PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

DOXRED LYO 10, powder for solution for infusion

10 mg Doxorubicin hydrochloride

Contains sugar (lactose monohydrate 50 mg)

DOXRED LYO 50, powder for solution for infusion

50 mg Doxorubicin hydrochloride

Contains sugar (lactose monohydrate 250 mg)

Read all of this leaflet carefully before you are given DOXRED LYO.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- DOXRED LYO 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 DOXRED LYO is and what it is used for

2. What you need to know before you take DOXRED LYO

3. How to take DOXRED LYO

4. Possible side effects

5. How to store DOXRED LYO

6. Contents of the pack and other information

1. What DOXRED LYO is and what it is used for

DOXRED LYO contains a medicine called doxorubicin, which belongs to a group of medicines called cytotoxics used for chemotherapy. Doxorubicin is used to treat a variety of cancers, either alone or in combination with other medicines, including the following:

- Acute leukaemias (blood cancer), lymphomas (cancer of lymph glands or spleen) and a number of solid tumours.
- Cancer of the breast that has spread to other organs, bladder cancer, cancer of the airways and cancers of nerve or brain tissue.
- Thyroid cancer that has spread to other organs, cancer of the lining of the womb, cancers of the testes, prostate, cervix (neck of womb), and head and neck cancers, and certain types of white blood cell cancers.
- Cancer of the ovary if given in combination with other chemotherapeutic (anticancer) medicines (cisplatin and cyclophosphamide).
- Cancer of the breast and small (oat) cell cancer of the lung when given concurrently with other chemotherapeutic medicines.
- Cancers arising in connective tissue (called sarcomas) that may involve bone tissue or other soft tissues.
- Hodgkin's disease, a cancer of lymph tissue (lymphoma), if given with other chemotherapeutic medicines.

- Non-Hodgkin's lymphomas if administered concurrently with other chemotherapeutic medicines. Your doctor will decide whether or not you qualify for treatment with DOXRED LYO.

2. What you need to know before you are given DOXRED LYO

Do not receive DOXRED LYO if you:

- are known to be hypersensitive (allergic) to doxorubicin or to other medicines belonging to the same class (anthracyclines) or to any of the other ingredients of DOXRED LYO (listed in **See what DOXRED LYO contains** below).
- have low white blood cell or red blood cell counts or low platelet counts.
- have impairment of liver function.
- have heart failure or any other heart disease.
- recently suffered a heart attack (myocardial infarction).
- suffer from abnormal heart rhythm.
- have already received treatment with maximum cumulative doses of doxorubicin or other similar medicines.
- are pregnant or breast feeding.

Warnings and precautions

DOXRED LYO should be given to you only under the supervision of a doctor experienced in cancer chemotherapy.

Females are advised to use reliable contraception if they are of child-bearing age, since treatment with DOXRED LYO may harm their unborn babies.

Tell your doctor or health care provider before you are given DOXRED LYO if you:

- developed complications from treatment with other anticancer medicines, such as mouth ulcers, low blood cell or platelet counts, or generalised infections, you should first recover from these before you begin treatment with DOXRED LYO.
- have or have ever had heart disease, either before or during radiotherapy.
- have liver disease.
- are currently taking or have recently taken cyclophosphamide or 6-mercaptopurine (medicines used in the treatment of certain cancers).
- have had or are due to have live or live-attenuated vaccinations.

DOXRED LYO may also cause the following:

- Damage to the heart which may present as early or late events:
    - Early events: abnormal heart rhythm or ECG abnormalities such as rapid or slow heart rate.
    - Late events (can occur two to three months or several months to years after completion of treatment): heart failure with symptoms such as swelling of the feet or ankles or even stomach or face, shortness of breath, inability to lie down due to shortness of breath, coughing of pink sputum and generally feeling tired and unwell.
- Decreased blood cells and bone marrow function including blood cancer (leukaemia). If you develop a fever, bleeding or think you may be suffering from an infection, please inform your doctor immediately.
- Infertility in women, absence of menstruation or development of premature menopause. Ovulation and menstruation appear to return after treatment is stopped.
- Damage to chromosomes in sperm. Low sperm counts and absence of sperm may be permanent. Men who are receiving treatment with DOXRED LYO should use effective contraceptive measures.

- Severe nausea and vomiting. In addition, it may also cause inflammation with sores in the mouth or on the lips. This may progress to ulcers. Most patients recover from this adverse event by the third week of therapy.
- Severely impaired liver function. Your doctor will monitor your liver function through periodic blood tests.
- Pain, swelling and redness or other changes surrounding the injection area as well as hardening of the blood vessel walls.
- Clotting blockages in blood flow.
- High levels of uric acid in the blood. Your doctor may prescribe a urinary alkaliniser and allopurinol (medicine used to decrease high uric acid levels) to prevent high levels of uric acid. In addition, you should remain well hydrated by drinking lots of water.

