1.3.2 Patient Information Leaflet

SCHEDULING STATUS

S4

DOXOPEG, liposomal infusion

Doxorubicin hydrochloride 2 mg/ml

Contains sucrose

Read all of this leaflet carefully before you receive DOXOPEG

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

1. What DOXOPEG is and what it is used for

DOXOPEG belongs to the general group of medicines known as antineoplastics or anti-cancer medicines.

DOXOPEG is used to treat AIDS-related Kaposi's sarcoma (a cancer that causes patches of abnormal tissue to grow under the skin, in the lining of the mouth, nose, and throat or in other organs).

DOXOPEG is used for treating other types of cancers, such as breast and ovarian cancer.

DOXOPEG is also used in combination with another medicine called bortezomib, to treat multiple myeloma, a cancer of the blood, in patients who have received at least 1 prior therapy and who have had a bone marrow transplant, or are unsuitable to have a bone marrow transplant.

2. What you need to know before you receive DOXOPEG

Before you receive your DOXOPEG treatment, you and your doctor should discuss the effects and side effects of DOXOPEG**.**

Do not receive DOXOPEG:

- If you are allergic to doxorubicin hydrochloride or any of the other ingredients of DOXOPEG (see What DOXOPEG contains).
- If you are pregnant or breastfeeding (see Pregnancy and breastfeeding).
- If you have a condition called AIDS-related Kaposi's sarcoma that may be treated effectively with other treatment, such as local therapy or systemic alpha-interferon.
- If you or your child is under the age of 18 years.

Warnings and precautions

Take special care with DOXOPEG:

- If you have or develop a bone marrow disorder or mouth ulcers after treatment with DOXOPEG. Your doctor will perform blood counts if this occurs.

- If you have a liver disorder. You doctor will draw blood prior to the treatment to test your liver function.
- If you have a heart disorder, as DOXOPEG may worsen your condition.
- If you develop any heart problems during your treatment with DOXOPEG. Your doctor will do regular tests to monitor your heart function. You are at higher risk of developing heart problems if you are elderly, a child or if you have Down's syndrome.
- If you develop blood clots in your veins or your lungs while you receive DOXOPEG (pain in the area affected, swelling of your ankles or feet, difficult or rapid breathing, or pain when you breathe).
- If you are taking other anti-cancer medicines.
- If you develop a severe skin condition affecting the palms of your hands and the soles of your feet (redness, swelling and pain), inform your doctor as soon as possible.
- If you notice sores, discolouration or any discomfort in your mouth.
- If you have high blood sugar (diabetes). DOXOPEG contains sucrose (see Important information about some of the ingredients of DOXOPEG).
- The cases of Interstitial lung diseases have been observed in patients receiving liposomal doxorubicin as contained in DOXOPEG, including fatal cases. The symptoms of Interstitial lung disease are cough and shortness of breath sometimes with fever which are not caused by physical activity. Seek immediate medical attention, if you experience symptoms that may be signs of Interstitial lung disease.

DOXOPEG can temporarily lower the number of white blood cells in your blood, increasing your chance of getting an infection. It can also lower the number of platelets, which are necessary for proper blood clotting.

If this occurs, there are certain precautions you can take, especially when your blood count is low, to reduce the risk of infection or bleeding:

- If possible, avoid people with infections.
- Check with your doctor immediately if you notice any unusual bleeding or bruising.
- Do not touch your eyes or the inside of your nose unless you have just washed your hands and have not touched anything else in the meantime.
- Be careful not to cut yourself when you are using sharp objects such as razors, knives or scissors.
- Avoid contact sports or other situations where bruising or injury can occur.
- Be careful when using a regular toothbrush, dental floss or toothpick.

Other medicines and DOXOPEG

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

Not all interactions with DOXOPEG are included in this leaflet.

The following medicines could cause an interaction when used in combination with DOXOPEG:

- Other anti-cancer therapies (used to treat cancer).
- Cyclophosphamide or taxanes (used in the treatment of certain cancers).
- 6-mercaptopurine (used to treat leukaemia and inflammatory bowel disease).
- Cytotoxic agents (used to treat cancers, arthritis or related conditions).

- Myelotoxic agents (used to treat cancer).

DOXOPEG with food and drink:

DOXOPEG can be administered with or without food.

Pregnancy, 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 you receive DOXOPEG.

Do not use DOXOPEG if you are pregnant, suspect you are pregnant, planning to become pregnant or breastfeeding.

Women must avoid becoming pregnant and use contraception while taking DOXOPEG and in the eight months following discontinuation of DOXOPEG treatment.

