READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

TRUXIMA™ <<TROO-XEE-MA>>
Rituximab for Injection
Non-Hodgkin's Lymphoma & Chronic Lymphocytic Leukemia

Read this carefully before you start taking TRUXIMA™ and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about TRUXIMA™.

TRUXIMA™ is a biosimilar biologic drug (biosimilar) to the reference biologic drug Rituxan®. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.

Serious Warnings and Precautions

- Some side effects associated with TRUXIMA™ are severe and may be life-threatening. This drug should only be used by health professionals experienced in treating cancer in a facility where sudden and life-threatening reactions can be immediately treated.
- Fatal allergic reactions and tumour lysis syndrome (TLS) causing fatal kidney damage have occurred.
- Repeat and sometimes fatal attacks of hepatitis have occurred. Recurrence of hepatitis B virus infection has occurred in patients who show evidence of the virus in a blood test. It is advised that all patients be tested for hepatitis B virus infection before starting treatment with TRUXIMA™.
- Serious, including fatal infections can occur during or following treatment with TRUXIMA™. A rare brain infection called JC virus causing progressive multifocal leukoencephalopathy (PML) and death has been reported in patients with non-Hodgkin Lymphoma (NHL) and Chronic Lymphocytic Leukemia (CLL). It is hard to predict who will get PML, but it is more common in people with weakened immune systems.
- Serious infusion reactions can happen during your infusion or within 24 hours after your infusion of TRUXIMA™.
- Severe skin reactions such as Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) have been reported very rarely. Some cases have resulted in death.
- Serious and potentially fatal cardiovascular events have been reported rarely following treatment with TRUXIMA™.

What is TRUXIMA™ used for?
TRUXIMA™ (also known as rituximab for injection) is a cancer medicine that is used to stop cancer cell growth and ideally cause the death of cancer cells. It is a cancer medicine that must be prescribed by a doctor.

It is used to treat patients with certain types of non-Hodgkin's lymphoma and chronic lymphocytic leukemia.

How does TRUXIMA™ work?
Our bodies have a natural defence system against cancer cells.
When cancer cells appear, our bodies respond by making special proteins called antibodies. Researchers studied this response and learned how to create antibodies outside the body that help with cancer treatment. These are called monoclonal antibodies.

Monoclonal antibodies are now made to target tumours in an effort to control the growth of cancer.

TRUXIMA™ belongs to a family of medicine called monoclonal antibodies. It is an antibody that targets the CD-20 B-cell lymphocyte to stop its activity. TRUXIMA™ attaches to the CD20 marker that is located on the B-cell. When in place, it works to stop the growth of the cancer cells and may destroy them.

TRUXIMA™ is most active in patients whose lymphomas are of the B-cell type.

What are the ingredients in TRUXIMA™?
Medicinal ingredients: TRUXIMA™ contains the active ingredient rituximab for injection.
Non-medicinal ingredients: Hydrochloric acid, polysorbate 80, sodium chloride, tri-sodium citrate dihydrate, sodium hydroxide and water for injection.

TRUXIMA™ comes in the following dosage forms:
Liquid concentrate for intravenous (IV) administration.

Do not use TRUXIMA™ if:
- TRUXIMA™ (rituximab for injection) is contraindicated in patients with known Type I hypersensitivity or anaphylactic reactions to murine proteins, Chinese Hamster Ovary (CHO) cell proteins, or to any component of this product (See WARNNGS AND PRECAUTIONS).
- TRUXIMA™ is also contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML).
- TRUXIMA™ is not recommended for use in patients with severe, active infections.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TRUXIMA™. Talk about any health conditions or problems you may have, including if you:
Before beginning treatment with TRUXIMA™, make sure your doctor knows if:
- You ever had a bad reaction to rituximab for injection or any of the non-medicinal ingredients.
- You are allergic to other medications, food or dyes.
- You have a history of heart attack or stroke.
- You are taking any other medicines (including those not prescribed by the doctor). If you are taking medication to reduce blood pressure. If you are planning to be immunized with a vaccine during or after the completion of your TRUXIMA™ therapy.
- You have a pre-existing lung disease as you may have a greater chance of breathing difficulties during your TRUXIMA™ treatment infusion.
- You have a history of hepatitis B, current hepatitis B or tuberculosis infection.
- You are pregnant or could become pregnant or are breast-feeding a child.

