LM121110–LE001

Package leaflet: Information for the patient

Truxima™ 100mg

concentrate for solution for infusion

rituximab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read 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, 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 Truxima is and what it is used for

What Truxima is

Truxima contains the active substance "rituximab". This is a type of protein called a "monoclonal antibody". It is designed to stick to a type of white blood cell called "B Lymphocyte". When sticking to the surface of this cell, rituximab causes the cell to die.

What Truxima is used for

Truxima may be used for the treatment of several different conditions in adults. Your doctor may prescribe Truxima for the treatment of:

a) Non Hodgkin's Lymphoma

This is a disease of the lymph tissue (part of the immune system) that affects B Lymphocytes.
Truxima can be given alone or with other medicines called "chemotherapy".
If the treatment is working, Truxima may be continued for 2 years after completing the initial treatment.

b) Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is the most common form of adult leukaemia. CLL affects B lymphocytes, which originate in the bone marrow and develop in the lymph nodes. Patients with CLL have too many abnormal lymphocytes, which accumulate mainly in the bone marrow and blood. The spread of these abnormal B lymphocytes is the cause of symptoms you may have. Truxima in combination with chemotherapy destroys these cells.

c) Rheumatoid arthritis

Truxima is used for the treatment of rheumatoid arthritis. Rheumatoid arthritis is a disease of the joints. B lymphocytes are involved in the cause of some of the symptoms you have. Truxima is used to treat rheumatoid arthritis in people who have already tried other medicines which have either stopped working, have not worked well enough or have caused unacceptable side effects. Truxima is usually taken together with another medicine called methotrexate.
Truxima slows down the damage to your joints caused by rheumatoid arthritis and improves your ability to do normal daily activities.
Truxima works best in those who have a positive blood test for rheumatoid factor (RF) or for anti cyclic citrullinated peptide (anti CCP). Both tests are commonly positive in rheumatoid arthritis and aid in confirming the diagnosis.

d) Granulomatosis with polyangiitis or microscopic polyangiitis

Truxima is used for inducing remission in granulomatosis with polyangiitis (formerly called Wegener's granulomatosis) or microscopic polyangiitis, taken in combination with corticosteroids. Granulomatosis with polyangiitis and microscopic polyangiitis are two forms of inflammation of the blood vessels which mainly affects the lungs and kidneys, but may affect other organs as well. B lymphocytes are involved in the cause of these conditions.

2. What you need to know before you use Truxima

Do not take Truxima 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 have a severe active infection at the moment
- you have a weak immune system
- you have severe heart failure or severe uncontrolled heart disease and have rheumatoid arthritis, granulomatosis with polyangiitis or microscopic polyangiitis.

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

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given Truxima if:
- you have ever had or might now have a hepatitis infection. This is because in a few cases, Truxima 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 Truxima. Your doctor may need to take special care during your treatment with Truxima.

If you have rheumatoid arthritis, granulomatosis with polyangiitis or microscopic polyangiitis also tell your doctor

- if you think you may have an infection, even a mild one like a cold. The cells that are affected by Truxima help to fight infection and you should wait until the infection has passed before you are given Truxima. Also please tell your doctor if you have had a lot of infections in the past or suffer from severe infections.
- if you think you may need any vaccinations in the near future, including vaccinations for travel to other countries. Some vaccines should not be given at the same time as Truxima or in the months after you receive Truxima. Your doctor will check if you should have any vaccines before you receive Truxima.

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 Truxima in children and young people.

Other medicines and Truxima

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 Truxima can affect the way some other medicines work. Also some other medicines can affect the way Truxima 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 for 12 hours before you are given Truxima. This is because some people have a fall in their blood pressure while they are being given Truxima.
- 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 Truxima.

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 Truxima can transfer across 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 Truxima. You must also do this for 12 months after your last treatment with Truxima.
Do not breast-feed while you are being treated with Truxima. Also do not breast-feed for 12 months after your last treatment with Truxima. This is because Truxima may pass into breast milk.

Driving and using machines

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

3. How Truxima is given

How it is given

Truxima 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 Truxima as a drip (intravenous infusion).

Medicines given before each Truxima administration

Before you are given Truxima, 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

a) If you are being treated for non-Hodgkin's Lymphoma
- *If you are having Truxima alone*
  Truxima will be given to you once a week for 4 weeks. Repeated treatment courses with Truxima are possible.
- *If you are having Truxima with chemotherapy*
  Truxima will be given to you on the same day as your chemotherapy.This is usually given every 3 weeks up to 8 times.
- If you respond well to treatment, you may be given Truxima every 2 or 3 months for two years. Your doctor may change this, depending on how you respond to the medicine.

b) If you are being treated for chronic lymphocytic leukaemia

When you are treated with Truxima in combination with chemotherapy, you will receive Truxima every 28 days until you have received 6 doses. The chemotherapy should be given after the Truxima infusion. Your doctor will decide if you should receive other treatment at the same time.

c) If you are being treated for rheumatoid arthritis

Each course of treatment is made up of two separate infusions which are given 2 weeks apart. Repeated courses of treatment with Truxima are possible. Depending on the signs and symptoms of your disease, your doctor will decide when you should receive more Truxima. This may be months from the previous dose.

d) If you are being treated for granulomatosis with polyangiitis or microscopic polyangiitis

Treatment with Truxima uses four separate infusions given at weekly intervals. A corticosteroid medicine will usually be given by injection before the start of Truxima treatment. Corticosteroid medicines given by mouth may be started at any time by your doctor to treat your condition.
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 require treatment. Rarely, some of these reactions have been fatal.

