

PRODUCT MONOGRAPH

Pr**RITUXAN**[®]

rituximab

10 mg/mL Intravenous Infusion

Professed Standard

Antineoplastic

Hoffmann-La Roche Ltd.
7070 Mississauga Road
Mississauga, Ontario
L5N 5M8

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PART III: CONSUMER INFORMATION

P^rRITUXAN[®]
rituximab

Pronounced: rih TUCKS en

Non-Hodgkin's Lymphoma & Chronic Lymphocytic Leukemia

This leaflet is part III of a three-part "Product Monograph" published when RITUXAN was authorized for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about RITUXAN. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

RITUXAN (also known as rituximab) 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.

What is non-Hodgkin's lymphoma?

Non-Hodgkin's lymphoma is a cancer of the lymph cells (lymphocytes), which are found in the blood and in the lymph nodes. Lymph nodes are located in the head and neck area, under the arms, in the groin and throughout the chest and abdomen. Lymphocytes are a type of white blood cell. There are two types: B lymphocytes and T lymphocytes. B lymphocytes produce antibodies or proteins that help our immune system to fight foreign substances which enter the body. All B-cells have a marker on their surface. This marker is called CD20.

What is chronic lymphocytic leukemia?

Chronic lymphocytic leukemia is a cancer of the bone marrow (spongy tissue inside bones where blood cells are made). It affects lymph cells (lymphocytes) which are a type of white blood cell. There are two types: B lymphocytes and T lymphocytes. B lymphocytes produce antibodies or proteins that help our immune system to fight foreign substances which enter the body. All B-cells have a marker on their surface. This marker is called CD20.

What RITUXAN does:

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.

RITUXAN 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. RITUXAN 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.

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

Who should take RITUXAN?

RITUXAN is given alone for patients with low-grade CD20 antigen positive B-cell non-Hodgkin's lymphoma, who have not received prior treatment or who are no longer responding to their current anti-cancer treatment or where the lymphoma has returned despite previous anti-cancer treatment.

Depending on the type of lymphoma, RITUXAN may also be given in combination with chemotherapy regimens called CHOP or CVP. CHOP stands for the following drugs: cyclophosphamide, doxorubicin, vincristine and prednisone while CVP stands for cyclophosphamide, vincristine and prednisolone.

RITUXAN may also be used as a continuous (maintenance) treatment for patients who have responded to initial therapy.

RITUXAN may also be used to treat patients with moderate or severe [stage B or C] B-cell chronic lymphocytic leukemia. In the CLL trial RITUXAN was used with 2 other chemotherapy drugs FC [which stands for fludarabine and cyclophosphamide].

When it should not be used:

If you are allergic to rituximab or proteins of similar mouse or human origin or any other ingredient in RITUXAN or if you have ever had a rare infection of the brain called progressive multifocal leukoencephalopathy (PML) you should not take RITUXAN.

What should you tell your doctor before you start taking RITUXAN?

Before beginning treatment with RITUXAN, make

sure your doctor knows if:

- You ever had a bad reaction to RITUXAN 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 RITUXAN therapy.
- You have a pre-existing lung disease as you may have a greater chance of breathing difficulties during your RITUXAN 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.

This information will help your doctor and you decide whether you should use RITUXAN and what extra care may need to be taken while you are on the medication.

What the medicinal ingredient is:

RITUXAN contains the active ingredient rituximab.

What the non-medicinal ingredients are:

Hydrochloric acid, polysorbate 80, sodium chloride, sodium citrate, sodium hydroxide and water for injection.

What dosage forms it comes in:

Liquid concentrate for intravenous (IV) administration.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Some side effects associated with RITUXAN 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 RITUXAN.

Serious, including fatal infections can occur during or following treatment with RITUXAN. 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 RITUXAN.

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 RITUXAN.

RITUXAN 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 RITUXAN is right for you. Women should avoid pregnancy and use effective birth control methods during treatment with RITUXAN and for one year-after treatment.

RITUXAN is an infusion (“drip”) which is given intravenously (into your veins). Very commonly patients being given RITUXAN 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 RITUXAN. 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 RITUXAN.

One patient with CLL who had a tuberculosis infection had repeat and severe attacks when treated with RITUXAN. 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.

RITUXAN 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 RITUXAN. Your doctor will check if you should have any vaccines before or after you receive RITUXAN.

