PATIENT INFORMATION LEAFLET FOR RIXATHON

SCHEDULING STATUS: S4

RIXATHON 100 mg/10 ml (concentrate for solution for infusion)

RIXATHON 500 mg/50 ml (concentrate for solution for infusion)

rituximab

Read all of this leaflet carefully before you are given RIXATHON

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- RIXATHON has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What RIXATHON is and what it is used for
2. What you need to know before you receive RIXATHON
3. How to use RIXATHON
4. Possible side effects
5. How to store RIXATHON
6. Contents of the pack and other information

1. What RIXATHON is and what it is used for

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

What RIXATHON is used for:

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

- **Non-Hodgkin's Lymphoma**

This is a disease of the lymph tissue (part of the immune system) that affects a type of white blood cell called B-Lymphocytes. In adults, RIXATHON can be given alone or with other medicines called "chemotherapy". In adult patients where the treatment is working, RIXATHON may be used as a maintenance treatment for 2 years after completing the initial treatment. In children and adolescents, RIXATHON is given in combination with "chemotherapy".

- **Chronic lymphocytic leukaemia**

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

- **Granulomatosis with polyangiitis (GPA) and Microscopic polyangiitis (MPA)**

RIXATHON in combination with glucocorticoids is used for the treatment of patients with severely active Granulomatosis with polyangiitis (GPA, also known as Wegener's granulomatosis) and microscopic polyangiitis (MPA) (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).

- **Pemphigus vulgaris (PV)**

RIXATHON is used for the treatment of patients with moderate to severe pemphigus vulgaris (PV). PV is an autoimmune condition that causes painful blisters on the skin and lining of the mouth, nose, throat and genitals.

2. What you need to know before RIXATHON is administered to you

RIXATHON should not be administered to you:

- If you are hypersensitive (allergic) to rituximab, other proteins which are like rituximab, or any of the other ingredients of RIXATHON (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.

Warnings and precautions

Tell your doctor or health care provider before being given the injection:

- You have ever had or might now have a hepatitis infection. This is because in a few cases, rituximab 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.

Special care should be taken with RIXATHON:

- if you experience clumsiness or loss of coordination, difficulty walking, facial drooping, loss of vision, personality changes, trouble speaking, weak muscles.
- if you think you may have an infection, even a mild one like a cold. The cells that are affected by RIXATHON help to fight infection and you should wait until the infection has passed before you are given RIXATHON.
- if you had a lot of infections in the past or suffer from severe infections.
- if you have or had tuberculosis infections, including latent tuberculosis infections.
- if you think you may need any vaccinations in the near future, including vaccinations needed to travel to other countries. Some vaccines should not be given at the same time as RIXATHON or in the months after you receive RIXATHON. Your doctor will check if you should have any vaccines before you receive RIXATHON.
- if you are infected with HIV

Other medicines and RIXATHON

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

You should specifically tell your health care provider if you take any of the following medicines:

- If you are taking medicines for high blood pressure. You may be asked not to take these other medicines 12 hours before you are given RIXATHON. This is because

some people have a fall in their blood pressure while they are being given RIXATHON.

- If you have ever taken medicines which affect your immune system – such as chemotherapy or immune-suppressive medicines.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.
This is because RITUXIMAB can cross the placenta and may affect your baby.

If you are of child-bearing potential and using oral contraceptives, please speak to your doctor or health care provider before receiving treatment with RIXATHON.
This is because you should be on an effective method of contraception while using RIXATHON. You must also do this for 12 months after your last treatment with RIXATHON.
Do not breast-feed while you are being treated with RIXATHON. Additionally, do not breast-feed for 12 months after your last treatment with RIXATHON. This is because RIXATHON may pass into breast milk.

Driving and using machines

No studies have been performed on the ability to drive and use machines.

RIXATHON contains sodium

RIXATHON 100 and 500 contains 90 mg and 450 mg sodium per 10 ml and 50 ml vial respectively. This needs to be taken into consideration by patients on a controlled sodium diet.

3. How to use RIXATHON

You will not be expected to give yourself RIXATHON. It will be given to you by a person who is qualified to do so.

