

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### **Metronidazole 500 mg/100 ml Solution for Infusion**

(in the following text named with Metronidazole 500 mg/100 ml)

Metronidazole

**Read all of this leaflet carefully before you start using this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any of the 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 Metronidazole 500 mg/100 ml is and what it is used for
2. What you need to know before you receive Metronidazole 500 mg/100 ml
3. How Metronidazole 500 mg/100 ml will be given to you
4. Possible side effects
5. How to store Metronidazole 500 mg/100 ml
6. Contents of the pack and other information

#### **1. What METRONIDAZOLE 500 mg/100 ML is and what it is used for**

Metronidazole 500 mg/100 ml belongs to a group of medicines known as antibiotics and is used to treat severe infections caused by bacteria that can be killed by the active substance metronidazole.

You may be given Metronidazole 500 mg/100 ml for the treatment and prevention of any of the following diseases:

- Infections of the blood, brain, lung, bones, genital tract, pelvic area and stomach

If required, your treatment may be supplemented by other antibiotics. Metronidazole 500 mg/100 ml may be given as a preventive measure prior to operations.

#### **2. What you need to know before you receive METRONIDAZOLE 500 MG/100 ML**

**You must not be given Metronidazole 500 mg/100 ml**

- if you are allergic (hypersensitive) to metronidazole, other similar substances or any of the other ingredients of Metronidazole 500 mg/100 ml (listed in section 6).

#### **Warnings and precautions**

Talk to your doctor before receiving Metronidazole 500 mg/100 ml. Please tell your doctor

if you have:

- severe liver damage or occurrence of confusion, altered level of consciousness and coma as a result of severe liver damage (hepatic encephalopathy)
- a disease of brain, spinal cord or nerves.

Therefore, your doctor will very carefully determine whether you should be treated with Metronidazole 500 mg/100 ml.

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.)

Cases of severe liver toxicity/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.

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.

Other medicines and Metronidazole 500 mg/100 ml

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other 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 500 mg/100 ml' 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.

**Metronidazole 500 mg/100 ml with Alcohol**

You must not drink any alcoholic beverages or drugs containing alcohol while you are being given metronidazole and up to 48 hours afterwards because this may cause intolerance reactions such as dizziness and vomiting.

### **Pregnancy, breast-feeding and fertility**

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

#### **Fertility**

Animal studies only indicate a potential negative influence of metronidazole on the male reproductive system if high doses lying well above the maximum recommended dose for humans were administered.

#### **Contraception in males and females**

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

#### **Pregnancy**

If you are pregnant, your doctor will not treat you with metronidazole unless she/he considers this absolutely necessary.

#### **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.

#### **Driving and using machines**

While taking Metronidazole 500 mg/100 ml 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 500 mg/100 ml contains sodium**

This medicine contains 322 mg sodium (main component of cooking/table salt) in each 100 ml. This is equivalent to 16% of the recommended maximum daily dietary intake of sodium for an adult.

### **3. How METRONIDAZOLE 500 mg/100 ml will be given to you**

#### **Dosage**

Dosage depends on the nature and severity of your illness, your age and body weight, and your individual response to treatment.

The following dosages are usually prescribed:

#### **Adults and adolescents**

##### Treatment of infections:

You may be given 100 ml of the medicine (corresponding to 500 mg of metronidazole) every 8 hours.

As an alternative you may receive 200 - 300 ml (corresponding to 1000 - 1500 mg of metronidazole) as a single dose. In most cases treatment will take 7 days. Only exceptionally treatment may be continued beyond this time, although a duration of 10 days should not normally be exceeded.

The dose will be the same for patients with kidney diseases.

For patients with liver diseases, lower doses may be required.

If you were treated by artificial kidney your doctor will schedule your infusion after dialysis has been finished. No routine dose adjustment is necessary.

#### Prevention of infections that might occur after operations

When used for prevention of infection in surgery, you may be given 500 mg of the medicine before the operation. The dose will be repeated 8 and 16 hours after the operation.

#### **The Elderly:**

Your doctor will give you this medicine only with special caution.