Cases of Progressive Multifocal Leukoencephalopathy (PML) have been reported during use of RITUXAN 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 RITUXAN. 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 RITUXAN with chemotherapy medicines to treat non-Hodgkin's lymphoma. Tell your doctor immediately if you have any abdominal pain during treatment with RITUXAN.

INTERACTIONS WITH THIS MEDICATION

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. RITUXAN should not be used with other drugs unless your doctor has told you it is safe to do so.

PROPER USE OF THIS MEDICATION

Your doctor has prescribed RITUXAN 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 RITUXAN is based on your body surface area which your doctor will calculate for you.

RITUXAN is not taken by mouth, but given with fluids 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 RITUXAN is given intravenously, it is called an infusion.

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

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

Missed Dose

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

Overdose

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

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Unwanted effects are possible with all medicines. Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well while you are receiving treatment with RITUXAN.

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

- 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, which 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 RITUXAN. The treatment can be restarted once the symptoms have resolved.
- Giving a fever reducer, such as **TYLENOL®**, an antihistamine, such as **BENADRYL®**, and a steroid such as Prednisone which can be given for allergic reactions, before each infusion of RITUXAN. 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 RITUXAN is complete. Please ask your doctor for specific instructions.

- Because some of the medications given with RITUXAN 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 RITUXAN 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, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common (1% to less than 10% of patients)	New fever or if your temperature becomes higher than 38°C		✓	
	Shortness of breath, difficulty breathing, wheezing, coughing		✓	
	Symptoms of infection that include: -fever, temperature at 38°C 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		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	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.		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	Redness or blistering of the skin and the 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.		✓	✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	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.		✓	

This is not a complete list of side effects. For any unexpected effects while taking RITUXAN, contact your doctor or pharmacist.

This document does not provide all known information about RITUXAN. If you have any questions or concerns about your treatment, please speak with your doctor, nurse or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program

Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Hoffmann-La Roche Limited at: www.rochecanada.com or by contacting the sponsor, Hoffmann-La Roche Limited, at: 1-888-762-4388.

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Hoffmann-La Roche Limited
Mississauga, ON L5N 5M8

PART III: CONSUMER INFORMATION

PrRITUXAN®
rituximab

Pronounced: rih TUCKS en

Rheumatoid Arthritis & Granulomatosis with Polyangiitis and Microscopic Polyangiitis

This leaflet is part III of a three-part "Product Monograph" published when RITUXAN was authorized for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about RITUXAN. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

- RITUXAN (also known as rituximab) is an injectable medicine that is used to reduce signs and symptoms of rheumatoid arthritis (in combination with methotrexate).
- RITUXAN in combination with glucocorticoids or "steroids" is also used to reduce inflammation associated with severe Granulomatosis with Polyangiitis (GPA, also known as Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) and helps to control your disease.

What is rheumatoid arthritis?

Rheumatoid Arthritis (RA) is an inflammatory disease of the joints. Characteristics of RA include redness, swelling, pain, and limited movement around joints of the hands, feet, elbows, knees and neck. It is considered an autoimmune disease, a disease which produces antibodies against its own immune system or against its own body proteins.

What is Granulomatosis with Polyangiitis (GPA, also known as Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)?

GPA/MPA are disorders that causes blood vessel inflammation (vasculitis). GPA/MPA are characterized by inflammation associated with autoantibodies called ANCAs (anti-neutrophil cytoplasm antibodies). ANCAs contribute to inflammation that damages the blood vessel walls in different tissues and organs in the body. The signs and symptoms of vasculitis vary depending on which blood vessels/organ systems are affected.

What RITUXAN does:

B cells are an important element in the immune system, helping the body to fight off infection. However in

diseases such as RA and GPA/MPA, the immune system acts abnormally leading to an attack on normal healthy tissue such as the joints. In GPA/MPA patients, the immune system can attack the respiratory tract [sinuses, nose, trachea (windpipe), and lungs], kidneys, eyes, nerves and skin.

RITUXAN is a monoclonal antibody. Antibodies are proteins which are produced to bind to another protein called an antigen. RITUXAN binds to an antigen on the surface of a type of white blood cell, the B lymphocyte. When RITUXAN binds to the surface of this cell, it causes the cell to die.

Who should take RITUXAN?

