Package leaflet: Information for the user

MetroNor 5 mg/ml solution for infusion
Metronidazole

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- 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 signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What is MetroNor 5 mg/ml solution for infusion and what is it used for

Metronidazole belongs to a group of medicines called antibiotics and is used to treat serious infections caused by bacteria that may be killed by the active ingredient metronidazole.

Antibiotics are used to treat bacterial infections and are not suitable for treating viral infections (such as colds or flu).

It is important that you follow the instructions regarding the dose, the administration interval and the treatment duration indicated by your doctor.

Do not store or reuse this medicine. If you have any antibiotic left over after treatment, return it to the pharmacy for proper disposal. Do not throw away any medicines via wastewater or household waste.

MetroNor is used in adults and children.

You may be given MetroNor 5 mg/ml for the treatment of any of the following diseases:
- central nervous system infections such as abscesses (local infection with pus) in the brain, inflammation of the meninges (lining of the brain),
- infections of the lungs and the lining of the lungs, such as pneumonia accompanied by tissue destruction, pneumonia after entry of stomach contents into the lungs, abscesses in the lungs,
- infections of the gastrointestinal tract, such as inflammation of the inner lining of the pelvic walls and abdomen, abscesses in the liver, surgery of the large intestine or rectum, infections with pus in the abdomen and pelvis,

- infections of the female genital organs, such as inflammation in the uterus after processes such as removal of the uterus, caesarean section, miscarriage accompanied by blood poisoning (sepsis) or childbirth fever,
- infections of the ears, nose and throat, and teeth, jaw, and mouth, such as acute ulcerative gingivitis (inflammation of the gums in which ulcers are formed),
- inflammation of the inner lining of the heart,
- bone and joint infections, such as inflammation of the bone marrow
- gas gangrene
- blood poisoning from thrombosis or inflammation of the veins

If necessary, your treatment will be supplemented with other antibiotics.

MetroNor 5 mg/ml may be administered as a preventive measure prior to surgeries associated with an increased risk of infection caused by those known as anaerobic bacteria, mainly in gynaecology or stomach and intestinal surgery.

2. What you need to know before you take MetroNor 5 mg/ml solution for infusion

Do not use MetroNor
- If you are allergic to metronidazole, other similar substances, or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before receiving MetroNor 5 mg/ml solution for infusion.

Take special care with metronidazole 5 mg/ml if you suffer from:
- severe hepatic impairment,
- a disturbance of blood formation or
- a brain, spinal cord, or nerve disease.

Therefore, your doctor will carefully determine whether you should be treated with MetroNor 5 mg/ml solution for infusion.

If seizures or any other nerve problems or symptoms (for example, numbness in the limbs) become apparent during treatment, your treatment will be reviewed immediately.

Treatment with metronidazole 5 mg/ml should generally not be prolonged for more than 10 days; the treatment period will only be extended in exceptional circumstances and if it is absolutely necessary. Repetition of the metronidazole therapy will be limited to when absolutely necessary. In such a case, it will be supervised with special attention.

- Treatment should be stopped or reviewed immediately if you develop severe diarrhoea which may be due to a serious disease of the large intestine called 'pseudomembranous colitis' (see also section 4).

Cases of severe liver toxicity/acute liver failure, some with fatal outcome, have been reported in patients with Cockayne syndrome with medicinal products containing metronidazole.
If you have Cockayne syndrome, your doctor should monitor your liver function frequently while you are receiving metronidazole treatment and afterwards.

Tell your doctor immediately and stop taking metronidazole if you develop:

• stomach pain, anorexia, nausea, vomiting, fever, malaise, tiredness, jaundice, dark urine, clay-coloured stools, or itching.

Serious bullous skin reactions such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), or acute generalised exanthematous pustulosis (AGEP) have been reported with metronidazole (see "Possible side effects"). If symptoms or signs of AGEP, SJS or TEN occur, treatment with MetroNor should be stopped immediately.

Since long-term use of metronidazole may affect blood formation (see section 'Possible side effects'), your blood count will be monitored during treatment.

Other medicines and MetroNor
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

There is no type of therapeutic incompatibility with any of the generally used anti-infective drugs. It may be administered simultaneously, although separately (i.e., not in the same container) with other anti-infective drugs.

Amiodarone (used to treat irregular heartbeat)
When you receive this medicine, your heart function should be monitored. You should see your doctor if you notice any abnormal heart function, dizziness, or fainting.

Barbiturates (active substance in medicines to treat epilepsy or seizures).
Phenobarbital reduces the duration of action of metronidazole; therefore, your dose of metronidazole may need to be increased.

Contraceptive pills
Your birth control pill may be less reliable while you are receiving metronidazole.

Busulfan
Metronidazole should not be given to patients receiving busulfan because toxic effects are more likely to occur in that case.

Carbamazepine (a medicine for the treatment of epilepsy).
This combination also requires caution because metronidazole may increase the action duration of carbamazepine.

Cimetidine (a medicine for the treatment of stomach upset).
Cimetidine may reduce metronidazole clearance in isolated cases and subsequently lead to increased serum metronidazole concentrations.

