Baxter

Package leaflet: Information for the user

Metronidazole 500 mg/100 ml Intravenous Infusion

02282

Read all of this leaflet carefully before you start using 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 500 MG/100 ML 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 postoperative 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 USE METRONIDAZOLE 500 MG/100 ML

Do not use Metronidazole 500 mg/100 ml:

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

Warnings and precautions

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.

Talk to your doctor before using Metronidazole 500 mg/100 ml:

- if you are suffering from liver disease
- if you are actively suffering from disease of the nervous system. In this case you should inform your doctor, particularly if you experience poor coordination (ataxia), dizziness or confusion during the treatment.
- if you have blood cells disorders
- if you are undergoing kidney dialysis

Your doctor may want to carry out some tests if you receive this medicine for more than 10 days.

Other medicines and Metronidazole 500 mg/100 ml

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

- warfarin (medicine to thin the blood) as your blood clotting time will need to be monitored more frequently
- vecuronium (medicine used to relax your muscles during surgery)
- disulfiram (to treat alcohol addiction)
- 5-Fluoro-uracile (used to treat some forms of cancer)
- Lithium (used to treat depression) as lithium treatment should be reduced or stopped before you are given Metronidazole
- medicines to treat epilepsy such as phenobarbital, phenytoin and carbamazepine
- cholestyramine (used to lower cholesterol)
- cimetidine (used to treat stomach ulcers)
- medicines used following organ transplants such as ciclosporin and tacrolimus
- medicines used to correct irregular heartbeats such as amiodarone and quinidine
- busulfan (used to treat leukemia which is a cancer of the blood cells)

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

Metronidazole 500 mg/100 ml with food and 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

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

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.

Driving and Using machines

You should not drive or use machines while being treated with this medicine.

Metronidazole 500 mg/100 ml contains sodium chloride

This medicinal product contains 310 mg sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE METRONIDAZOLE 500 MG/100 ML

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

Dosage and Method of Administration

Each bag is one dose and will be administered through a plastic tube into a vein using a drip. It will be given at a rate of approximately 5 ml/minute (equivalent to the infusion of one bag over 20 to 60 minutes). As soon as possible after the infusion has been completed, 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 you will be given depends upon

- 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 to 1500 mg (2 to 3 bags) up to one hour before surgery or
- 500 mg (1 bag) immediately before, during or after the operation.

A 500 mg dose (1 bag) will then usually be repeated every 8 hours as necessary.

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 (2 to 3 bags) or 500 mg (1 bag) 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.

– **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.

If you received more Metronidazole 500 mg/100 ml 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, although not everybody gets them.

Severe side effects:

The following severe side effects can occur rarely (may affect up to 1 in 1,000 people):

- severe allergic reaction (which may cause sudden faintness, severe breathlessness, abdominal pain, or swelling of the face and/or of the tongue and throat.)
- severe neurological effects: convulsion or fits, brain disease, disorder of the nerves which can causes loss of vision, brain fever not caused by bacterials (aseptic meningitis) or speech disorder
- inflammation of your pancreas which may cause pain in your belly with radiation through the back (pancreatitis)
- severe skin effects (erythema, serious illness with blistering of the skin, mouth and genitals and skin peeling)
- Unexpected infections, mouth ulcers, bruising, bleeding gums, or severe tiredness. This could be caused by a blood problem.

If you experience any of these severe side effects, please tell your doctor immediately. The doctor will stop the infusion.

Tell your doctor if any of the following side effects occur:

- feeling sick (nausea, malaise), vomiting, sweating, chills, chest pain, diarrhea, constipation, decreased or loss of appetite
- fever
- headache, drowsiness, dizziness, confusion or hallucinations
- depressed mood, poor sleep
- itching, inflammation, swelling, eruption/rash of your skin all of which may sometimes be severe
- unpleasant metallic taste, inflammation of mouth and/or tongue, tongue discoloration, dry mouth
- numbness, tingling, pain, or a feeling of weakness in arms or legs
- clumsiness, or poor coordination
- alteration of your blood that can modify results of your blood tests, abnormal liver test results
- yellowing of the skin and eyes (jaundice)
- darkening of your urine, painful urination
- fast or irregular heartbeat
- pain in in muscles and/or joints
- double vision or nearsightedness

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in:

United Kingdom:

Via the Yellow Card Scheme at:

www.mhra.gov.uk/yellowcard

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.

