.
If you are addicted to alcohol, talk to your doctor or pharmacist before taking this medicine.
Mezyl contains sodium; doses over about 8.87 ml oral suspension Mezyl contain over 23 mg sodium. This should be considered by patients who are following a salt-controlled diet.
Mezyl contains approximately 560 mg sorbitol in 5 ml oral suspension. Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive this medicine. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

3. HOW TO TAKE MEZYL

Always take Mezyl exactly as your doctor has told you. If you are not sure, talk to your doctor or pharmacist. Talk to your doctor or pharmacist if the effects are too weak or too strong.
Shake well before use!
The doses are as below:
Urogenital trichomoniasis
Adults and children over 10 years old: 1000 mg per day, in 2 divided doses, for 5 - 7 days or as a single 2 g dose (if necessary, sexual partners should be treated concomitantly).
Alternatively, adults may be treated with a short regimen as a 2-day course of 2 g per day, in two divided doses.
Children: 15 mg / kg per day in 3 divided doses.
Treatment should be continued for 7 days.

Acute ulcerative gingivitis
Adults and children over 10 years old: 750 mg per day, in 3 divided doses, for 3 days.

Amoebiasis
Adults and children over 10 years old: 500 mg, 3 – 4 times daily.
Children: 35 mg / kg per day in divided doses.
Treatment usually lasts from 5 to 10 days.

Giardiasis

Adults and children over 10 years old: 2000 mg, once daily, for 3 days or 500 mg twice daily for 7 – 10 days.

Children 7-10 years old: 1000 mg, once daily, for 3 days.

Children 3-7 years old: 600 mg - 800 mg, once daily, for 3 days.

Children 1-3 years old: 500 mg, once daily, for 3 days.

Anaerobic infections

Treatment

Adults: 500 mg, every 8 hours.

Children: 7.5 mg / kg every 8 hours.

Treatment should be stopped by clinical and bacteriological evaluation of the doctor, but 7 days should be sufficient.

Prophylaxis against anaerobic infections

Adults: 400 mg every 8 hours in the 24 hours before surgery, followed postoperatively by intravenous or rectal administration until oral therapy is possible.

Children: 7.5 mg / kg every 8 hours.

Dental infections

Adults: the usual total daily dose is 750 mg, in divided doses. Usually the treatment should be continued for 3 to 7 days.

Ulcerations

Adults: 400 mg, 3 times daily, for 7 days.

In eradication of *Helicobacter pylori*

According to the physician's recommendation, combined with other drugs.

Dose adjustment does not seem necessary in patients with renal impairment.

In case of children whose weight is lower than the normal weight for their age or in case of infants under 10 kg, the dose of metronidazole should be reduced proportionally.
Metronidazole is removed during haemodialysis and for this reason it should be administered after the procedure has been completed.
Elderly: Special care should be taken with higher doses. There is no information regarding the dose modification.

Hepatic encephalopathy and severe liver disease
The daily dosage should be reduced to one third and may be administered once daily.

If you take more Mezyl than you should
If you take more Mezyl than you should, or if the children have taken this medicine by accident, please contact your doctor, the hospital, or call the emergency to get an opinion of the risk and advice on the actions to be taken.
Symptoms reported after a single oral dose up to 12 g of metronidazole, are: vomiting, ataxia and slight disorientation.
Treatment: there is no specific antidote for metronidazole overdosage. In cases of suspected acute overdose, symptomatic treatment should be instituted (gastric lavage, activated charcoal, hemodialysis).

If you forget to take Mezyl
If you forget to take one or more doses, take the next dose at the next prescribed time. Do not take a double dose (or a higher dose) to make up for the forgotten dose(s).
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Mezyl can also cause side effects, although not everybody may get them. Mezyl is well tolerated in the recommended dose. Tell your doctor about the side effects that may appear.

Gastrointestinal effects:

- nausea, vomiting, diarrhoea;
- epigastric pain, impaired sense of taste, furred tongue, oral mucositis;
- dry mouth, anorexia, special and reversible cases of pancreatitis.

Hypersensitivity reactions:

- rash, pruritus, eczema, urticaria;
- fever, angioedema, erythema multiforme, exceptional cases of anaphylactic shock;
- very rare cases of acne eruptions;
- severe skin reactions.

Central and peripheral nervous system:

- headache, dizziness, ataxia, convulsions, transient epileptiform seizures (on prolonged or intensive therapy);
- encephalopathy, peripheral neuropathy, drowsiness, paraesthesia;
- very rare reports of encephalopathy (e.g., confusion) and subacute cerebellar syndrome (e.g., ataxia, dysarthria, gait impairment, nystagmus and tremor) which may resolve on discontinuation of the drug;
- aseptic meningitis.

Psychiatric disorders:

- psychotic disorders that include confusion, hallucinations;
- depressed mood.

Visual disorders:

- vision disorders such as diplopia and myopia;

- optic neuropathy / neuritis.

Hematological effects:

- cases of agranulocytosis, leucopenia, neutropenia, pancythopenia and thrombocytopenia, have been reported very rarely.

In the liver:

- cases of cholestatic hepatitis, sometimes associated with jaundice, have been reported very rarely.
- other hepatic disorders

Other: darkening of urine, hearing impairment, hearing loss, ringing in the ears (tinnitus), muscle pain, joint pain.

If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.
If any of the above side effects appears, the treatment with Mezyl should be discontinued and you should talk to your doctor or pharmacist.

5. HOW TO STORE MEZYL

Keep out of the reach and sight of children!
Do not use Mezyl after the expiry date which is stated on the package.
Store below 25°C!
Store in the original package to protect it from light.

6. FURTHER INFORMATION

What Mezyl contains

The active substance is metronidazole benzoate.
5 ml suspension contain 200 mg of metronidazole benzoate equivalent to 125 mg of metronidazole base.

The other ingredients: sodium carboxymethylcellulose, sucrose, sorbitol 70%, glycerol, polysorbate 80, citric acid monohydrate, disodium hydrogen phosphate dihydrate, methyl hydroxybenzoate, propyl hydroxybenzoate, ethanol 96%, vanilla, purified water.

Content of the pack

Box with one glass bottle of 120 ml.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,
St. “Skënder Vila”,
Tirana, Albania
.Tel.: +355 4 23 89 602

This leaflet was last revised in December 2023.