Infusion reactions

During or within the first 2 hours of the first infusion you may develop fever, chills and shivering. Less frequently, some patients may get pain at the infusion site, blisters, itching, sickness, tiredness, headache, breathing difficulties, tongue or throat swelling, itchy or runny nose, vomiting, flushing or palpitations, heart attack or low number of platelets. If you have heart disease or angina, these infusion reactions might get worse. **Tell the person giving you the infusion immediately** if you develop any of these symptoms, as the infusion may need to be slowed down or stopped. You may require additional treatment such as an antihistamine or paracetamol. When these symptoms go away, or improve, the infusion can be continued. These reactions are less likely to happen after the second infusion. Your doctor may decide to stop your Truxima 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 Truxima.
These are often colds, but there have been cases of pneumonia or urinary infections. These are listed below under "Other side effects".
If you are being treated for rheumatoid arthritis, you will also find this information in the Patient Alert Card you have been given by your doctor. It is important that you keep this Alert Card and show it to your partner or caregiver.

Skin reactions

Very rarely, severe blistering skin conditions that can be life-threatening may occur. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present. **Tell your doctor immediately if you have any of these symptoms.**

Other side effects include:

a) If you are being treated for non-Hodgkin's Lymphoma or chronic lymphocytic leukaemia

Very common side effects (may affect more than 1 in 10 people):
- bacterial or viral infections, bronchitis
- low number of white blood cells sometimes with fever, or low number of 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 "lactate dehydrogenase(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 and 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
- 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. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present.
- kidney failure
- severe vision loss

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

b) If you are being treated for rheumatoid arthritis

Very common side effects (may affect more than 1 in 10 people):
- infections such as pneumonia (bacterial)
- pain on passing water (urinary tract infection)
- allergic reactions that are most likely to occur during an infusion, but can occur up to 24- hours after infusion
- changes in blood pressure, nausea, rash, fever, feeling itchy, runny or blocked nose and sneezing, shaking, rapid heartbeat, and tiredness
- headache
- changes in results of laboratory tests carried out by your doctor. These include a decrease in the amount of some specific proteins in the blood (immunoglobulins) which help protect against infection.

Common side effects (may affect up to 1 in 10 people):
- infections such as bronchial tube inflammation (bronchitis)
- a feeling of fullness or a throbbing pain behind the nose, cheeks and eyes (sinusitis), pain in the abdomen, vomiting and diarrhoea, breathing problems
- fungal foot infection (athlete's foot)
- high cholesterol levels in the blood
- abnormal sensations of the skin, such as numbness, tingling, pricking or burning, sciatica, migraine, dizziness
- loss of hair
- anxiety, depression
- indigestion, diarrhoea, acid reflux, irritation and /or ulceration of the throat and the mouth
- pain in the tummy, back, muscles and/or joints

Uncommon side effects (may affect up to 1 in 100 people):
- excess fluid retention in the face and body
- inflammation, irritation and /or tightness of the lungs and throat, coughing
- skin reactions including hives, itching and rash
- allergic reactions including wheezing or shortness of breath, swelling of the face and tongue, collapse

Very rare side effects (may affect up to 1 in 10,000 people):
- a complex of symptoms occurring within a few weeks of an infusion of Truxima including allergic like reactions such as rash, itching, joint pain, swollen lymph glands and fever
- severe blistering skin conditions that can be life-threatening. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present.

Other rarely-reported side-effects due to Truxima include a decreased number of white cells in the blood (neutrophils) that help to fight against infection. Some infections may be severe (please see information on ***Infections*** within this section).

c) If you are being treated for granulomatosis with polyangiitis or microscopic polyangiitis

Very common side effects (may affect more than 1 in 10 people):
- infections, such as chest infections, urinary tract infections (pain on passing water), colds and herpes infections
- allergic reactions that are most likely to occur during an infusion, but can occur up to 24-hours after infusion
- diarrhoea
- coughing or shortness of breath
- nose bleeds
- raised blood pressure
- painful joints or back
- muscle twitches or shakiness
- feeling dizzy
- tremors (shakiness, often in the hands)
- difficulty sleeping (insomnia)
- swelling of the hands or ankles

Common side effects (may affect up to 1 in 10 people):
- indigestion
- constipation
- skin rashes, including acne or spots
- flushing or redness of the skin
- blocked nose
- tight or painful muscles
- pain in the muscles or in the hands or feet

- low number of red blood cells (anaemia)
- low numbers of platelets in the blood
- an increase in the amount of potassium in the blood
- changes in the rhythm of the heart, or the heart beating faster than normal

Very rare side effects (may affect up to 1 in 10,000 people):
- severe blistering skin conditions that can be life-threatening. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present.
- recurrence of a previous Hepatitis B infection

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

Reporting of side effects

If you get any side effects talk to your doctor, pharmacist or nurse. This includes any side effects not listed in this leaflet. You can also report side effects directly via
UK: Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard
and
Ireland: HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Truxima

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 the vial after EXP. The expiry date refers to the last day of that month.
Store in a refrigerator (2 °C – 8 °C). 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 that you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Truxima contains

- The active ingredient in Truxima is called rituximab. The vial contains 100 mg of rituximab. Each mL of concentrate contains 10 mg of rituximab.
- The other ingredients are sodium chloride, tri-sodium citrate dihydrate, polysorbate 80 and water for injections.

What Truxima looks like and contents of the pack

Truxima is a clear, colourless solution, supplied as a concentrate for solution for infusion in a glass vial.
Pack of 2 vials.

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And

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu