

## Package leaflet: Information for the user

### Metronidazole 500 mg/100 ml Solution for infusion

**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.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

#### What is in this leaflet

1. What Metronidazole Solution for infusion is and what it is used for
2. What you need to know before you are given Metronidazole Solution for infusion
3. How Metronidazole Solution for infusion is given
4. Possible side effects
5. How to store Metronidazole Solution for infusion
6. Contents of the pack and other information

#### 1. What Metronidazole Solution for infusion is and what it is used for

##### What is this medicine?

The active ingredient in your medicine is metronidazole. It is an antimicrobial agent (an agent that kills micro-organisms or suppresses their multiplication and growth).

Your medicine contains metronidazole 500 mg per 100 ml (5 mg per ml). This is a sterile solution for intravenous infusion free from bacterial endotoxin (substances causing fever reactions).

##### What is it used for?

This medicine is used when oral medication is not possible, for the prevention and treatment of infections caused by certain species of bacteria. It is used in adults and children for:

- the prevention of post-operative infections due to sensitive bacteria in surgical procedure with a high risk of occurrence of this type of infection
- the treatment of severe established abdominal and gynaecological infections where sensitive bacteria have been identified as the cause or are suspected to be the cause

Metronidazole 500 mg/100 ml must only be used under medical supervision.

If you need any further information on your condition, please ask your doctor.

#### 2. What you need to know before you are given Metronidazole Solution for infusion

##### **Do not use Metronidazole Solution for infusion:**

- if you are allergic to metronidazole or any of the other ingredients of this medicine (listed in section 6).

##### **Warnings and precautions**

Talk to your doctor, pharmacist before being given metronidazole if you have:

- severe liver damage
- a blood formation disorder or
- a disease of brain, spinal cord or nerves

Therefore, your doctor will very carefully determine whether you should be treated with metronidazole.

If convulsive fits or any other nerve affections (e.g. numbness in limbs) become apparent during therapy, your treatment will promptly be revised.

Treatment must be stopped or revised immediately if you get severe diarrhoea which may be due to a severe large bowel disease called "pseudomembranous colitis" (see also section 4.)

As prolonged use of metronidazole may impair blood formation (see section "Possible side effects"), your blood counts will be monitored during treatment.

If you received this medicine your urine may be darkened.

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.

Treatment with Metronidazole should not usually be continued for longer than 10 days; the treatment period will only be extended in exceptional circumstances and if absolutely necessary. Repeat therapy with metronidazole will be restricted to cases where this is absolutely necessary. In such a case, you will be monitored particularly carefully.

### **Other medicines and Metronidazole**

Certain medicines are known to change the normal effect of this infusion.

Certain medicines can have their effect changed by this infusion.

These medicines should not be used at the same time as Metronidazole 500 mg/100 ml Solution for infusion.

Please tell your doctor if you are taking, have recently taken or might take any of the following medicines:

*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 heart function abnormalities, dizziness or fainting.

*Barbiturates* (the active substance in sleeping pills)

The duration of action of metronidazole is reduced by phenobarbital; your metronidazole dose may therefore have to be increased.

*Birth control pills*

Your birth control pill may be less reliable while you are being given metronidazole.

*Busulfan*

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

*Carbamazepine* (a drug for the treatment of epilepsy)

This combination also warrants caution because metronidazole may increase the duration of action of carbamazepine.

*Cimetidine* (a drug for the treatment of stomach disorders)

Cimetidine may reduce the elimination of metronidazole in isolated cases and subsequently leads to increased serum metronidazole concentrations.

*Coumarin derivatives* (drugs that inhibit blood clotting)

Metronidazole may enhance the blood clotting inhibition brought about by coumarins. So, if you are taking a medicine that inhibits blood clotting (for example warfarin), you may need less of it during treatment with metronidazole.

*Cyclosporin* (a drug used to suppress undesirable immune responses)

When cyclosporin is given together with metronidazole, the blood levels of cyclosporin may increase; your doctor will therefore have to adjust your cyclosporin dose as appropriate.

*Disulfiram* (used in alcohol withdrawal therapy)

If you are taking disulfiram, you must not be given metronidazole, or disulfiram must be stopped. Combined use of these two drugs may lead to states of confusion up to the point of a serious mental disorder (psychosis).

*Drugs containing alcohol*

Please refer to section 'Using Metronidazole' with food and drink.

*Fluorouracil* (an anticancer drug)

The daily dose of Fluorouracil may have to be reduced when giving it together with Metronidazole because metronidazole may lead to an increase of the blood level of Fluorouracil.

*Lithium* (used to treat mental illness)

Treatment with lithium preparations requires particularly careful monitoring during treatment with metronidazole, and the dose of the lithium preparation may need to be re-adjusted. Lithium treatment should be tapered or withdrawn before administration of metronidazole.

*Mycophenolate mofetil* (used for the prevention of rejection reactions after organ transplant).