Other medicines and DOXRED LYO

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

In particular, tell your doctor or pharmacist if you are taking any of the following medicines:

- Some medicines effect the concentration and clinical effect of doxorubicin:
    - Increased concentration and clinical effect:
        - verapamil (for high blood pressure and chest pain)
    - Decreased concentration and clinical effect:
        - phenobarbital (for seizures), phenytoin (for seizures), St. John's Wort (herbal medicine for depression). Please tell your doctor or pharmacist if you are taking any of these medicines.
- Ciclosporin (immunosuppressive medicine): which can make the effects of doxorubicin stronger and may result in prolonged decrease in bone marrow and blood cells (coma and

seizures have also been described with administration together with ciclosporin and doxorubicin).

- Calcium channel blockers (medicines for your heart): can increase the toxic effects on the heart if taken together with doxorubicin.
- Sorafenib (used to treat inoperable liver cancer and advanced kidney cancer): may decrease the effect of doxorubicin.
- Paclitaxel (a medicine used in the treatment of certain cancers): which can make the effects of doxorubicin stronger.
- Trastuzumab (a medicine used in the treatment of certain cancers): Trastuzumab can remain in the body for up to 7 months. As trastuzumab may affect the heart, you should not use doxorubicin for up to 7 months after you have stopped taking trastuzumab. If doxorubicin is used before this time, then your heart function should be carefully monitored.

DOXRED LYO with food and drink and alcohol

Taking DOXRED LYO with alcohol beverages should be avoided.

Pregnancy and breastfeeding and fertility

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 healthcare provider for advice before taking this medicine.

DOXRED LYO should not be used during pregnancy and breastfeeding as safety in pregnant women and breastfeeding mothers has not been established.

Pregnancy

There is a risk that use of DOXRED LYO during pregnancy may cause birth defects in your child. If you are sexually active, you are advised to use effective birth control to prevent pregnancy during treatment, whether you are male or female.

Breastfeeding

You should stop breastfeeding before starting treatment with DOXRED LYO as some of the medicine may get into your breast milk and possibly harm your child.

Driving and using machines

DOXRED LYO has no or negligible effects on your ability to drive or use machinery.
It is not always possible to predict to what extent DOXRED LYO may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which DOXRED LYO affects them.

DOXRED LYO contains:

DOXRED LYO contains sugar (lactose monohydrate). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking DOXRED LYO.

After reconstitution, DOXRED LYO 10 and DOXRED LYO 50 contains 17,7 mg and 88,5 mg sodium respectively (main component of cooking/table salt) in each. This is equivalent to 0,9 % for DOXRED LYO 10 and 4,43 % for DOXRED LYO 50 of the recommended maximum daily dietary intake of sodium for an adult.

3. How to receive DOXRED LYO

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

DOXRED LYO will be given to you by a doctor or nurse through a drip (infusion) into a vein.

The usual dose is:

Your doctor will decide what dose to give and the number of days treatment you will receive depending on your condition. The dose is decided by taking into account the condition you have, your height and weight. From your height and weight, the doctor will work out your body surface area; and it is this that your dose is calculated from.

During treatment your doctor will be making regular checks of your:

- Blood: To check for low blood cell counts that may need treatment.
- Heart function: Heart damage can occur when high doses of doxorubicin are given. This may not be detected for several weeks; so regular tests may be required during this period.
- Liver: Using blood tests, your doctor will check that this medicine is not affecting the way it functions in a harmful way.
- Blood uric acid levels: Doxorubicin may increase uric acid levels in the blood which might cause gout. Another medicine may be given if your uric acid levels are too high.

People with liver problems

You may be given a different dose to the usual dose. Your doctor will decide how much DOXRED LYO you will need and will check you closely depending on the severity of the liver disease.

If you are given more DOXRED LYO than you should

Since a healthcare provider will administer DOXRED LYO, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If a dose of DOXRED LYO is missed

Since a healthcare provider will administer DOXRED LYO, it is unlikely that the dose will be missed.

If you stop receiving DOXRED LYO

While one course of treatment may sometimes be enough, more often your doctor will advise further courses in either one, three or four weeks time. It may take several courses before your illness is under control and you feel better.

4. Possible side effects:

DOXRED LYO can have side effects.

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

If any of the following happens, stop taking DOXRED LYO and tell your doctor immediately:

- Sudden signs of allergy – including skin rash, itching or hives; swelling of the face, lips or tongue, shortness of breath or difficulty breathing.