Other warnings you should know about:

- Rituximab for injection has not been studied in pregnant or breast-feeding women. If you are pregnant, could become pregnant or are or breast-feeding, be sure to discuss with your doctor whether TRUXIMA™ is right for you. Women should avoid pregnancy and use effective birth control methods during treatment with TRUXIMA™ and for one year after treatment.
- TRUXIMA™ is an infusion ("drip") which is given intravenously (into your veins). Very commonly patients being given rituximab for injection have some side effects while the infusion is being given. Most patients are also given medication such as acetaminophen [TYLENOL®], antihistamines, and steroids for allergic reactions [such as prednisone] before the infusion to prevent these reactions. If you notice any trouble breathing, feel hot or shivery, have hives or an itchy rash, tell the person giving you the infusion immediately.
- These side effects are more common with the first infusions of rituximab for injection. If you develop any of these symptoms, the infusion will be slowed down or stopped for a while. Once these symptoms go away, or improve, the infusion can be continued.
- If you have ever had heart disease [for example angina (heart pain), arrhythmia (palpitations/ irregular heart beat),or heart failure] or breathing problems, your doctor will take special care of you during therapy with TRUXIMA™.
- One patient with CLL who had a tuberculosis infection had repeat and severe attacks when treated with rituximab for injection. Tell the doctor if you think you had tuberculosis; you will be carefully checked for signs of tuberculosis infection.
- In some cases, patients who have had hepatitis B might have a repeat attack of hepatitis. Tell the doctor if you think you have had hepatitis in the past.
- Infection with hepatitis B virus causes inflammation of the liver which may show as mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue. If you experience any of these symptoms immediately contact your doctor. If you show evidence of hepatitis B virus infection you may be referred to a liver disease expert for ongoing monitoring and management.
- TRUXIMA™ is not to be used in patients with active hepatitis B viral disease. Tell your doctor if you think you have hepatitis B.
- Live viral vaccines should not be given with TRUXIMA™. Your doctor will check if you should have any vaccines before or after you receive TRUXIMA™.
- Cases of Progressive Multifocal Leukoencephalopathy (PML) have been reported during use of rituximab for injection in NHL and CLL. PML is a condition that causes nerve damage within the brain. Tell your doctor immediately if you have memory loss, trouble thinking, and difficulty with walking, clumsiness, falls or weakness on one side of the body, changes in mood or loss of vision. Your doctor will check if you need to see a neurologist.
- Cases of Tumour Lysis Syndrome [TLS] have been reported during the use of rituximab for injection. TLS is a condition that causes sudden kidney failure and abnormal heart rhythms due to changes in blood chemistry, which may be fatal. Tell your doctor immediately if you have palpitations/irregular heartbeats; vomiting; fatigue/weakness; difficulty concentrating/trouble thinking; swelling, numbness or tingling in hands, face or feet; back pain; muscle cramps; fainting or trouble breathing.
- Some patients with TLS in its early stages have no symptoms, and your doctor will be performing blood tests for this and other side effects.
- Bowel problems, including blockage or tears in the bowels that can sometimes lead to death can happen if you receive TRUXIMA™ with chemotherapy medicines to treat non-Hodgkin's lymphoma. Tell your doctor immediately if you have any abdominal pain during treatment with TRUXIMA™.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with TRUXIMA™:

- Before starting treatment, make sure your doctor knows if you are taking or have recently taken any other medicines (including those you have bought for yourself from a pharmacy, supermarket or health store). This is extremely important, as using more than one medicine at the same time can strengthen or weaken their effect. TRUXIMA™ should not be used with other drugs unless your doctor has told you it is safe to do so.

How to take TRUXIMA™:

Your doctor has prescribed TRUXIMA™ after carefully studying your case. Other people may not benefit from taking this medicine, even though their problems may seem similar to yours.

Usual dose:

The usual dose of TRUXIMA™ is based on your body surface area which your doctor will calculate for you.

TRUXIMA™ is not taken by mouth, but given through an intravenous line. An intravenous line, or I.V., is a thin, plastic tube placed in a vein in your hand or arm. When TRUXIMA™ is given intravenously, it is called an infusion.

A healthcare professional in a healthcare facility will give you TRUXIMA™ as prescribed by your doctor.

Your first TRUXIMA™ infusion may take most of the day. Usually the remaining infusions will take less time.

Overdose:

It is unlikely that you will receive too much TRUXIMA™ as you will be closely monitored by Healthcare Professionals during your infusion. However, if you suspect you received too much TRUXIMA™ contact your physician and poison control centre immediately.

If you think you have taken too much TRUXIMA™, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of TRUXIMA™, contact your physician immediately. Your physician will decide when you should receive your next dose.