Its effect may be weakened by metronidazole, so careful monitoring of the effect of the medicine is recommended.

*Phenytoin* (a drug for the treatment of epilepsy)

If you are taking phenytoin, your doctor will treat you with metronidazole only with caution because metronidazole may increase the duration of action of phenytoin. On the other hand, phenytoin may reduce the effect of metronidazole.

*Tacrolimus* (used to suppress unwanted immune reactions)

The blood levels of this agent and your kidney function should be checked when starting and stopping treatment with metronidazole.

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

### **Metronidazole with food and alcohol**

*Alcohol*

Do not drink any alcohol while receiving your medicine, and for 72 hours afterwards. This might cause unpleasant side effects, such as feeling sick and vomiting, abdominal pain, hot flushes, palpitations, and headache.

### **Pregnancy and breast-feeding**

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

#### Pregnancy

This medicine should be avoided during pregnancy or breast-feeding unless your doctor considers it essential.

#### Breast-feeding

You should not breast-feed during treatment with metronidazole and not resume nursing for another 2–3 days thereafter because metronidazole passes into breast milk.

#### Contraception in males and females

If you are taking a birth-control pill, please refer to section "Taking or using other medicines".

### **Driving and using machines**

While taking Metronidazole you may feel sleepy, dizzy, confused, see or hear things that are not there (hallucinations), have fits (convulsions) or temporary eyesight problems (such as blurred or double vision). If this happens, do not drive or use any machinery or tools.

### **Metronidazole contains sodium**

This medicinal product contains 310 mg (13.5 mmol) of sodium per 100 ml. This is equivalent to 16% of the adult recommended maximum daily dietary intake for sodium. This should be particularly taken into account for those on a low salt (sodium) diet.

### **3. How Metronidazole Solution for infusion is given**

Your doctor will decide how much you need and when it will be given to you.

#### **Dosage and Method of Administration**

Metronidazole Solution for infusion is administered into a vein using a drip. It will be given at a rate of 5 ml / minute.

As soon as possible after being given the injection, your treatment will be continued using oral medication. Your doctor will decide when you can start to take oral medication instead of the drip.

The amount of metronidazole you will be given will depend on the reason it is being prescribed for you and the following:

- your age
- your weight
- your clinical condition and
- the reason it is being prescribed for you

#### **Prevention of infection after abdominal or gynaecological surgery:**

The preventive treatment duration will be short and mostly limited to the post-operative period (24 hours but no more than 48 hours).

*Adults* will usually receive

- a single dose of 1000 mg – 1500 mg up to one hour before surgery or
- 500 mg immediately before, during or after the operation. A

A 500 mg dose will then usually be repeated every 8 hours as necessary.

As soon as feasible, oral medication of metronidazole will then replace the drip and will be given every 8 hours.

*Children less than 12 years* will receive a smaller dose which is calculated from their body weight as a single dose of 20 – 30 mg/kg given one to two hours before surgery.

*Newborn infants born prematurely (gestational age less than 40 weeks)* will receive one single dose of 10 mg/kg body weight prior to surgery.

#### **Treatment of severe established abdominal or gynaecological infection:**

This medicine will be used for the treatment of established infections when you are unable to take the medicine by mouth.

*Adults* will usually receive a single daily dose of 1000 to 1500 mg or 500 mg every 8 hours

*Children more than 8 weeks to 12 years of age* will receive a smaller dose which is calculated from their body weight as:

- Either a single daily dose of 20 – 30 mg/kg
- Or alternatively 3 doses of 7.5 mg/kg given every 8 hours
- The daily dose may be increased to 40 mg/kg, depending on the severity of the infection. Duration of treatment is usually 7 days.

*Newborn infants (less than 8 weeks old)* will receive one single daily dose of 15 mg/kg of body weight or 7.5 mg/kg every 12 hours.

*Newborn infants born prematurely (gestational age less than 40 weeks)* will have their level of metronidazole in blood controlled after a few days of therapy as accumulation of the drug substance in the blood might occur during the first week of life.

### **Other types of infections**

For treatment of other infections caused by parasites and some bacteria your doctor will decide how much Metronidazole Solution for infusion you need to take and how often. This will depend on your illness and how bad it is.

### **Elderly:**

Metronidazole will be administered to the elderly with caution, especially where high doses are required. Your doctor will modify your dose as required.

### **Patients with renal failure:**

There is no need to adjust the dosage if you have problems with your kidneys.

Your doctor will most probably not adjust the dosage of your medicine if you are undergoing peritoneal dialysis. Your doctor can however take the decision to reduce the dosage of metronidazole if excessive levels of metabolites are found in your blood.

If you are undergoing haemodialysis your doctor will re-administer your medicine just after haemodialysis.

### **Patients with advanced liver deficiency:**

Your doctor will reduce the dosage. Your doctor will at the same time monitor the level of metronidazole in your blood.

### **Duration of Treatment**

Duration of treatment for ongoing infections is usually 7 to 10 days.

