

Package leaflet: Information for the patient

MabThera 1600 mg solution for subcutaneous injection rituximab

Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1 WHAT MABTHERA IS AND WHAT IT IS USED FOR

What MabThera is

MabThera contains the active substance “rituximab”. This is a type of protein called a “monoclonal antibody”. It sticks to the surface of a type of white blood cell called “B-Lymphocyte”. When rituximab sticks to the surface of this cell, the cell dies.

MabThera is available as a medicine given as a drip (called MabThera 100 mg or MabThera 500 mg, concentrate for solution for infusion) and as a medicine for injection under your skin: called MabThera 1400 mg or MabThera 1600 mg, solution for subcutaneous injection).

What MabThera is used for

MabThera 1600 mg is used to treat chronic lymphocytic leukaemia -in adults.

- Chronic lymphocytic leukaemia (CLL) is the most common form of adult leukaemia. CLL affects a type of white blood cell called B-lymphocytes, which originates from the bone marrow and develops in the lymph nodes. Patients with CLL have too many abnormal lymphocytes, which accumulate mainly in the bone marrow and blood. The proliferation of these abnormal B-lymphocytes is the cause of symptoms you may have.
MabThera in combination with chemotherapy destroys these cells which are gradually removed from the body by biological processes-

You will be given MabThera 1600 mg with other medicines called “chemotherapy”.

You will always be given MabThera as a drip (intra-venous infusion) at the start of your treatment.

After this, you will be given MabThera as an injection under your skin. Your doctor will decide when to start MabThera injections.

2 WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN MABTHERA

Do not have MabThera if:

- you are allergic to rituximab, other proteins which are like rituximab, or any of the other ingredients of this medicine (listed in section 6)

you are allergic to hyaluronidase (an enzyme that helps to increase the absorption of injected active substance)

- you have a severe active infection at the moment
- you have a weak immune system.

Do not have MabThera if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before you are given MabThera.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given MabThera if:

- you have ever had or might now have a hepatitis infection. This is because in a few cases, MabThera could cause hepatitis B to become active again, which can be fatal in very rare cases. Patients who have ever had hepatitis B infection will be carefully checked by their doctor for signs of this infection
- you have ever had heart problems (such as angina, palpitations or heart failure) or breathing problems.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given MabThera. Your doctor may need to take special care of you during your treatment with MabThera.

Also talk to your doctor if you think you may need any vaccinations in the near future, including vaccinations needed to travel to other countries. Some vaccines should not be given at the same time as MabThera or in the months after you receive MabThera. Your doctor will check if you should have any vaccines before you receive MabThera.

Children and adolescents

Talk to your doctor, pharmacist or nurse before you are given this medicine if you, or your child, are under 18 years of age. This is because there is not much information about the use of MabThera in children and adolescents.

Other medicines and MabThera

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because MabThera can affect the way some other medicines work. Also some other medicines can affect the way MabThera works.

In particular, tell your doctor:

- if you are taking medicines for high blood pressure. You may be asked not to take these other medicines 12 hours before you are given MabThera. This is because some people have a fall in their blood pressure while they are being given MabThera
- if you have ever taken medicines which affect your immune system – such as chemotherapy or immune-suppressive medicines.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given MabThera.

Pregnancy and breast-feeding

You must tell your doctor or nurse if you are pregnant, think that you might be pregnant or are planning to become pregnant. This is because MabThera can cross the placenta and may affect your baby.

If you can get pregnant, you and your partner must use an effective method of contraception while using MabThera. You must also do this for 12 months after your last treatment with MabThera. MabThera passes into breast milk in very small amounts. As the long-term effects on breastfed infants are not known, for precautionary reasons,

breast-feeding is not recommended during treatment with MabThera and for 6 months after the treatment.

Driving and using machines

It is not known whether MabThera has an effect on you being able to drive or use any tools or machines.

Sodium

MabThera 1600 mg contains less than 1 mmol sodium (main component of the cooking/table salt) per dose, i.e. it is essentially sodium-free.

3 HOW MABTHERA IS GIVEN

How it is given

MabThera will be given to you by a doctor or nurse who is experienced in the use of this treatment. They will watch you closely while you are being given this medicine. This is in case you get any side effects.

You will always be given MabThera as a drip (intra-venous infusion) at the start of your treatment.

After this, you will be given MabThera as an injection under your skin (subcutaneous injection) over approximately 7 minutes. There is a peel-off sticker on the glass vial that specifies the medication.

Your doctor or nurse will place the sticker on the syringe before injection. Your doctor will decide when to start MabThera injections.

When injected under your skin, it is given in the stomach area, not in other sites of the body, and not into areas of the stomach where the skin is red, bruised, tender, hard or where there are moles or scars.

Medicines given before each MabThera administration

Before you are given MabThera, you will be given other medicines (pre-medication) to prevent or reduce possible side effects.

How much and how often you will receive your treatment

When you are treated with MabThera in combination with chemotherapy, you will receive a MabThera infusion on day 0 of cycle 1, then subcutaneous injections on day 1 of each subsequent cycle. The total number of cycles is of 6. Each cycle has a duration of 28 days. The chemotherapy should be given after the MabThera administration.

Your doctor will decide if you should receive concomitant supportive therapy.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4 POSSIBLE SIDE EFFECTS

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

Most side effects are mild to moderate but some may be serious and need treatment. Rarely, some of these side effects have been fatal.

Reactions where the medicine is injected

Many patients get some local side effects where MabThera is injected. These include: pain, swelling, bruising, bleeding, skin redness, itching and rash.

Your doctor may decide to stop your MabThera treatment if these reactions are serious.

Infections

Tell your doctor immediately if you get signs of an infection including:

- fever, cough, sore throat, burning pain when passing urine or feeling weak or generally unwell
- memory loss, trouble thinking, difficulty walking or sight loss – these may be due to a very rare, serious brain infection, which has been fatal (Progressive Multifocal Leukoencephalopathy or PML).

You might get infections more easily during your treatment with MabThera. These are often colds, but there have been cases of pneumonia or urinary infections. These are listed below under “Other side effects”.

Other side effects include:

Very common side effects (may affect more than 1 in 10 people):

- bacterial or viral infections, bronchitis
- low number of white blood cells with or without fever or blood cells called “platelets”
- feeling sick (nausea)
- bald spots on the scalp, chills, headache
- lower immunity – because of lower levels of anti-bodies called “immunoglobulins” (IgG) in the blood which help protect against infection.

Common side effects (may affect up to 1 in 10 people):

- infections of the blood (sepsis), pneumonia, shingles, cold, bronchial tube infections, fungal infections, infections of unknown origin, sinus inflammation, hepatitis B
- low number of red blood cells (anaemia), low number of all blood cells
- allergic reactions (hypersensitivity),
- high blood sugar level, weight loss, swelling in the face and body, high levels of the enzyme “LDH” in the blood, low calcium levels in the blood
- unusual feelings of the skin – such as numbness, tingling, pricking, burning, a creeping skin feeling, reduced sense of touch
- feeling restless, problems falling asleep
- becoming very red in the face and other areas of the skin as a consequence of dilation of the blood vessels
- feeling dizzy or anxious
- producing more tears, tear duct problems, inflamed eye (conjunctivitis)
- ringing sound in the ears, ear pain
- heart problems – such as heart attack, uneven or fast heart rate
- high or low blood pressure (low blood pressure especially when standing upright)
- tightening of the muscles in the airways which causes wheezing (bronchospasm), inflammation, irritation in the lungs, throat or sinuses, being short of breath, runny nose
- being sick (vomiting), diarrhoea, pain in the stomach, irritation or ulcers in the throat and mouth, problems swallowing, constipation, indigestion
- eating disorders, not eating enough, leading to weight loss
- hives, increased sweating, night sweats
- muscle problems – such as tight muscles, joint or muscle pain, back and neck pain
- tumour pain
- general discomfort or feeling uneasy or tired, shaking, signs of flu
- multiple-organ failure.

Uncommon side effects (may affect up to 1 in 100 people):

- blood clotting problems, decrease of red blood cell production and increase of red blood cell destruction (aplastic haemolytic anaemia), swollen or enlarged lymph nodes
- low mood and loss of interest or enjoyment in doing things, feeling nervous
- taste problems – such as changes in the way things taste
- heart problems – such as reduced heart rate or chest pain (angina)
- asthma, too little oxygen reaching the body organs
- swelling of the stomach.

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

- short term increase in the amount of some types of anti-bodies in the blood (called immunoglobulins – IgM), chemical disturbances in the blood caused by break-down of dying cancer cells
- nerve damage in arms and legs, paralysed face
- heart failure
- inflammation of blood vessels including those leading to skin symptoms
- respiratory failure
- damage to the intestinal wall (perforation)
- severe skin problems causing blisters that can be life-threatening
- kidney failure
- Severe vision loss (sign of brain nerves damage).

Not known (it is not known how often these side effects happen):

- a reduction in white blood cells which does not happen straight away
- reduced platelets number just after the infusion – this can be reversed, but can be fatal in rare cases
- hearing loss, loss of other senses.

MabThera may also cause changes in laboratory tests carried out by your doctor.

If you are having MabThera with other medicines, some of the side effects you may get may be due to the other medicines.

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 this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5 HOW TO STORE MABTHERA

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 after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C). Do not freeze. Keep the container in the outer carton in order to protect from light.

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 MabThera 1600 mg solution for subcutaneous injection contains

- The active ingredient is rituximab. Each vial contains **1600 mg**/13.4 mL of rituximab. Each mL contains 120 mg of rituximab.
- The other ingredients are recombinant human hyaluronidase (rHuPH20), L-histidine, L-histidine hydrochloride monohydrate, α,α -trehalose dihydrate, L-methionine, polysorbate 80 and water for injections.

What MabThera 1600 mg solution for subcutaneous injection looks like and contents of the pack

MabThera is a ready to use, clear to opalescent, colourless to yellowish liquid, supplied as a solution for subcutaneous injection in a colourless glass vial with a butyl rubber stopper with aluminium overseal and a blue plastic flip-off disk.

Each vial contains 1600 mg/13.4 mL of rituximab. Each carton contains one vial.

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This leaflet was last revised in Other sources of information

Detailed information on this medicine is available on the European Medicines Agency (EMA) website: <http://www.ema.europa.eu>.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.