What are possible side effects from using TRUXIMA™?

These are not all the possible side effects you may feel when taking TRUXIMA™. If you experience any side effects not listed here, contact your healthcare professional.

The most common possible unwanted effects are infusion related events, and happen to more than 30% of patients treated with TRUXIMA™:

- Fever and chills
- Nausea, vomiting, fatigue (feeling tired or weak), headache, skin rash, redness of the skin, itchiness, wheezing or tightness in the chest, shortness of breath, difficulty

breathing, sensation of the tongue or throat swelling, throat irritation, rhinitis (runny nose), temporary low blood pressure, flushing, dizziness on standing up, fast heart beat, chest pain, pain where the non-Hodgkin's lymphoma is located.

If these unwanted effects occur, it is most common within 30 minutes to 2 hours after starting the first infusion, but may also occur after the infusion has finished. The symptoms are usually mild to moderate, and can be easily treated. Rarely, these reactions can be severe. These unwanted effects are less common after the first treatment.

These unwanted effects can be prevented or managed by:

- Slowing or interrupting your infusion of TRUXIMA™. The treatment can be restarted once the symptoms have resolved.
- Giving a fever reducer, such as TYLENOL®, and an antihistamine, such as BENADRYL®, and a steroid such as prednisone, which can be given for allergic reactions, before each infusion of TRUXIMA™. Sometimes additional medications are needed to be given to treat these unwanted effects.

Additionally:

- Your doctor may instruct you not to take your blood pressure medication 12 hours before and delay taking until after your infusion of TRUXIMA™ is complete. Please ask your doctor for specific instructions.
- Because some of the medications given with TRUXIMA™ may cause some dizziness or sleepiness, you should arrange for someone else to drive you home after each treatment.

There are also possible unwanted effects which could be serious but occur less commonly:

- Chest pain, fast or irregular or uneven heart beat.
- Decreased of the white blood cells, red blood cells and platelets in the blood, infection and bleeding.
- Rapid destruction of cells sometimes leading to kidney, heart or breathing problems (Tumour Lysis Syndrome).
- Redness or blistering of the skin and the inside of the mouth.
- Recurrence of Hepatitis B infection. Signs and symptoms of Hepatitis B include mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.
- Increasing weakness on one side of the body, clumsiness or falls, trouble with thinking or memory, changes in mood, change in vision.

If you have been given TRUXIMA™ in combination with chemotherapy, the following additional unwanted effects may occur:

- Sudden loss of speech, weakness or numbness of part or all of one side of the body, loss of vision or blurred vision, unexplained dizziness and/or sudden falls.
- Herpes zoster also known as shingles. Symptoms of shingles include itching, tingling or severe burning pain with red patches that develop into blisters and are grouped in a cluster usually on the trunk of the body.

Please consult your doctor, nurse or pharmacist for possible unwanted effects that may be caused by CHOP, CVP or FC chemotherapy.

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	

	Only if severe	In all cases	Stop taking drug and get immediate medical help
COMMON (1% to less than 10% of patients)		✓	
New fever or if your temperature becomes higher than38ºC		✓	
Shortness of breath, difficulty breathing, wheezing, coughing		✓	
Symptoms of infection that include: - fever, temperature at 38ºC or higher. - Sore throat - Cough - Any redness or swelling - Pain when you pass your urine		✓	
Any bleeding or unusual bruising		✓	
Skin rash, itching, hives or sore joints		✓	
Swelling of the face, lips, mouth or throat which may cause difficulty in swallowing or breathing, swelling of the hands, feet or ankles		✓	
Symptoms of Hepatitis B such as mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.		✓	
Uncommon (0.1% to less than 1% of patients)		✓	
Chest pain, fast heart rate or an irregular or uneven heart rate		✓	
Kidney problems such as lower back or side pain, swelling of feet or lower legs, numbness or tingling in feet or hands.		✓	✓
Redness or blistering of the skin and inside of the mouth		✓	✓
Sudden loss of speech, increasing weakness or numbness of part or all of one side of the body, loss of vision or blurred vision, unexplained dizziness and/or clumsiness or sudden falls, trouble with thinking or memory, changes in mood, change in vision, change in mental status (for example, confusion), seizures.		✓	
Symptoms of shingles such as itching, tingling, or severe burning pain with red patches that develop into blisters and are grouped		✓	

in a cluster usually on the trunk of the body.			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reporting Suspected Side Effects

For the general public: Should you experience a side effect following immunization, please report it to your doctor, nurse, or pharmacist.