Your doctor will tell you how long your treatment with RIXATHON will last.
If you have the impression that the effect of RIXATHON is too strong or too weak, tell your doctor or pharmacist.

RIXATHON will be administered to you as an intravenous infusion (drip) through a dedicated line.
Your doctor will choose the dose that is right for you. Your dose will be shown clearly on the label that your pharmacist puts on your medicine. If it does not, or you are not sure, ask your doctor or pharmacist.

a) If you are being treated for (Non-Hodgkin's Lymphoma) NHL:

- If you are being treated with RIXATHON alone, it will be given to you once a week for 4 weeks (days 1, 8, 15 and 22), so that a course of treatment usually lasts for 22 days.

  Repeated treatment courses with RIXATHON are possible.

- If you are having RIXATHON with chemotherapy, RIXATHON 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 RIXATHON as a maintenance treatment every 3 months for two years. Your doctor may change this, depending on how you respond to the disease.

b) If you are being treated for CLL:

- When you are treated with RIXATHON in combination with chemotherapy, you will receive RIXATHON infusions on day 0 cycle 1 then day 1 of each cycle for 6 cycles in total. Each cycle has a duration of 28 days.
- The chemotherapy should be given after the RIXATHON infusion. Your doctor will decide if you should receive concomitant supportive therapy.

c) If you are being treated for GPA or MPA

- You will receive RIXATHON once weekly for 4 weeks.

Maintenance treatment

Following induction of remission with RIXATHON, maintenance treatment should be initiated no sooner than 16 weeks after the last RIXATHON infusion.

Following induction of remission with other standard of care immunosuppressants, RIXATHON maintenance treatment should be initiated during the 4-week period that follows disease remission.

RIXATHON should be administered as two 500 mg IV infusions separated by two weeks, followed by 500 mg IV infusion every 6 months thereafter. Patients should receive RIXATHON for at least 24 months after achievement of remission (absence of clinical

signs and symptoms). For patients who may be at higher risk for relapse, physicians should consider a longer duration of RIXATHON maintenance therapy, up to 5 years.

d) If you are being treated for PV

Each course of treatment is made up of two separate infusions which are given 2 weeks apart. If you respond well to treatment, you may be given RIXATHON as a maintenance treatment. This will be administered 1 year and 18 months after the initial treatment and then every 6 months as needed or your doctor may change this, depending on how you respond to the medicine.

Maintenance treatment

A maintenance infusion of 500 mg IV should be administered months 12 and 18, and then every 6 months thereafter if needed, based on clinical evaluation.

Treatment of relapse

In the event of relapse, patients may receive 1000 mg IV. The healthcare provider should also consider resuming or increasing the patient's glucocorticoid dose based on clinical evaluation.

Subsequent infusions may be administered no sooner than 16 weeks following the previous infusion.

If you are given more RIXATHON than you should receive

Since a healthcare professional will administer RIXATHON, he/she will control the dosage. In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

You may experience flu-like symptoms and respiratory conditions if too much RIXATHON has been administered to you.

If you forget to use RIXATHON

Since a health care provider will administer RIXATHON, it is unlikely that the dose will be missed.

4. Possible side effects

RIXATHON can have side effects.

Not all side effects reported for RIXATHON are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving RIXATHON, please consult your health care provider for advice.

During the injection with RIXATHON the following reactions may occur:

- Fever, cough, sore throat, burning pain when passing urine or feeling weak or generally unwell
- Memory loss, trouble thinking, and 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).

These are all very serious side effects. If you have them, you may have had a serious reaction to RIXATHON. You may need urgent medical attention or hospitalisation.

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

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.

These are all serious side effects. You may need urgent medical attention.

Other side effects include:

a) If you or your child are being treated for non-Hodgkin’s Lymphoma or chronic lymphocytic leukaemia:

Frequent side effects:

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

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

- muscle problems – such as tight muscles, joint or muscle pain, back and neck pain
- general discomfort or feeling uneasy or tired, shaking, signs of flu
- multiple-organ failure.

