DR. REDDY'S LABORATORIES (PTY) LTD.
APPROVED PATIENT INFORMATION LEAFLET:
REDDITUX® 100/500
(concentrate for solution for infusion)

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

REDDITUX® 100 concentrate for solution for infusion

REDDITUX® 500 concentrate for solution for infusion

rituximab

Read all of this leaflet carefully before you start receiving REDDITUX®

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- REDDITUX® 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 REDDITUX® is and what it is used for
2. What you need to know before you take REDDITUX®
3. How to take REDDITUX®
4. Possible side effects
5. How to store REDDITUX®
6. Contents of the pack and other information

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1. What REDDITUX® is and what it is used for

REDDITUX® 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 REDDITUX® sticks to the surface of this cell, it destroys the cell.

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

a) Non Hodgkin Lymphoma (NHL)

- This is a disease of the lymph tissue (part of the immune system) that affects a type of white blood cell called B-lymphocytes.
- REDDITUX® can be given alone or with other medicines called chemotherapy.

In patients where the treatment is working, REDDITUX® may be used as a continuous or maintenance treatment for 2 years after completing the initial treatment.

b) Chronic lymphocytic leukaemia (CLL)

- This 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 B-lymphocytes, which accumulate mainly in the bone marrow and blood.
- REDDITUX® in combination with chemotherapy destroys these cells which are gradually removed from the body by biological processes.

c) Granulomatosis with polyangiitis (GPA) and Microscopic polyangiitis (MPA)

- REDDITUX® 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).

d) Pemphigus vulgaris (PV)

- REDDITUX® 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 you are given REDDITUX®

You should not be administered with REDDITUX® if you:

- are hypersensitive (allergic) to rituximab or any of the ingredients of REDDITUX® (See section 6)
- have an active and severe active infection
- have a weak immune system
- have heart disease or heart failure

Warnings and precautions

Special care should be taken with REDDITUX®:

- if you experience clumsiness or loss of coordination, difficulty walking, facial drooping, loss of vision, personality changes, trouble speaking, weak muscles
- if you have ever had heart problems (such as angina, palpitations or heart failure) or breathing problems

- if you are taking treatment for high blood pressure. You may be asked not to take your medicines for 12 hours before your infusion of REDDITUX®. Some people experience a drop in their blood pressure during the infusion
- if you have or ever had a hepatitis infection. This is because in a few cases, REDDITUX® could cause hepatitis B to become active again, which can be fatal in very rare cases. Patients who have had hepatitis B infection will be carefully checked by their doctor for signs of this infection
- if you have taken or are taking medicines such as chemotherapy or immunosuppressive medicines which may affect your immune system
- if you think you may have an infection, even a mild one like a cold. The cells that are affected by REDDITUX® help to fight infection and you should wait until the infection has passed before you are given REDDITUX® if you had a lot of infections in the past or suffer from severe infections
- if you think you may need any vaccinations in the near future, including vaccinations needed to travel to other countries. Some vaccines should not be given at the same time as REDDITUX® or in the months after you receive REDDITUX®. Your doctor will check if you should have any

  vaccines before you receive REDDITUX®
- if you have or had tuberculosis infections, including latent tuberculosis infections
- if you are infected with HIV

Children and adolescents

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

Using other medicines with REDDITUX®

Always tell your healthcare professional if you are taking any other medicine.
(This includes complementary or traditional medicines).

In particular, tell your doctor if you are using other medicines and especially 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 REDDITUX®. This is because some people have a drop in their blood pressure while they are being given REDDITUX®.
- if you have ever taken medicines which affect your immune system – such as chemotherapy or immune-suppressive medicines.

This may not be a complete list of all interactions that may occur. Know the medicines you take. Keep a list of them with you to show your doctor and pharmacist each time you get a new medicine.
If you are to have an operation, tell the doctor about your REDDITUX® treatment as it may alter the effects of certain medicines used during operations.

Receiving REDDITUX® with food and drink

There is no information to suggest that the consumption of food and drink affects the way REDDITUX® works.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking REDDITUX®.