Should you require information related to the management of the side effect, please contact your healthcare provider. The Public Health Agency of Canada, Health Canada and Celltrion Healthcare Co., Ltd. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) appropriate for your province/territory and send it to your local Health Unit.

Storage:
Store in a refrigerator (2 °C – 8 °C). Keep the container in the outer carton in order to protect from light.
Keep out of reach and sight of children.

If you want more information about TRUXIMA™:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); Teva Canada Innovation site (http://www.tevacanadainnovation.ca), or by calling 1-833-662-5644.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

TRUXIMA™ <<TROO-XEE-MA>>
Rituximab for Injection
Rheumatoid Arthritis

Read this carefully before you start taking TRUXIMA™ and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about TRUXIMA™.

TRUXIMA™ is a biosimilar biologic drug (biosimilar) to the reference biologic drug Rituxan®. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.

Serious Warnings and Precautions

- Several side effects are associated with TRUXIMA™, some may be severe and life-threatening. This drug should only be used by health professionals experienced in treating rheumatoid arthritis in a setting where medication and supportive care measures are immediately available in the event of an allergic reaction during administration (see DOSAGE AND ADMINISTRATION).
- Serious infusion reactions can happen during your infusion or within 24 hours after your infusion of TRUXIMA™.
- Recurrence of hepatitis B virus infection has occurred in patients who show evidence of the virus in a blood test. It is advised that all patients be tested for hepatitis B virus infection before starting treatment with TRUXIMA™.
- Serious, including fatal infections can occur during or following treatment with TRUXIMA™. A rare brain infection called JC virus causing progressive multifocal leukoencephalopathy (PML) and death has been reported in patients with autoimmune diseases treated with TRUXIMA™. It is hard to predict who will get PML, but it is more common in people with weakened immune systems.
- Severe skin reactions such as Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) have been reported very rarely. Some cases have resulted in death.
- Serious and potentially fatal cardiovascular events have been reported rarely following treatment with TRUXIMA™.

What is TRUXIMA™ used for?

- TRUXIMA™ (also known as rituximab for injection) is an injectable medicine that is used to reduce signs and symptoms of rheumatoid arthritis (in combination with methotrexate).

How does TRUXIMA™ work?
B cells are an important element in the immune system, helping the body to fight off infection. However in diseases such as RA, the immune system acts abnormally leading to an attack on normal healthy tissue such as the joints. TRUXIMA™ is a monoclonal antibody. Antibodies are proteins which are produced to bind to another protein called an antigen. TRUXIMA™ binds to an antigen on the surface of a type of white blood cell, the B lymphocyte. When TRUXIMA™ binds to the surface of this cell, it causes the cell to die.

What are the ingredients in TRUXIMA™?
Medicinal ingredients: TRUXIMA™ contains the active ingredient rituximab for injection.
Non-medicinal ingredients: Hydrochloric acid, polysorbate 80, sodium chloride, tri-sodium citrate dihydrate, sodium hydroxide and water for injection.

TRUXIMA™ comes in the following dosage forms:
Liquid concentrate for intravenous (IV) administration.

Do not use TRUXIMA™ if:
- TRUXIMA™ (rituximab for injection) is contraindicated in patients with known Type I hypersensitivity or anaphylactic reactions to murine proteins, Chinese Hamster Ovary (CHO) cell proteins, or to any component of this product (See WARNNGS AND PRECAUTIONS).
- TRUXIMA™ is also contraindicated in patients who have or have had progressive multifocal leukoencephalopathy (PML).
- TRUXIMA™ is not recommended for use in patients with severe, active infections.
- TRUXIMA™ is not recommended unless patients' moderate-to-severe rheumatoid arthritis has not been controlled with medicines called TNF antagonists.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TRUXIMA™. Talk about any health conditions or problems you may have, including if you:

- You ever had a bad reaction to rituximab for injection or any of the non-medicinal ingredients.
- You are allergic to other medications, food or dyes.
- You have a history of heart disease, heart attack or stroke.
- You are taking any other medicines (including those not prescribed by the doctor). If you are taking or took another biologic medicine called a TNF antagonist or a DMARD (disease modifying anti-rheumatic drug). If you are taking medication to reduce blood pressure. If you are planning to be immunized with a vaccine during or after the completion of your TRUXIMA™ therapy.
- You have a pre-existing lung disease as you may have a greater chance of breathing difficulties during your TRUXIMA™ treatment infusion.
- You have a history of hepatitis B or current hepatitis B infection.
- You have a history of chronic or recurrent infection.
- You are pregnant or plan on becoming pregnant or are breast-feeding a child.

