1.3.2 Proposed Patient Information Leaflet (clean copy)

SCHEDULE STATUS

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PATIENT INFORMATION LEAFLET

ZALCAREN powder for injection

STERILE DILUENT FOR ZALCAREN solution for injection

Melphalan (anhydrous) hydrochloride

Sugar free.

Read all of this leaflet carefully before you you are given ZALCAREN.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.

What is in this leaflet?

1. **What ZALCAREN is and What it is used for?**

ZALCAREN injection contains a medicine called melphalan. This belongs to a group of medicines called cytotoxics (also called chemotherapy). ZALCAREN is used to treat cancer. It works by reducing the number of abnormal cells your body makes.

ZALCAREN is used for:

Multiple myeloma - a type of cancer that develops from cells in the bone marrow called plasma cells. Plasma cells help to fight infection and disease by producing antibodies.

Advanced **cancer of the ovaries**

Childhood neuroblastoma - cancer of the nervous system

2. What you need to know before you receive ZALCAREN

ZALCAREN should not be administered to you:

- If you are allergic (hypersensitive) to melphalan or any of the other ingredients of ZALCAREN injection (listed in section 6).
- If you are pregnant.
- Mothers receiving ZALCAREN should not breastfeed.
- If you are planning or recently been vaccinated with live vaccine.

Warnings and precautions

Take special care with ZALCAREN:

Before you use ZALCAREN, tell your doctor or nurse if:

- you have had radiotherapy or chemotherapy, now or recently.
- you have a kidney problem.

- Ensure adequate performance and organ function before using high-dose ZALCAREN Injection in elderly patients. If you are not sure if any of the above apply to you, talk to your doctor or nurse before having ZALCAREN.

Tell your doctor:

- If you are already pregnant, it is important to talk to your doctor before having ZALCAREN.
- If you are going to have a vaccination because some vaccines (like polio, measles, mumps and rubella) may give you an infection if you have them whilst you are being treated with ZALCAREN.
- You must talk to a doctor if you do not feel better or if you feel worse.

Taking other medicines with ZALCAREN

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

Other medicines and ZALCAREN

ZALCAREN may have an effect on other medicines or other medicines may have an effect on **ZALCAREN**.

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

- other cytotoxic medicines (chemotherapy) such as doxorubicin or methotrexate.
- Nalidixic acid (an antibiotic used to treat urinary tract infections)
- Ciclosporin (used to prevent rejection of organs or tissues following a transplant or to treat certain skin conditions like psoriasis and eczema or to treat rheumatoid arthritis).
- Vaccines: If you are going to have a vaccination speak to your doctor or nurse before you have it. This is because some vaccines (like polio, measles, mumps and rubella) may give you an infection if you have them whilst you are being treated with ZALCAREN.

Pregnancy, breastfeeding and fertility:

You should not receive ZALCAREN if you are pregnant or breastfeeding your baby. 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 receiving ZALCAREN.

Highly effective contraceptive precautions must be taken to avoid pregnancy whilst you or your partner are receiving ZALCAREN.

Fertility

Melphalan, as in ZALCAREN, can affect ovaries or sperm, which may cause infertility (inability to have a baby). In women, menstruation can stop (amenorrhoea) and in men, a complete lack of sperm can be observed (azoospermia) as a result of ZALCAREN treatment. Therefore, men are advised to have a consultation on sperm preservation before treatment.

Driving and using machinery:

ZALCAREN has no or negligible influence on the ability to drive and use machines.

It is not always possible to predict to what extent ZALCAREN 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 ZALCAREN affects them.

Important information about some of the ingredients of ZALCAREN

This medicinal product contains small amounts of ethanol (96 % alcohol) - 0,52 mL per 10 mL.

3. How to take ZALCAREN

expected to give yourself ZALCAREN. It will be given to you by a person who is qualified to do so.

Always take ZALCAREN exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. Your doctor will tell you how long your treatment with ZALCAREN will last. If you have the impression that the effect of ZALCAREN is too strong or too weak, talk to your doctor or pharmacist.

ZALCAREN should only be prescribed for you by a medical practitioner who is experienced in treating blood problems or cancer. ZALCAREN will only be prepared by a health professional who is experienced in the preparation of such medication.

Method of administration

ZALCAREN can be given:

- as an infusion (drip) into your vein, or
- into an artery, administered to a certain body part (perfusion).

Your doctor will decide how much ZALCAREN you will have.

The amount of ZALCAREN depends on:

- your body weight or body surface area (a specific measurement taking into account your weight and your size)
- other medicines you are taking
- your disease
- your age
- whether or not you have kidney problems.

When you are given ZALCAREN, your doctor will take regular blood tests. This is to check the number of cells in your blood. Your doctor may sometimes change your dose as a result of these tests.

Your doctor will tell you how long your treatment with **ZALCAREN** will last. Do not stop treatment early because this may cause reoccurrence of your condition. If you have the impression that the effect of **ZALCAREN** is too strong or too weak, tell your doctor or pharmacist.

If you receive more ZALCAREN than you should:

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

Symptoms of Overdose

Symptoms of oral overdose may include nausea, vomiting, diarrhoea, sometimes bloody stools.

Treatment

In the event of an overdose, your healthcare professional will institute general supportive measures together with appropriate blood transfusion.

There is no specific antidote.

The blood picture will be closely monitored for at least four weeks following over-dosage until there is evidence of recovery.

If you forget to take ZALCAREN:

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

4. POSSIBILE SIDE EFFECTS

ZALCAREN can have side effects.