#### **Children**

Dosing in children is based on body weight (BW).

#### Treatment of infections:

<b>Age</b>	<b>Dosage</b>
8 weeks to 12 years	20 - 30 mg of metronidazole per kg BW per day as a single dose or divided into 7.5 mg of metronidazole per kg BW every 8 hours. The daily dose may be increased to 40 mg of metronidazole per kg BW if infection is severe.
Under 8 weeks	15 mg of metronidazole per kg BW as a single dose daily or divided into 7.5 mg per kg BW every 12 hours.
Newborns of less than 40 weeks gestational age	As metronidazole may accumulate in these patients during the first week of life, the concentration of metronidazole in the blood will be checked after a few days of treatment

Usually treatment will take 7 days.

#### Prevention of infections that might occur after operations:

<b>Age</b>	<b>Dosage</b>
Less than 12 years	20 - 30 mg of metronidazole per kg BW as a single dose given 1 - 2 hours before surgery
Newborns of less than 40 weeks gestational age	10 mg of metronidazole per kg BW as a single dose before surgery

#### **Method of administration and duration of treatment**

Metronidazole 500 mg/100 ml is administered through a drip directly into a vein (intravenous infusion).

The infusion of one bottle usually takes 60 minutes, but it should not be done within less than 20 minutes.

This medicine may be diluted in a suitable vehicle solution for infusion.

The entire metronidazole treatment period is usually 7 days and must not exceed 10 days unless this is absolutely necessary (see also “Take special care with Metronidazole 500 mg/100 ml”).

If you are concurrently receiving other antibiotics your doctor will give you those medicines separately.

### **If you use more Metronidazole 500 mg/100 ml than you should**

Undesirable effects, as described in the next section, may occur as signs or symptoms of an overdose. Single oral doses of metronidazole, up to 12 g have been reported in suicide attempts and accidental overdoses. Symptoms were limited to vomiting, ataxia and slight disorientation. There is no known specific antidote or specific treatment of a massive overdose, but metronidazole can be removed by dialysis (that is treatment with artificial kidney) from the body.

## **4. POSSIBLE SIDE EFFECTS**

Like all medicines, this medicine can cause side effects, although not everybody gets them. Side effects occur mostly at high doses or with prolonged use.

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

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 (isolated reports) • Brain disorders, lack of coordination
- 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, toxic epidermal necrolysis)

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
- Brain fever not caused by bacteria (aseptic meningitis)
- Acute liver failure in patients with Cockayne Syndrome (see section 2 “Warnings and precautions”)

### **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)
- 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, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the Yellow Card Scheme at: [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 500 MG/100 ML**

Keep this medicine out of the sight and reach of children.  
Keep bottles in the carton in order to protect from light.

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

Use only if the solution is clear and free of visible particles, and the bottle and closure are intact.

This medicinal product is intended for single use only. Discard any unused portions.

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 to protect environment.

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

### **What METRONIDAZOLE 500 MG/100 ML contains:**

– The active substance is metronidazole. 1 ml Metronidazole 500 mg/100 ml solution for infusion contains 5 mg metronidazole. One 100ml polyethylene bottle contains 500 mg metronidazole.

– The other ingredients are sodium chloride, disodium phosphate dodecahydrate, citric acid monohydrate, water for injections

### **What Metronidazole 500 mg/100 ml looks like and contents of the pack**

Metronidazole 500 mg/ 100 ml is a clear, colourless or slightly yellowish aqueous solution.

Metronidazole 500 mg/ 100 ml is supplied in

- 100ml polyethylene bottles, available in packs of 10 × 100 ml, 20 × 100 ml

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder**

Braun Melsungen AG  
Carl-Braun-Straße 1  
34212 Melsungen,  
Germany

### **Postal address:**

34209 Melsungen,  
Germany  
Tel. +49-5661-71-0  
Fax +49-5661-71-4567

### **Manufacturer(s)**

Braun Melsungen AG  
Carl-Braun-Straße 1  
34212 Melsungen, Germany

Braun Medical, S.A.  
Carretera de Terrassa 121  
08191 Rubí, Barcelona, Spain

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