Coumarin derivatives (medicines which inhibit blood clotting)

Metronidazole may increase the inhibition of blood clotting caused by coumarins. Therefore, if you are taking a medicine that inhibits blood clotting (e.g., warfarin), you may need less amount of it during treatment with metronidazole.

Cyclosporin (a drug used to suppress undesirable immune responses)
When cyclosporine is co-administered with metronidazole, blood levels of cyclosporine may increase; therefore, your doctor will need to adjust your cyclosporine dose accordingly. In addition, your kidney function will be monitored.

Disulfiram (used to treat alcohol withdrawal)
If you are taking disulfiram, you should not receive metronidazole, or you should stop taking disulfiram. The combined use of these two drugs may lead to confusional states to the point of a serious mental disorder (psychosis).

Fluorouracil (a medicine to treat cancer) The daily dose of fluorouracil may need to be lowered when given together with metronidazole because metronidazole may cause an increase in the blood level of fluorouracil.

Lithium (used to treat mental illness)
Treatment with lithium-based preparations requires especially careful monitoring during metronidazole treatment, and the dose of lithium-based preparation may require readjustment.

Mycophenolate mofetil (used to prevent rejection reactions after organ transplantation)
Its effect may be weakened by metronidazole, therefore, careful monitoring of the effect of mycophenolate mofetil is recommended.

Phenytoin (a drug to treat epilepsy)
If you are taking phenytoin, your doctor will treat you with metronidazole only with caution because metronidazole may increase the action duration of phenytoin. On the other hand, phenytoin may reduce the effect of metronidazole.

Tacrolimus
Blood levels of this agent and kidney function should be monitored after initiation or discontinuation of metronidazole treatment.

MetroNor 5 mg/ml with alcohol
You should not drink alcoholic beverages while you are receiving metronidazole, or for 48 hours after the end of treatment. Drinking alcohol while using metronidazole 5 mg/ml may cause you to feel unwell, with symptoms such as palpitations, hot flashes, sweating, dizziness, and vomiting.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

<u>Pregnancy</u>
If you are pregnant, your doctor will not treat you with metronidazole unless absolutely necessary.

<u>Breast-feeding</u>

Breast-feeding should be discontinued during treatment with metronidazole and should not be resumed for another 2-3 days because metronidazole is excreted in human milk.

Fertility

Animal studies have indicated a negative influence on the male reproductive system; however, this was only seen at very high doses that far exceeded the recommended dose for humans.

Driving and using machines
You should not drive or use machines while you are taking metronidazole, as metronidazole may alter your alertness. This may happen especially at the beginning of treatment or in combination with alcohol intake.

This medicine contains 359 mg of sodium (main ingredients of table salt/kitchen salt) per 100 ml. This equals 18% of the maximum daily sodium intake recommended for an adult.

3. How to use MetroNor 5 mg/ml solution for infusion

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The dose depends on the nature and severity of your disease, your age and body weight, and your individual response to treatment.

The recommended dose is:

Adults and adolescents

- Infection treatment

You will be given 100 ml of this medicine (corresponding to 500 mg of metronidazole) every 8 hours. In most cases, treatment will last for 7 days.
Alternatively, you may receive 300 ml of the medicine (corresponding to 1500 mg of metronidazole) on the first day of treatment.
In most cases, treatment will last for 7 days. Exceptionally, treatment may be prolonged, although, in general, treatment should not exceed 10 days.
The dose will be the same for patients with kidney disease. For patients with liver disease, lower doses will be required. If you are being treated with a hemodialyzer, your doctor will adjust the dose on the days of treatment.

- Prevention of infections that may occur after surgical interventions

When used to prevent infection in surgery, you will be given 500 mg of medicine before surgery. The dose will be repeated 8 and 16 hours after the intervention.

Use in children
Dosage in children is based on body weight.

Infection treatment

In children older than 8 weeks to 12 years of age: The usual daily dose is 20-30 mg/kg/day as a single dose or divided into 7.5 mg/kg every 8 hours. The daily dose could be increased to 40 mg/kg, depending on the severity of the infection. The treatment duration is usually 7 days.

In children less than 8 weeks old: 15 mg/kg as a single daily dose or divided into 7.5 mg/kg every 12 hours.

In new-born babies with a gestational age less than 40 weeks, accumulation of metronidazole may occur during the first week of life, therefore, plasma concentrations of metronidazole should preferably be monitored after a few days of treatment.

- Prevention of infections that may occur after surgical interventions

In children under 12 years: 20-30 mg/kg as a single dose administered 1-2 hours before surgery.

In new-born babies with a gestational age less than 40 weeks: 10 mg/kg weight as a single dose before surgery.

Method of administration

MetroNor 5 mg/ml is given as a drip directly into a vein (intravenous infusion). The infusion from a bottle usually takes 60 minutes but should not be done in less than 30 minutes.

If you are receiving other antibiotics at the same time, your doctor will give you these drugs separately.