Men must use contraception while taking DOXOPEG and in the six months following discontinuation of DOXOPEG, so that their partner does not become pregnant.

Driving and using machines

DOXOPEG may cause dizziness or drowsiness. Take care before you drive a vehicle or operate machinery, until you know how DOXOPEG affects you.

Important information about some of the ingredients of DOXOPEG:

DOXOPEG contains sucrose, a type of sugar (see What DOXOPEG contains). If you have been told by your doctor that you have an intolerance to some sugars, tell your doctor before receiving DOXOPEG.

3. How to receive DOXOPEG

Do not share medicines prescribed for you with any other person.

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

DOXOPEG is an infusion into the vein, which will be given to you by your doctor every 2 to 3 weeks.

DOXOPEG will be administered under the supervision of a qualified oncologist specialised in the administration of cytotoxic agents (cancer medication).

Your doctor will determine the correct dose for you according to your condition.

Inform your doctor if you see skin reactions on the site where the infusion was inserted, including swelling, small blisters or ulcers, redness or peeling of your skin.

Your doctor will tell you how long your treatment with DOXOPEG will last.

If you have the impression that the effect of DOXOPEG is too strong or too weak, tell your doctor or pharmacist.

If you receive more DOXOPEG than you should

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

If you missed a dose of DOXOPEG

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

4. Possible side effects

DOXOPEG can have side effects.

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

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

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting.
- yellowing of your skin and eyes, also called jaundice.

These are all very serious side effects. If you have them, you may have had a serious reaction to DOXOPEG. 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:

Side effects that occur frequently:

- you develop fever, feel tired, or if you have signs of bruising or bleeding;
- redness, swelling, peeling or tenderness, mainly on the hands or feet ('hand-foot' syndrome). These effects have been seen very commonly and are sometimes severe. In severe cases, these effects may interfere with certain daily activities, and may last for 4 weeks or longer before resolving completely. The doctor may wish to delay the start and/or reduce the dose of the next

treatment;

- sores in mouth, severe diarrhoea or vomiting or nausea;
- infections, including lung infections (pneumonia) or infections that may affect your vision;
- being short of breath;
- severe stomach pain;
- severe weakness/ fainting.

Side effects that occur less frequently:

- cardiac arrest (heart stops beating); heart failure, in which the heart does not pump enough blood to the rest of the body, which makes you short of breath and may lead to swollen legs;
- blood clot that moves to the lungs, causes chest pain and makes you short of breath;
- swelling, warmth, or tenderness in the soft tissues of your leg, sometimes with pain which gets worse when you stand or walk;
- severe or life-threatening rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome) or over most of the body (toxic epidermal necrolysis).

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

Tell your doctor if you notice any of the following:

Side effects that occur frequently:

- decrease in the number of white blood cells, which can increase the chances of infections. In rare cases, having low white blood cells may lead to severe

infection. Anaemia (reduction in red blood cells) may cause tiredness, and decreased platelets in the blood may increase the risk of bleeding. It is because of the potential changes in your blood cells that you will have regular blood tests;

- decreased appetite;
- constipation;
- skin rashes, including redness of the skin, allergic skin rash, red or raised rash on the skin;
- hair loss;
- pain including in the muscles and chest muscle, joint, arm, or leg, pain in your fingers or toes (extremities);
- feeling very tired;
- infections, including severe infection throughout the body (sepsis), lung infections, herpes zoster virus infections (shingles), a type of bacterial infection (mycobacterium avium complex infection), urinary tract infection, fungal infections (including thrush and oral thrush in the mouth) infection of the hair roots, infected or irritated throat, infected nose, sinuses or throat (cold), infection of the vagina;
- low number of a type of white blood cell (neutrophils), with a fever;
- severe weight loss and muscle wasting, not enough water in the body (dehydration), low level of potassium, sodium, or calcium in the blood;
- feeling confused, feeling anxious, depression, difficulty sleeping;
- nerve damage that may cause tingling, numbness, pain or loss of pain sensation, nerve pain, unusual feeling in the skin (such as tingling or a crawling feeling), decreased feeling or sensitivity, especially in the skin;
- change in sense of taste, headache, feeling very sleepy with low energy, feeling

dizzy;

- inflamed eyes (conjunctivitis);
- fast heart beat;
- high or low blood pressure, flushing;
- shortness of breath that may be brought on by physical activity, nose bleeds, cough;
- inflamed stomach lining or food
- ulcers (sores) in the mouth, indigestion, difficulty swallowing, mouth pain, dry mouth;
- skin problems, including flaky or dry skin, redness of the skin, blister or ulcer (sore) on the skin, itching, dark skin patches;
- excessive sweating;
- muscle spasms or aches;
- pain including in the muscles, bone, or back;
- pain when passing urine, redness of the skin of the scrotum;
- allergic reaction to infusion of the medicine, flu-like illness, chills, inflamed lining of the cavities and passages in the body, such as the nose, mouth or windpipe, feeling weak, generally feeling unwell, swelling caused by fluid build-up in the body, swollen hands, ankles or feet;
- swelling of the legs (oedema);
- weight loss.