Do not use this medicine after the expiry date which is stated on the label after Exp:. The expiry date refers to the last day of that month. You will not be given this medicine if this date has passed.

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

Do not remove the unit from overwrap until ready for use.

Do not use if the solution is not clear, or if the unit is damaged in any way.

Discard any unused portion.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

This leaflet does not contain all the information about this medicine. If you have any questions or are not sure about anything, ask your doctor or nurse.

What Metronidazole 500 mg/100 ml contains

It is an isotonic solution.

The active substance is Metronidazole. Each 100 ml consists of:
Metronidazole 500 mg

The other inactive ingredients (excipients) are Disodium phosphate dodecahydrate, Citric acid monohydrate, Sodium chloride and Water for injections.

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

It is a clear solution for infusion intended for intravenous administration.

The solution is in 100 ml polyolefin/polyamide transparent plastic containers protected by a transparent plastic overwrap.

The pack size is: 20 x 100 ml, 50 x 100 ml and 60 x 100 ml.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

The company responsible for the product (also known as the marketing authorization holder) is:

Baxter Healthcare Ltd.
Caxton Way
Thetford
Norfolk
IP24 3SE
UK

Manufacturer:

The product may be made by:

Baxter Healthcare S.A.,
Moneen Road, Castlebar, County Mayo, Ireland

Bieffe Medital Sabiñánigo,
Ctra de Biescas, Senegüé, 22666 Sabiñánigo (Huesca), Spain

The medicinal product is authorised in the Member States of the EEA under the following names:

United Kingdom	Metronidazole 500 mg/100 ml Intravenous Infusion
Denmark	Metronidazol “Baxter” VIAFLO Infusionsvæske, opløsning
Norway	Metronidazol Baxter VIAFLO 5 mg/ml Infusjonsvæske, oppløsning

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Metronidazole 500 mg/100 ml Intravenous Infusion

The following information is intended for medical or healthcare professionals only:

Posology and method for administration:

Method of Administration

Metronidazole 500 mg/100 ml should be infused intravenously at an approximate rate of 5 ml/minute (or one bag infused over 20 to 60 minutes). Oral medication should be substituted as soon as feasible.

Prophylaxis against postoperative infections caused by anaerobi bacteria

Primarily in the context of abdominal, (especially colorectal) and gynaecological surgery.

Antibiotic prophylaxis duration should be short, mostly limited to the post operative period (24 hours but never more than 48 hours). Various schedules are possible.

Adults: Intravenous injection of single dose of 1000 mg – 1500 mg, 30 – 60 minutes preoperatively or alternatively 500 mg immediately before, during or after operation, then 500 mg 8 hourly.

Children < 12 years:
20 – 30 mg/kg as a single dose given 1 – 2 hours before surgery.

Newborns with a gestation age < 40 weeks:
10 mg/kg body weight as a single dose before operation.

Anaerobic infections

Intravenous route is to be used initially if patients symptoms preclude oral therapy. Various schedules are possible.

Adults: 1000 mg – 1500 mg daily as a single dose or alternatively 500 mg every 8 hours.

Children > 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 may be increased to 40 mg/kg, depending on the severity of the infection. Duration of treatment is usually 7 days.

Children < 8 weeks of age:
15 mg/kg as a single dose daily or divided into 7.5 mg/kg every 12 hours.

In newborns with a gestation age < 40 weeks, accumulation of metronidazole can occur during the first week of life, therefore the concentrations of metronidazole in serum should preferably be controlled after a few days of therapy.

Oral medication could be given, at the same dose regimen. Oral medication should be substituted as soon as feasible.

Duration of Treatment

Treatment for seven to ten days should be satisfactory for most patients but, depending upon clinical and bacteriological assessments, the physician might decide to prolong treatment e.g.; for the eradication of infection from sites which cannot be drained or are liable to endogenous recontamination by anaerobic pathogens from the gut, oropharynx or genital tract.

Bacterial vaginosis

Adolescents: 400 mg twice daily for 5 – 7 days or 2000 mg as a single dose.

Urogenital trichomoniasis

Adults and adolescents:
2000 mg as a single dose or 200 mg 3 times daily for 7 days or 400 mg twice daily for 5 – 7 days.