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

Tell your doctor immediately if you notice any of the following:

- Blood poisoning. Symptoms include fever, difficulty breathing, low blood pressure, fast heart rate and mental confusion.
- Acute lymphoblastic leukemia (ALL) - a type of blood cancer that starts in white blood cells in your bone marrow. Symptoms may include enlarged lymph nodes, bruising, fever, bone pain, bleeding from the gums and frequent infections.
- Acute myeloid leukemia (AML) - a cancer of the blood and bone marrow. Symptoms include fatigue, recurrent infections and bruising easily.
- Low white blood cell counts. Symptoms may include fever or chills, cough or hoarseness, lower back or flank pain, painful or difficult urination or a sore throat.
- High blood uric acid levels causing attacks of gout, which usually presents with severe pain, swelling and redness of a joint, such as those of the big toe or knee. This occurs most commonly during initial treatment of patients with leukaemia or lymphoma as a result of rapid cell breakdown that leads to elevated blood uric acid concentrations.
- You may notice your heart beating abnormally quickly, with an increase in pulse rate. In some cases, you may notice heart problems several months or years after medication has been completed.
- Increased heart rate, chest pain which could indicate heart problems, shock (low blood pressure and circulation).
- Heart failure – Symptoms may include swelling of the feet or legs, or shortness of breath accompanied by an inability to lie down or coughing of pink-coloured sputum.
- Inflammation of veins, blockage of a blood vessel by a clot (thromboembolism), hot flushes.
- Any bleeding complications, including vomiting of blood or blood per rectum.

- Irritation or bleeding in the intestines, inflammation of the lining of the stomach, heartburn, soreness or ulcers in the mouth, which may not appear until 3-10 days after treatment.
- Severe foul-smelling diarrhoea accompanied by stomach cramps and fever as this may indicate infection or inflammation of the large bowel.

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

Tell your doctor if you notice any of the following:

Frequent side effects

- Infection
- Low red blood cell counts (presenting with tiredness or shortness of breath) and low platelet counts (presenting with easy bruising, pinpoint red spots on the skin, or bleeding from the gums).
- Abnormal ECG (this is an electrical trace of your heart) results.
- Inflammation of the throat and gullet, nausea, vomiting, diarrhoea, sores or inflammation in the mouth, stomach pain, lack of appetite, dehydration.
- Hair loss, rash, itching, skin changes.
- Weakness, tiredness, fever, chills, redness and swelling may develop at site of injection.
- In women, doxorubicin may cause infertility during the time DOXRED LYO is taken. Women may also find that their periods stop, but their periods should return to normal after treatment is stopped. In some cases early menopause can occur.
- In men, doxorubicin may cause an absence or decrease in sperm count, but this may return to normal after treatment is stopped.
- Redness and swelling may develop at site of injection.

Less frequent side effects

- Conjunctivitis (usually causing red watery eyes), inflamed cornea, watery eyes.
- Hot flushes.
- Darkening of the membrane inside the mouth, stomach ulcer.
- Changes in liver enzyme levels. (as detected by a blood test can determine if the medicine is having an abnormal effect on your liver.)
- Nails and skin may appear darker than usual, inflammation reaction which could occur soon after treatment or years later, increased sensitivity of the skin to the sunlight, hives, reddening of the skin covering fingers, toes, ears and other peripheral parts.
- Red colouration of urine for 1 to 2 days after administration.
- In women, doxorubicin may cause infertility during the time DOXRED LYO is taken. Women may also find that their periods stop, but their periods should return to normal after treatment is stopped. In some cases early menopause can occur.
- In men, doxorubicin may cause an absence or decrease in sperm count, but this may return to normal after treatment is stopped.
- Pain, swelling or red streaks at the injection site.
- Laboratory test may show the following:
    - Ejection fraction (EF) (a measurement, expressed as a percentage, of how much blood the left ventricle of the heart pumps out with each contraction) is decreased.
    - Electrocardiogram (ECG) test is abnormal.
    - blood test results for liver function differing from normal.
    - weight gain.

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 or nurse. This includes any possible side effects not listed in this leaflet. 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 DOXRED LYO.

5. How to store DOXRED LYO

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Before reconstitution: Store below 30 °C. Protect from light. Keep vial in the outer carton until required for use.

After reconstitution: The reconstituted solution is stable for 7 days at room temperature (below 25 ºC) and under normal room light and 15 days under refrigeration (2 ° to 8 °C). It should be protected from exposure to sunlight. Discard any unused solution.

6. Contents of the pack and other information

What DOXRED LYO contains

DOXRED LYO 10: Each 5 ml vial contains doxorubicin hydrochloride 10 mg as the active substance. Contains sugar (lactose monohydrate 50 mg/vial).

DOXRED LYO 50: Each 25 ml vial contains doxorubicin hydrochloride 50 mg as the active substance. Contains sugar (lactose monohydrate 250 mg/vial).

The other ingredients are: Lactose monohydrate, methyl paraben, hydrochloric acid and sodium hydroxide.

What DOXRED LYO looks like and contents of the pack

A red coloured lyophilized mass.

DOXRED LYO 10: Carton containing a 5 ml clear, transparent glass vial closed by a grey slotted rubber stopper and 20 mm red flip-off seal.

DOXRED LYO 50: Carton containing a 25 ml clear, transparent glass vial closed by a grey slotted rubber stopper and 20 mm red flip-off seal.

Holder of Certificate of Registration

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This leaflet was last revised in

Not applicable.

Registration number

DOXRED LYO 10: 57/26/0698

DOXRED LYO 50: 57/26/0699