Depending upon your clinical condition and results of bacteriological assessment, your doctor may decide to prolong the treatment. This is intended to eradicate infections from parts of your body where the anti-infective metronidazole has difficulties to access or where self-recontamination is possible.

This should be taken into consideration for patients on a low sodium diet.

### **If you received more Metronidazole than you should**

#### **Symptoms:**

If you have received more infusion than you should, the following symptoms could appear:

- feeling sick (nausea)
- vomiting
- poor coordination (ataxia) and
- slight disorientation

No symptoms developed where too much of this medicine is given to *newborn infant born prematurely*.

#### **Treatment:**

Please inform your doctor immediately if any of these symptoms occur.

In the event of accidental over-infusion, your doctor will stop the infusion.

Your doctor will take the appropriate measures according to the symptoms you have developed.

If you have any further question on the use of this medicinal product please ask your doctor

## **4. Possible side effects**

Like all medicines, this medicine can cause side effects, particularly when you first start taking it, although not everybody gets them. Side effects occur mostly at high doses or with prolonged use.

**Contact your doctor at once** if you notice any of the following side effects:

*Rare (may affect up to 1 in 1,000 people):*

- Severe persistent diarrhoea (possibly a symptom of a severe bowel infection called pseudomembranous colitis, see below)
- Severe acute hypersensitivity reactions up to allergic shock

*Very rare (may affect up to 1 in 10,000 people):*

- White blood cell and platelet counts may decrease during treatment (granulocytopenia, agranulocytosis, pancytopenia, thrombocytopenia)
- Hepatitis (liver inflammation), jaundice, inflammation of the pancreas.
- Brain disorders, lack of coordination
- Brain fever not caused by bacterials (aseptic meningitis)
- Severe inflammatory rash on mucous membranes and the skin with fever, redness and blistering, in extremely rare cases up to skin detachment over extended areas (Stevens-Johnson Syndrome)

*Not known (frequency cannot be estimated from the available data):*

- Mild to moderate hypersensitivity reactions, swelling of your face, mouth, throat and/or tongue (angioedema)
- Gaze spasm, damage or inflammation of the nerves of your eyes
- Reduced white blood cell, count (leucopenia), severe anaemia (aplastic anaemia)
- Seizures, nervous disorders such as numbness, pain, furry sensation or tingling in the arms or legs
- Toxic epidermal necrolysis

#### Other side effects include

*Common (may affect up to 1 in 10 people)*

- Infections with yeasts (e.g. genital infections)

*Uncommon (may affect up to 1 in 100 people)*

- Darkened urine (due to a metabolite of metronidazole)

*Rare (may affect up to 1 in 1,000 people)*

- Changes in ECG

*Very rare (may affect up to 1 in 10,000 people)*

- Psychotic disorders, including states of confusion, hallucination
- Headache, dizziness, drowsiness, fever, disturbance of sight and movement, giddiness, speech defects, convulsions
- Visual disturbances, e.g. double vision, short-sightedness
- Liver function disorders (such as elevated serum levels of certain enzymes and bilirubin)
- Allergic skin reactions like itching, hives
- Joint and muscle pain

*Not known (frequency cannot be estimated from the available data):*

- Sickness, feeling sick, diarrhoea, inflammation of tongue or mouth, belching and bitter taste, metallic taste, pressure above the stomach, furry tongue
- Difficulty swallowing
- Anorexia
- Sad (depressed) mood
- Sleepiness or sleeplessness, muscle twitching
- Reddening and itching of the skin (erythema multiforme)
- Vein wall irritation (to the point of inflamed veins and thrombosis) after intravenous administration, states of weakness, fever

#### Emergency management of pseudomembranous enterocolitis:

In the event of severe persistent diarrhoea, you must promptly inform your doctor because this may be due to pseudomembranous colitis, a serious condition that must be treated immediately. Your doctor will stop metronidazole and provide appropriate treatment.

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

### **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. You can also report side effects directly via the Yellow Card Scheme.

Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

### **5. How to store Metronidazole**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and bottle after EXP. The expiry date refers to the last day of that month.

Keep the bottle in the outer carton in order to protect from light.

After first opening the medicinal product should be used immediately. For single use only.

Do not use this medicine if the bottle is found leaking or solution is not clear or pale-yellow.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

### **6. Contents of the pack and other information**

#### **What Metronidazole Solution for infusion contains**

- The active substance is metronidazole
- The other ingredients are disodium phosphate dihydrate, citric acid monohydrate, sodium chloride and water for injections.

#### **What Metronidazole Solution for infusion looks like and contents of the pack**

Metronidazole Solution for infusion is a clear to pale yellow solution packed in a 100 ml polypropylene bottle sealed with a chlorobutyl stopper.

Metronidazole Solution for infusion is available in packs containing 30 x 100 ml bottles.

#### **Marketing Authorisation Holder**

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#### **Manufacturer**

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