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

If any of the following happens, stop taking ZALCAREN and tell your doctor immediately or go to the casualty department at your nearest hospital:

- sudden wheeziness, difficulty breathing, chest pain or chest tightness,
- swelling of the hands, feet, ankles, eyelids, face, lips, mouth or tongue/throat, which may cause difficulty in swallowing or breathing,
- lumpy skin rash, itching or “hives” anywhere on the body.

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

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

- break down of skeletal muscles (rhabdomyolysis) leading to tenderness, swelling and weakness of affected muscles,
- blood clot in a deep vein or arteries, symptoms may include but are not limited to swelling in your foot, ankle, or leg, usually on one side. Cramping pain in your affected leg that usually begins in your calf. Severe, unexplained pain in your foot and ankle. An area of skin that feels warmer than the skin on the surrounding area,
- blood clots in the lungs. Symptoms may include but are not limited to anxiety, clammy or bluish skin, chest pain that may extend into your arm, jaw, neck, and shoulder, fainting, irregular heartbeat and

light headedness, effects on the blood may occur. Your doctor will do regular blood tests, but you should tell him/her at once if you notice any signs of fever or infection, or any unexpected bruising or bleeding,

- haemolytic anaemia. This results from the destruction of red blood cells. As a result, you may feel tired and dizzy, get headaches, look pale with a yellowing of the skin and/or eyes,
- any signs of jaundice (yellowing of the whites of the eyes or the skin) as this may be due to hepatitis (inflammation/infection of the liver). If you have any blood tests to check how your liver is working, ZALCAREN may affect the results,
- your muscles are achy, stiff or weak, your urine is darker than usual or brown or red in colour,
- that you are gradually becoming more breathless than usual,
- a drop in the number of blood cells and platelets,
- ZALCAREN has been reported to cause cancers in some patients who have been treated with ZALCAREN.

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:

- Bleeding from gums or nose, blue or purple bruises on skin. This could be due to low platelets in your blood (thromobocytopenia). feeling sick (nausea), being sick (vomiting) and diarrhoea,
- hair loss,
- a tingling or warm feeling where ZALCAREN was injected,
- a muscle problem which can cause pain, tightness, tingling, burning or numbness, called compartment syndrome.

Less frequent side effects:

- sore mouth,
- allergic reaction,

- rash.

Side effects with an unknown frequency:

- muscle pain,
- in women, periods may stop,
- in men, sperm production may be reduced or stopped.

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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via

https://www/sahpra.org.za/Publications/Index/8.

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

5. How to store ZALCAREN

Your ZALCAREN will be prepared for use by a healthcare professional. Once prepared it should be used immediately and must not be stored or refrigerated.

Store at or below 25°C.

Protect from light.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What ZALCAREN contains

MELPHALAN 50 mg POWDER FOR INJECTION/INFUSION

Melphalan hydrochloride equivalent to 50 mg Melphalan per vial.

The other ingredients of ZALCAREN are:

- Melphalan Ph.Eur
- Tert – butanol HP
- Hydrochloric acid, concentrated Ph.Eur
- Povidone Ph.Eur (Kollidone® 12 PF)
- Water for injection USP/Ph.Eur/IH
- Nitrogen USNF/Ph.Eur/IH
-

Solvent for solution for Melphalan powder for injection/ infusion

- Sodium citrate (Tri Sodium Citrate Anhydrous)
- Propylene Glycol Ph.Eur
- Ethanol Ph.Eur (96 %)
- Water for injection USP/Ph.Eur/IH
- Nitrogen USNF/Ph.Eur/IH
-

What ZALCAREN looks like and contents of the pack

ZALCAREN 50 mg POWDER FOR INJECTION/INFUSION

Before Reconstitution:

White to off-white Lyophilized cake or powder in clear glass vial stoppered with gray igloo lyo rubber stopper and sealed with aluminium seal having sky blue colour PP disc.

After Reconstitution

(Reconstitution with 10 mL of Solvent for solution for Melphalan powder for injection/infusion)

A clear colourless to pale yellow coloured solution essentially free from visible particles.

SOLVENT FOR SOLUTION FOR MELPHALAN POWDER FOR INJECTION/INFUSION)

Clear colourless solution, essentially free from visible particles filled in clear glass vial stoppered with gray rubber stoppers and sealed with aluminium seal having sky blue colour pp disc.

Melphalan powder for injection/infusion

1 Vial

19 ml Tubular Type I Clear Glass vial

White to off – white lyophilized cake or powder filled in Type – I, clear tubular glass vial with 20 mm neck stoppered with 20 mm grey igloo lyophilized bromobutyl rubber stopper and sealed with cleared lacquered Aluminium seal having sky blue colour PP disc.

These vial shall be placed in pre thermoformed tray along with one vial of solvent diluent*. This combo pack of pre thermoformed tray is further packed in one printed carton along with package insert.

Solvent for solution for Melphalan powder for injection/infusion

1 Vial

10R Tubular Type I Clear BB Glass vial

Clear colourless solution is filled in 10R tubular Type – I, clear BB glass vial with 20 mm neck stoppered with 20 mm dark grey colour rubber stopper with bromobutyl based rubber formulation and sealed with cleared lacquered Aluminium seal having sky blue colour PP disc.

These vial shall be placed in pre thermoformed tray along with one vial of Melphalan 50 mg Powder for Injection*. This combo pack of pre thermoformed tray is further packed in one printed carton along with package insert.

Holder of Certificate of Registration

AUROGEN SOUTH AFRICA (PTY) Ltd

Woodhill Office Park,

Building 1 53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12, 1448

Johannesburg

South Africa

This leaflet was last revised in

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