- RITUXAN is used to reduce signs and symptoms of moderate-to-severe rheumatoid arthritis in people who have tried other medicines called TNF antagonists, which have either stopped working or have not worked well enough. RITUXAN is taken together with another medicine called methotrexate. When taken with methotrexate, RITUXAN has been shown to reduce the rate of progression of joint damage as measured by x-ray.
- RITUXAN is also used in the treatment of severe Granulomatosis with Polyangiitis (GPA, also known as Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA). RITUXAN is taken together with other medicines referred to as glucocorticoids or "steroids". RITUXAN has been shown to reduce inflammation, and helps to control your disease.

When it should not be used:

If you are allergic to rituximab or proteins of similar origin or any other non-medicinal ingredient in RITUXAN or if you have ever had a rare infection of the brain called progressive multifocal leukoencephalopathy (PML) you should not take RITUXAN.

RITUXAN is not recommended unless patients' moderate-to-severe rheumatoid arthritis has not been controlled with medicines called TNF antagonists.

What should you tell your doctor before you start taking RITUXAN?

Before beginning treatment with RITUXAN, make sure your doctor knows if:

- You ever had a bad reaction to RITUXAN 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 RITUXAN therapy.
- You have a pre-existing lung disease as you may have a greater chance of breathing difficulties during your RITUXAN 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.

This information will help your doctor and you decide whether you should use RITUXAN and what extra care may need to be taken while you are on the medication.

What the medicinal ingredient is:

RITUXAN contains the active ingredient rituximab.

What the non-medicinal ingredients are:

Hydrochloric acid, polysorbate 80, sodium chloride, sodium citrate, sodium hydroxide and water for injection.

What dosage forms it comes in:

Liquid concentrate for intravenous (IV) administration.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Several side effects are associated with RITUXAN, 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 RITUXAN.

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 RITUXAN.

Serious, including fatal infections can occur during or following treatment with RITUXAN. A rare brain infection called JC virus causing progressive multifocal leukoencephalopathy (PML) and death has been reported in patients with autoimmune diseases treated with Rituxan. 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 RITUXAN.

RITUXAN 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 RITUXAN 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 RITUXAN.

RITUXAN is an infusion (“drip”) which is given into your veins. Some patients being given RITUXAN 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 RITUXAN. 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 RITUXAN.

The cells that are killed by RITUXAN help to fight infection. RITUXAN 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 RITUXAN 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.

RITUXAN 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 RITUXAN. Your doctor will check if you should have any vaccines before or after you receive RITUXAN.

Cases of Progressive Multifocal Leukoencephalopathy (PML) have been reported following use of RITUXAN 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.

INTERACTIONS WITH THIS MEDICATION

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. RITUXAN should not be used with other drugs unless your doctor has told you it is safe to do so.

PROPER USE OF THIS MEDICATION

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

The JointEffort[®] program has been established to facilitate the administration of RITUXAN in RA and GPA/MPA. Information about the JointEffort[®] program can be obtained by calling 1-888-748-8926.

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

RITUXAN 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 RITUXAN is given intravenously, it is called an infusion.

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 RITUXAN are possible. Depending on the signs and symptoms of your disease, your doctor will decide when you should receive more RITUXAN.

GPA/MPA

RITUXAN is administered as a weekly intravenous infusion for 4 weeks.

Overdose

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

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Unwanted effects are possible with all medicines. Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well while you are receiving treatment with RITUXAN.

The most common possible unwanted 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 RITUXAN. 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 RITUXAN. 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 RITUXAN is complete. Please ask your doctor for specific instructions.
- Because some of the medications given with RITUXAN may cause some dizziness or sleepiness, you should arrange for someone else to drive you home after each treatment.

In addition to the unwanted effects described above, there are certain adverse events identified which are specific to GPA/MPA patients, namely muscle spasms, increases in liver enzymes and nose bleeds.

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 RITUXAN in combination with other medicines, some of the side effects you may experience may be due to the other medicine.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common (1% to less than 10% of patients)	New fever or if your temperature becomes higher than 38°C		✓	
	Shortness of breath, difficulty breathing, wheezing, coughing		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	Symptoms of infection that include: <ul style="list-style-type: none"> - fever, temperature at 38°C 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		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	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)	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		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	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 are concerned about these or any other unexpected effects while on treatment with RITUXAN, talk with your doctor, nurse or pharmacist.

This document does not provide all known information about RITUXAN. If you have any questions or concerns about your treatment, please speak with your doctor, nurse or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Hoffmann-La Roche Limited at: www.rochecanada.com or by contacting the sponsor, Hoffmann-La Roche Limited, at: 1-888-762-4388.

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