REDDITUX® is an antibody and can cross the placenta and affect your baby. If you can get pregnant, you must use an effective method of birth control during treatment with REDDITUX® and for 12 months after your last treatment with REDDITUX®.

REDDITUX® may pass into breast milk and therefore you should not breast feed your baby during treatment with REDDITUX® and for 12 months after your last treatment with REDDITUX®.

If you are a male patient you should not father a child while receiving treatment with REDDITUX®. You must use an effective method of contraception while using REDDITUX® and for at least 3 months after stopping treatment with REDDITUX®.

Driving and using machines

There is no information to suggest that REDDITUX® affects your ability to drive or operate machinery.

REDDITUX® contains sodium

REDDITUX® 100 and 500 contains 2,27 mmol (or 52,26 mg) and 11,36 mmol (or 261,34 mg) sodium per 10 ml and 50 ml vial respectively. This needs to be taken into consideration if you are on a low- sodium diet.

3. How to use REDDITUX®

REDDITUX® will always be prepared and given to you by a healthcare professional, as an intravenous infusion (drip).

Your doctor will give you a medicine to prevent or reduce possible reactions to REDDITUX®.

You will be observed by a healthcare professional while you are given the infusion in case you experience side effects.

Your doctor will decide on the most suitable treatment for you including:

- the correct dose
- how often and for how long you should be treated and whether you should also receive other medicines with REDDITUX® or not.

Your doctor will give you all the necessary information on your treatment plan.

a) If you are being treated for NHL:

- If you are being treated with REDDITUX® 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 REDDITUX® are possible.
- If you are having REDDITUX® with chemotherapy, REDDITUX® 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 REDDITUX® 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 REDDITUX® in combination with chemotherapy, you will receive

REDDITUX® 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 REDDITUX® 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 REDDITUX® once weekly for 4 weeks.

Maintenance treatment

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

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

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 REDDITUX® 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 at 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 have the impression that the effect of REDDITUX® is too strong or too weak, tell your doctor or another healthcare professional.

Do not stop treatment early without discussing this with your doctor.

If you are receiving more REDDITUX® than you should

The treatment schedule and dose will be decided by your doctor, who will monitor your response. If you are concerned that you have been given too much REDDITUX®, contact your doctor or another healthcare professional immediately.

If you forget to receive REDDITUX®

If you forget to receive REDDITUX® for any reason, discuss this with your doctor or another healthcare professional immediately.

If you stop receiving REDDITUX®

Discuss the effects of stopping treatment with REDDITUX® if you choose to do so with your doctor.

4. Possible side effects

REDDITUX® can have side effects. Side effects are mild to moderate but some may be serious and fatal.

Not all side effects reported for REDDITUX® are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking REDDITUX®, please consult your doctor, pharmacist or other health care professional for advice.

Tell your doctor immediately if you experience any of these symptoms:

Infusion reactions:

- During or within the first 1 to 2 hours of the first infusion you may develop fever, chills and shivering.
- Less frequently, some patients may experience pain at the infusion site, blisters, itching, sickness, tiredness, headache, breathing difficulties, tongue or throat swelling, itchy or runny nose, vomiting, flushing or palpitations, heart attack or low number of platelets.
- If you have heart disease or angina, these reactions might get worse.
- Tell the person giving you the infusion immediately if you develop any of these symptoms, the infusion may need to be slowed down or stopped.
- You may require additional treatment such as an antihistamine or paracetamol. When these symptoms go away, or improve, the infusion can be continued. These reactions are less likely to happen after the second infusion.

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

Infections:

- fever, cough, sore throat, burning pain when passing urine or feeling weak or generally unwell.

- memory loss, trouble thinking, difficulty walking or sight loss – these may be due to a very rare, serious brain infection, which has been fatal (Progressive Multifocal Leukoencephalopathy (PML)).

You might get infections more easily during your treatment with REDDITUX®.

These are often colds, but there have been cases of pneumonia or urinary infections. These are listed below under "Other side effects".