Side effects that occur less frequently:

- herpes simplex virus infections (cold sores or genital herpes), fungal infection;
- low number of all types of blood cells, increased number of ‘platelets’ (cells that

help blood to clot);

- allergic reaction;
- high level of potassium in the blood, low level of magnesium in the blood, high levels of uric acid in the blood;
- nerve damage affecting more than one area of the body;
- fits (seizures), fainting;
- unpleasant or painful sensation, especially to touch, feeling sleepy;
- blurred vision, watery eyes;
- heartbeat feels fast (palpitations) or uneven (dysrhythmia), heart muscle disease, heart damage;
- tissue damage (necrosis) where the injection is given, inflamed veins that cause swelling and pain, feeling dizzy upon sitting up or standing up;
- chest discomfort;
- passing wind, inflamed gums (gingivitis);
- skin problems or rashes, including flaky or peeling skin, allergic skin rash, ulcer (sore) or hives on the skin, discoloured skin, change in the natural colour (pigment) of the skin, small red or purple spots caused by bleeding under the skin, nail problems, acne, the painless separation of the nail from the nail bed, increased pigmentation of the skin or mucosa;
- muscle weakness;
- breast pain;
- irritation or pain where the injection is given;
- swollen face, high body temperature;
- symptoms (such as inflammation, redness or pain) come back at a part of the body that previously received radiation therapy or was previously damaged by

a chemotherapy injection into a vein;

- infection that occurs in people with a weak immune system;
- low number of blood cells made in the bone marrow;
- inflamed retina, which may cause changes in vision or blindness;
- abnormal heart rhythm, abnormal heart tracing on an ECG (electrocardiogram) and may be with a slow heartbeat, problem with the heart that affects the heart beat and rhythm, blue colour to the skin and mucosa caused by low oxygen in the blood;
- widening of blood vessels;
- tight feeling in the throat;
- sore and swollen tongue, ulcer (sore) on the lip;
- skin rash with fluid-filled blisters;
- vaginal infection, redness of the scrotum;
- problems with the lining of the cavities and passages in the body, such as the nose, mouth or windpipe;
- abnormal liver blood test results, increased level of ‘creatinine’ in the blood.

Side effects with frequency unknown:

- cancer of the blood that develops quickly and affects the blood cells (acute myeloid leukaemia), bone marrow disease that affects the blood cells (myelodysplastic syndrome), cancer of the mouth or lip;
- serious side effects on your blood;
- coughing and shortness of breath, possibly accompanied by fever, that is not brought on by physical activity (Interstitial lung disease).

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

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions 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 DOXOPEG.

5. How to store DOXOPEG

Store all medicines out of reach of children.

- Store between 2 to 8 °C.
- Do not freeze.
- Keep the vials in the outer carton until required for use.

After dilution:

- After dilution with dextrose 5 % in water for intravenous infusion, the diluted DOXOPEG solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. Diluted product not for immediate use should be stored between 2 to 8 °C for no longer than 24 hours.
- For single use only.
- Discard any remaining solution.

- Do not use after the expiry date stated on the label or carton.

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

DOXOPEG contains

- The active substance is doxorubicin hydrochloride.

  Each ml of the liposomal infusion contains 2 mg of doxorubicin hydrochloride.

  Contains sugar: sucrose.
- The other ingredients are ammonium sulphate, cholesterol, ethanol, histidine, hydrogenated soy phosphatidyl choline, methoxy polyethylene glycol (MPEG 2000), sucrose and water for injection.

What DOXOPEG looks like and contents of the pack

A red, translucent, sterile and pyrogen-free suspension.

Contents of the pack:

The container is a Type 1, clear glass, 15 ml vial, with a grey Teflon stopper, an aluminium seal and red plastic flip-off cap.

The DOXOPEG vial is packed in an outer carton.

DOXOPEG is supplied as a single pack or packs of ten vials.

Each 15 ml vial of DOXOPEG contains 10 ml doxorubicin hydrochloride 2 mg/ml.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

The professional information can be found on the SAHPRA website.