Other warnings you should know about:
- Rituximab for injection has not been studied in pregnant or breast-feeding women. If you are pregnant or breast-feeding, be sure to discuss with your doctor whether TRUXIMA™ is right for you. Women in whom there is a possibility of conceiving a child should avoid becoming pregnant and use effective contraceptive methods during and up to 12 months

after treatment with TRUXIMA™.

- TRUXIMA™ is an infusion ("drip") which is given into your veins. Some patients being given rituximab for injection have some side effects while the infusion is being given. If you notice any difficulty breathing, feel hot or shivery, have hives or an itchy rash, tell the person giving you the infusion immediately.
- These effects mainly occur with the first infusion of rituximab for injection. If you develop any of these symptoms, the infusion will be slowed down or stopped for a while. Some patients will need to take an antihistamine or acetaminophen. When these symptoms go away, or improve, the infusion can be continued.
- If you have ever had heart disease (i.e. angina, palpitations, or heart failure) or a history of breathing problems, your doctor will take special care of you during therapy with TRUXIMA™.
- The cells that are killed by TRUXIMA™ help to fight infection. TRUXIMA™ should not be given to people who have an active infection. Tell your doctor if you think you may have an infection, even a mild one like a cold, before he gives you the medicine. Also please tell your doctor if you have a lot of infections or suffer from severe infections.
- You might get infections more easily following TRUXIMA™ therapy. It is very important to tell your doctor if you get any symptoms of an infection, for example fever, cough, sore throat, burning pain when passing urine, or you start to feel weak or generally unwell.
- In some cases, patients who have had hepatitis B might have a repeat attack of hepatitis. Tell the doctor if you think you have had hepatitis in the past.
- Infection with hepatitis B virus causes inflammation of the liver which may show as mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue. If you experience any of these symptoms immediately contact your doctor. If you show evidence of hepatitis B virus infection you may be referred to a liver disease expert for ongoing monitoring and management.
- TRUXIMA™ is not to be used in patients with active hepatitis B viral disease. Tell your doctor if you think you have hepatitis B.
- Live viral vaccines should not be given with TRUXIMA™. Your doctor will check if you should have any vaccines before or after you receive TRUXIMA™.
- Cases of Progressive Multifocal Leukoencephalopathy (PML) have been reported following use of rituximab for injection for the treatment of autoimmune diseases, including RA. PML is a condition that causes nerve damage within the brain. Tell your doctor immediately if you have memory loss, trouble thinking, difficulty with walking, clumsiness, falls or weakness on one side of the body, changes in mood or loss of vision. Your doctor will check if you need to see a neurologist.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with TRUXIMA™:

- Before starting treatment, make sure your doctor knows if you are taking or have recently taken any other medicines (including those you have bought for yourself from a pharmacy, supermarket or health store). This is extremely important, as using more than one medicine at the same time can strengthen or weaken their effect. TRUXIMA™ should not be used with other drugs unless your doctor has told you it is safe to do so.

How to take TRUXIMA™:

Your doctor has prescribed TRUXIMA™ after carefully studying your case. Other people may not benefit from taking this medicine, even though their problems may seem similar to yours.

Before the infusion is given you will be given medicines to prevent or reduce possible reactions to TRUXIMA™.

TRUXIMA™ is not taken by mouth, but given through an intravenous line. An intravenous line, or I.V., is a thin, plastic tube placed in a vein in your hand or arm. When TRUXIMA™ is given intravenously, it is called an infusion.

Usual dose:
RA
Each course of treatment is made up of two separate infusions which are given at least 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™.

Overdose:
It is unlikely that you will receive too much TRUXIMA™ as you will be closely monitored by Healthcare Professionals during your infusion. However, if you suspect you received too much TRUXIMA™ contact your physician and poison control centre immediately.

Missed Dose:
If you miss a dose of TRUXIMA™, contact your physician immediately. Your physician will decide when you should receive your next dose.

If you think you have taken too much TRUXIMA™, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using TRUXIMA™?
These are not all the possible side effects you may feel when taking TRUXIMA™. If you experience any side effects not listed here, contact your healthcare professional.

The most common possible unwanted side effects are infusion related events:

- Fever and chills
- Nausea, vomiting, fatigue (feeling tired or weak), headache, skin rash, hives, redness of the skin, itchiness, wheezing or tightness in the chest, shortness of breath, difficulty breathing, sensation of the tongue or throat swelling, throat irritation, rhinitis (runny nose), temporary low blood pressure, high blood pressure, flushing, dizziness on standing up, fast heartbeat, pain in the mouth/throat, swelling of the hands and feet.