Skin Reactions:

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

Other side effects include:

a/b) If you are being treated for NHL or CLL

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

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

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

- infections of the blood (sepsis), pneumonia, shingles, cold, bronchial tube infections,

fungal infections, infections of unknown origin, sinus inflammation, hepatitis B

- low number of red blood cells (anaemia), low number of all blood cells
- allergic reactions (hypersensitivity)
- high blood sugar level, weight loss, swelling in the face and body, high levels of the enzyme "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.

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

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

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

- short term increase in the amount of some types of anti-bodies in the blood (called immunoglobulins – IgM), chemical disturbances in the blood caused by break-down of dying cancer cells
- nerve damage in arms and legs, paralysed face
- heart failure
- inflammation of blood vessels including those leading to skin symptoms
- respiratory failure
- damage to the intestinal wall (perforation)
- severe skin problems causing blisters that can be life-threatening. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present.
- kidney failure
- severe vision loss.

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

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

c) If you are being treated for GPA or MPA

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

- 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.

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

- indigestion

- constipation
- skin rashes, including acne or spots
- flushing or redness of the skin
- 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.

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

- severe blistering skin conditions that can be life-threatening. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present
- recurrence of a previous Hepatitis B infection.

d) If you are being treated for PV

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

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

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

- infections such as herpes infections and eye infection
- mood disorders such as irritability and depression
- skin disorders such as itching, hives, and benign lumps
- feeling tired or dizzy
- fever
- headache
- pain in the tummy
- pain in the muscles
- heart beating faster than normal.

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

If you are taking REDDITUX® with other medicines, some of the side affects you may experience may be due to the other medicines.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

By reporting side effects, you can help provide more information on the safety of REDDITUX®.

5. How to store REDDITUX®

Storage of unopened vials

Store vials in a refrigerator between 2 °C to 8 °C. Protect vials from light. Do not freeze. Store in the outer carton until required for use.

Storage of reconstituted vials

The prepared infusion solution is physically and chemically stable for 48 hours at 2 °C to 8 °C and subsequently 48 hours at room temperature (25 °C).

The prepared infusion solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should normally not be longer than 48 hours at 2 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic

conditions.

Do not use this medicine after the expiry date.

Keep this medicine out of the sight and reach of children.

Do not dispose medicines in drains or sewerage systems (e.g., toilets).

Return all unused and expired medicines to your pharmacist.

6. Contents of the pack and other information

What REDDITUX® contains

Each vial of REDDITUX® 100 contains 100 mg of rituximab concentrate for solution for infusion.

Each vial of REDDITUX® 500 contains 500 mg of rituximab concentrate for solution for infusion.

The other ingredients of REDDITUX® are polysorbate 80, sodium chloride, sodium citrate dihydrate and water for injection.

What REDDITUX® looks like and contents of the pack

REDDITUX® is a clear to opalescent; colourless to yellowish solution, essentially free from visible particles.

REDDITUX® 100: Clear USP Type I 10 ml glass vials or clear USP Type I 10 ml European Bow Back (EBB) glass vial. The vials are closed with 20 mm grey butyl rubber stoppers laminated with

a fluoro-polymer coating. The stoppers are smooth-finished, with a small cavity at the centre. Stoppered vials are capped with 20 mm, flip-off seals. The aluminium seal completely covers the rubber stopper and is capped with an orange polypropylene disc.

REDDITUX® 500: Clear USP Type I 50 ml glass vials or clear USP Type I 50 ml European Bow Back (EBB) glass vial. The vials are closed with 20 mm grey butyl rubber stoppers laminated with a fluoro-polymer coating. The stoppers are smooth-finished, with a small cavity at the centre. Stoppered vials are capped with 20 mm, flip-off seals. The aluminium seal completely covers the rubber stopper and is capped with an orange polypropylene disc.

Holder of Certificate of Registration

Dr. Reddy's Laboratories (Pty) Ltd.

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Morningside

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2057

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Registration numbers

REDDITUX® 100: 56/26/0286

REDDITUX® 500: 56/26/0287

For any information about this medicine, please contact the local representative of the Holder of

Certificate of Registration:

Dr. Reddy's Laboratories (Pty) Ltd. Tel: +27 11 324 2100

Other sources of information

Detailed information on this medicine is available on the Dr. Reddy's Laboratories web site:

http://www.drreddys.co.za

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