Children < 10 years:
40 mg/kg orally as a single dose or 15 – 30 mg/kg/day divided in 2 – 3 doses for 7 days; not to exceed 2000 mg/dose.

Giardiasis

> 10 years: 2000 mg once daily for 3 days, or 400 mg three times daily for 5 days, or 500 mg twice daily for 7 to 10 days.

Children 7 to 10 years: 1000 mg once daily for 3 days.

Children 3 to 7 years: 600 to 800 mg once daily for 3 days.

Children 1 to 3 years: 500 mg once daily for 3 days.

Alternatively, as expressed in mg per kg of body weight:
15 – 40 mg/kg/day divided in 2 – 3 doses.

Amoebiasis

> 10 years: 400 to 800 mg 3 times daily for 5 – 10 days.

Children 7 to 10 years: 200 to 400 mg 3 times daily for 5 – 10 days.

Children 3 to 7 years: 100 to 200 mg 4 times daily for 5 – 10 days.

Children 1 to 3 years: 100 to 200 mg 3 times daily for 5 – 10 days.

Alternatively, doses may be expressed by body weight: 35 to 50 mg/kg daily in 3 divided doses for 5 to 10 days, not to exceed 2400 mg/day.

Eradication of Helicobacter pylori in paediatric patients

As a part of a combination therapy, 20 mg/kg/day not to exceed 500 mg twice daily for 7 – 14 days.

Official guidelines should be consulted before initiating therapy.

Elderly Population

Caution is advised in the elderly, particularly at high doses, although there is limited information available on modification of dosage.

Patients with renal failure

Routine adjustments of the dosage of Metronidazole are not considered necessary in the presence of renal failure.

No routine adjustment in the dosage of Metronidazole needs to be made in patients with renal failure undergoing intermittent peritoneal dialysis (IDP) or continuous ambulatory peritoneal dialysis (CAPD). However dosage reduction may be necessary when excessive concentrations of metabolites are found.

In patients undergoing haemodialysis, Metronidazole should be re-administered immediately after haemodialysis.

Patients receiving peritoneal dialysis should be monitored for signs of toxicity due to the potential accumulation of metronidazole metabolites.

Patients with advanced hepatic insufficiency

In patients with advanced hepatic insufficiency a dosage reduction with serum level monitoring is necessary.

Instructions for use and handling

See section 3 of this leaflet.

Use only if the solution is clear, without visible particles and if the container is undamaged. Administer immediately following the insertion of infusion set.

Do not remove unit from overpouch until ready for use.

The inner bag maintains the sterility of the product.

Do not connect bags to each other. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

In patients maintained on intravenous fluids, Metronidazole 500 mg/100 ml may be diluted with appropriate volumes of 0.9% sodium chloride solution, dextrose 5 % – 0.9 % sodium chloride solution, dextrose 5% w/v or potassium chloride infusions (20 and 40 mmol/litre).

Using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In the case of adverse reaction, infusion must be stopped immediately.

Additives:

Additives known or determined to be incompatible should not be used.

Before adding a substance or medication, verify that it is soluble and stable in metronidazole, and that the pH range of metronidazole is appropriate. Additives may be incompatible. When introducing additives, the instructions for use of the medication to be added and other relevant literature must be consulted (see Section 6.2).

Mix the solution thoroughly when additives have been introduced.

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After addition, if there is a color change and/or the appearance of precipitates, insoluble complexes or crystals, do not use.

Do not store solutions containing additives.

The product should be used immediately after opening.

Discard after single use.

Discard any unused portion.

Do not reconnect partially used bags.

1. Opening
   a. Remove the VIAFLO container from the overpouch just before use.
   b. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be impaired.
   c. Check the solution for limpidity and absence of foreign matters. If solution is not clear or contains foreign matters, discard the solution.
2. Preparation for administration

   Use sterile material for preparation and administration.
   a. Suspend container from eyelet support.
   b. Remove plastic protector from outlet port at bottom of container:
      – grip the small wing on the neck of the port with one hand,
      – grip the large wing on the cap with the other hand and twist,
      – the cap will pop off.
   c. Use an aseptic method to set up the infusion.
   d. Attach administration set. Refer to complete directions accompanying set for connection, priming of the set and administration of the solution.

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