If these unwanted effects occur, it is most common within 30 minutes to 2 hours after starting the first infusion, but may also occur after the infusion has finished. The symptoms are usually mild to moderate, and can be easily treated. Rarely, these reactions can be severe. These unwanted effects are less common after the first treatment.

These unwanted effects can be prevented or managed by:
- Slowing or interrupting your infusion of TRUXIMA™. The treatment can be restarted once the symptoms have resolved.
- Giving a fever reducer, such as TYLENOL®, and an antihistamine, such as BENADRYL® before each infusion of TRUXIMA™. Sometimes additional medications are needed to

be given to treat these unwanted effects.

Additionally:

- Your doctor may instruct you not to take your blood pressure medication 12 hours before and delay taking until after your infusion of TRUXIMA™ is complete. Please ask your doctor for specific instructions.
- Because some of the medications given with TRUXIMA™ may cause some dizziness or sleepiness, you should arrange for someone else to drive you home after each treatment.

There are also possible unwanted effects which could be serious but occur less commonly:

Some patients get infections after treatment. Often these are colds, but could be pneumonia or urinary infections. Some other effects might occur, but are less likely, including: pain in the tummy, back, chest, muscles and/or joints, at the infusion site, feeling unwell, changes in blood pressure, changes in heart rate, diarrhea, indigestion, cramp, dizziness, tingling or numbness, anxiety or nervousness, cough, watery or itchy eyes, runny or itchy nose, sweating, sinusitis.

Some patients also have some changes to blood tests including a fall in the number of red cells, white cells or both. Severe but rare reactions, in particular severe breathing difficulties and severe skin reactions including blistering, could be fatal. This is why your doctor will watch you closely, and why it is important for you to tell your doctor immediately if you experience any difficulty in breathing and any skin reactions.

Some patients also have increasing weakness on one side of the body, clumsiness or falls, trouble with thinking or memory, changes in mood, change in vision. You should report these to your doctor immediately.

If you are receiving TRUXIMA™ in combination with other medicines, some of the side effects you may experience may be due to the other medicine.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON (1% to less than 10% of patients)			
New fever or if your temperature becomes higher that 38ºC		✓	
Shortness of breath, difficulty breathing, wheezing, coughing		✓	
Symptoms of infection that include: - fever, temperature at 38ºC or higher. - Sore throat - Cough - Any redness or swelling - Pain when you pass your urine		✓	
Any bleeding or unusual bruising		✓	

Skin rash, itching, hives or sore joints		✓	
Swelling of the face, lips, mouth or throat which may cause difficulty in swallowing or breathing, swelling of the hands, feet or ankles		✓	
Symptoms of Hepatitis B such as mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.		✓	
Uncommon (0.1% to less than 1% of patients)			
< Condition: symptom / effect>			
Changes in blood pressure, changes in heart rate		✓	
Redness or blistering of the skin		✓	✓
Increasing weakness on one side of the body, clumsiness or falls, trouble with thinking or memory, changes in mood, change in vision		✓	
Sudden loss of speech, increasing weakness or numbness of part or all of one side of the body, loss of vision or blurred vision, unexplained dizziness and/or clumsiness or sudden falls, trouble with thinking or memory, changes in mood, change in vision, change in mental status (for example, confusion), seizures.		✓	
Symptoms of shingles such as itching, tingling, or severe burning pain with red patches that develop into blisters and are grouped in a cluster usually on the trunk of the body.		✓	
Kidney problems such as lower back or side pain, swelling of feet or lower legs, numbness or tingling in feet or hands.		✓	
Redness or blistering of the skin and inside the mouth.		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reporting Suspected Side Effects

For the general public: Should you experience a side effect following immunization, please report it to your doctor, nurse, or pharmacist.

Should you require information related to the management of the side effect, please contact your healthcare provider. The Public Health Agency of Canada, Health Canada and Celltrion Healthcare Co., Ltd. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) appropriate for your province/territory and send it to your local Health Unit.

Storage:
Store in a refrigerator (2 °C – 8 °C). Keep the container in the outer carton in order to protect from light.

Keep out of reach and sight of children.

If you want more information about TRUXIMA™:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); Teva Canada Innovation site (http://www.tevacanadainnovation.ca), or by calling 1-833-662-5644.

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