If you use more MetroNor than you should:
Your doctor or nurse will make sure you get the correct IV dose.
An accidental overdose could cause nausea, vomiting, cravings, a metallic taste, headache, dizziness, insomnia, drowsiness, oliguria, and dark urine, hearing problems, and seizures.
There is no specific antidote for metronidazole overdose. In cases where massive ingestion is suspected, treatment will be based on symptoms.

In case of overdose or accidental administration/ingestion, immediately consult your doctor or pharmacist, specifying the medicine and quantity ingested.

If you forget to use MetroNor
Do not take a double dose to make up for a forgotten dose.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Adverse effects mainly occur at high doses or with prolonged use.

The following terms are used to describe the frequency of side effects:
“Very common” affect more than 1 in every 10 treated patients
“Common” affect 1 to 10 in every 100 treated patients
“Uncommon” affect 1 to 10 in every 1000 treated patients
“Rare” affect 1 to 10 in every 10000 treated patients
“Very rare” affect less than 1 in every 10000 treated patients
“Not known” Frequency cannot be estimated from the available data.

The following side effects may be serious and, therefore, may require immediate treatment:

Rare:

- Persistent severe diarrhoea (possibly a symptom of a serious infection of the intestine called pseudomembranous colitis)

Emergency treatment of pseudomembranous enterocolitis

In case of persistent severe diarrhoea, you should inform your doctor immediately because it may be due to pseudomembranous colitis, a serious illness that must be treated immediately.

Your doctor will stop treatment with metronidazole and will prescribe you the adequate treatment.

- Acute and severe hypersensitivity reactions up to anaphylactic shock (swelling of the face, lips, and airways, as well as low blood pressure, shortness of breath, syncope and even death)

Very rare:

- Platelet and white blood cell counts may decrease during treatment (granulocytopenia, agranulocytosis, pancytopenia, thrombocytopenia). Regular monitoring of blood counts is required during prolonged use
- Hepatitis (liver inflammation), jaundice, inflammation of the pancreas (isolated reports)
- Brain disorders, lack of coordination
- Severe inflammatory rash on the mucous membranes and skin with fever, redness, and blisters, in extremely rare cases up to large area detachment of the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis)

Not known:

- Mild to moderate hypersensitivity reactions, a special type of rapid swelling of the skin of the face called angioedema
- Gaze spasm, damage, or inflammation of the nerves in the eyes
- Low white blood cell count, severe anaemia
- Seizures, nerve disorders such as numbness, pain, a coating sensation or tingling in the arms or legs.
- Inflammation of the meninges (or the lining of the brain) that is not bacterial in origin (aseptic meningitis)

Other side effects

Common

- Yeast infections (e.g., genital infections)

Uncommon

- Darkened urine (due to a metabolite of metronidazole)

Rare

- Changes in the ECG (electrical activity of the heart)

Very rare:

- Psychotic disorders, such as confusional states, hallucinations
- Headache, dizziness, drowsiness, fever, vision and movement disorder, vertigo, speech defects, seizures
- Visual disturbances, e.g., double vision, myopia

- Impaired hepatic function (such as elevated serum levels of certain enzymes and bilirubin)
- Allergic skin reactions such as itching, urticaria
- Pain in muscles and joints

Not known:
- Dizziness, nausea, diarrhoea, swelling of the tongue or mouth, belching and bitter taste, metallic taste, pressure on the stomach, coated tongue
- Difficulty in swallowing
- Decreased interest in food/appetite (anorexia)
- Sad (depressed) mood
- Drowsiness or insomnia, muscle spasms
- Redness and itching of your skin (erythema multiforme)
- Irritation of the venous walls (to the extent of presenting swollen veins and thrombosis) after intravenous administration, states of weakness, fever

The type and severity of the side effects in children is the same as in adults.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store MetroNor 5 mg/ml solution for infusion

Keep out of the sight and reach of children.

Bags: Store below 30ºC. Store in the original package to protect from light. Do not freeze or refrigerate. Because metronidazole is sensitive to light, the bag should only be removed from the overpouch immediately prior to administration.

Do not use this MetroNor after the expiry date which is stated on the container. The expiry date refers to the last day of that month.
Discard if alterations are observed in the container or in the liquid it contains.

Do not throw away any medicines via wastewater or household waste. If you are not sure, ask your pharmacist how to throw away medicines and packages you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What MetroNor contains:
The active substance is metronidazole.

Each 100 ml of solution contains 500 mg of metronidazole.
The other ingredients are: anhydrous disodium phosphate, citric acid monohydrate, sodium chloride and water for injections.

Each 300 ml of solution contains 1.5 g of metronidazole.

The other ingredients are: anhydrous disodium phosphate, citric acid monohydrate, sodium chloride and water for injections.

What the product looks like and contents of the pack
MetroNor is a clear, colourless, or slightly yellowish solution.
It is available in plastic bags of 100 and 300 ml.
Not all pack sizes may be marketed in all countries.

Marketing Authorisation Holder and Manufacturer:
LABORATORIOS NORMON, S.A.
Ronda de Valdecarrizo, 6 – 28760 Tres Cantos – Madrid (SPAIN)

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