Less frequent side effects:

- 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.
- 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

Side effects for which the frequency is not known:

- 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

Children and adolescents with non-Hodgkin's lymphoma: In general, side effects in children and adolescents with non-Hodgkin's lymphoma were similar to those in adults with non-Hodgkin's lymphoma or chronic lymphocytic leukaemia. The most frequent side effects seen were fever associated with low levels of a type of white blood cell (neutrophil), inflammation or sores in the lining of the mouth, and allergic reactions (hypersensitivity).

b) If you are being treated for GPA or MPA

Frequent side effects:

- infections, such as chest infections, urinary tract infections (pain on passing urine), 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
- indigestion
- constipation
- skin rashes, including acne or spots
- flushing or redness of the skin
- fever
- blocked or runny 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

Less frequent side effects:

- 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

c) If you or your child are being treated for pemphigus vulgaris patients

Frequent side effects:

- 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
- indigestion
- constipation
- skin rashes, including acne or spots
- flushing or redness of the skin
- fever
- blocked or runny 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

Less frequent side effects:

- 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

Children and adolescents with granulomatosis with polyangiitis or microscopic polyangiitis
In general, side effects in children and adolescents with granulomatosis with polyangiitis or microscopic polyangiitis were of a similar type to those in adults with granulomatosis with polyangiitis or microscopic polyangiitis. Most common side effects seen were infections, allergic reactions and feeling sick (nausea).

d) If you are being treated for pemphigus vulgaris

Frequent side effects:

- allergic reactions that are most likely to occur during an infusion, but can occur up to 24 hours after infusion
- headache
- infections such as chest infections
- long lasting depression
- loss of hair

- infections such as common cold, herpes infections, eye infection, oral thrush and urinary tract
- infections (pain on passing urine)
- mood disorders such as irritability and depression
- skin disorders such as itching, hives, and benign lumps
- feeling tired or dizzy
- fever
- painful joints or back
- pain in the tummy
- pain in the muscles
- heart beating faster than normal

RIXATHON may also cause changes in laboratory tests carried out by your doctor. If you are having RIXATHON with other medicines, some of the side effects you may get may be due to the other medicines.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of RIXATHON.

Suspected adverse reactions can also be reported directly to the HCR via he link https://pvi1j.solutions.iqvia.com or the e-mail address, adverse.event.sac@sandoz.com.

5. How to store RIXATHON

- Store in a refrigerator at 5 ± 3 °C.
- Store in the original packaging.
- Keep the vials in the carton until required for use.
- Keep the vial well closed.
- Do not use after the expiry date stated on the label / carton
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).
- **STORE ALL MEDICINES OUT OF REACH OF CHILDREN.**

6. Contents of the pack and other information

What RIXATHON contains:

The active substance is rituximab. Each 10 mL concentrate for solution for infusion contains 100 mg rituximab (10 mg/mL).

Each 50 mL concentrate for solution for infusion contains 500 mg rituximab (10 mg/mL).

The other ingredients are:

Citric acid monohydrate, polysorbate 80, sodium chloride, sodium hydroxide, hydrochloric acid and water for injection.

What RIXATHON looks like and contents of the pack

RIXATHON 100 mg/10 mL is filled in a clear, colorless vial made of tubular glass (hydrolytic class I, according to Ph. Eur. & USP) and closed with blow back rubber stoppers.
The vial stopper combination is crimped with an aluminum cap with a flip off component coloured “ivory”.

RIXATHON 500 mg/50 mL is filled in a clear, colorless vial made of tubular glass (hydrolytic class I, according to Ph. Eur. & USP) and closed with blow back rubber stoppers.
The vial stopper combination is crimped with an aluminum cap with a flip off component coloured “blue”.

Pack sizes:

2 x 10 mL ampoules per pack

1 x 50 mL ampoules per pack

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Sandoz SA (Pty) Ltd[1]

Waterfall 5-Ir

Magwa Crescent West

Waterfall City

Jukskei View

2090

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Registration numbers

RIXATHON 100 mg/10 ml: 55/26/0405

RIXATHON 500 mg/50 ml: 55/26/0406

Access to the corresponding Professional Information

[1]Company Reg. No.: 1990/001979/07