PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

DOXOLIP 2 mg/1 mL concentrate for infusion

2 mg/1 mL doxorubicin hydrochloride per vial

Contains sugar: Sucrose 100 mg/mL.

Please read this leaflet carefully before receiving DOXOLIP

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

What is in this leaflet

1. WHAT DOXOLIP IS AND WHAT IT CONTAINS

DOXOLIP belongs to the general group of medicines known as antineoplastics or anticancer medicines.

Each vial contains 2 mg/1 ml doxorubicin hydrochloride in a pegylated liposomal formulation and delivers 10 ml (20 mg) in a concentrate for infusion for single intravenous use.

DOXOLIP 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).
- To treat breast cancer and ovarian cancer.

- 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 DOXOLIP

Before you begin treatment with **DOXOLIP**, you and your doctor should talk about the good this medicine will do, as well as the risks of using it.

DOXOLIP should not be administered to you:

- If you are allergic to doxorubicin hydrochloride or any of the components of **DOXOLIP** (see **What DOXOLIP contains**).
- If you are pregnant or breastfeeding (see **Pregnancy and breastfeeding**).
- If you have a condition called AIDS-related Kaposi's sarcoma (a type of cancer that is very common in people with AIDS, causing patches of abnormal tissue to grow under the skin, in the lining of the mouth, nose, and throat or in other organs) that may be treated effectively with local therapy or systemic alpha-interferon.
- If you or your child is under the age of 18 years.
- If you have a pre-existing heart disease.

Warnings and precautions:

Special care should be taken with DOXOLIP.

Tell your doctor or healthcare professional before being given the injection:

- If you have or develop a bone marrow disorder (which includes symptoms such as bruising easily, nose bleeds, bleeding gums, tiny red spots on the skin, fever and chills, rash, diarrhoea, tiredness, paleness of skin, lips, and nail beds, increased heart rate or shortness of breath) after treatment with **DOXOLIP**. Your doctor will perform blood counts if this occurs.
- If you develop ulcers in your mouth after treatment with **DOXOLIP**.

- If you have a liver disorder. You doctor will draw blood prior to the treatment to test your liver function. The dosage of **DOXOLIP** may be reduced if necessary.
- If you have a heart disorder, as **DOXOLIP** may worsen your condition.
- If you are taking other anti-cancer medicines.
- If you are an elderly person.
- If your spleen has been removed.
- 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 have high blood sugar (diabetes). **DOXOLIP** contains sucrose.

DOXOLIP 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.

Cases of interstitial lung diseases have been observed in patients receiving pegylated liposomal doxorubicin 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.

You may experience an infusion-related reaction during the treatment with **DOXOLIP** which can be serious and sometimes life-threatening. The symptoms may include allergic reaction, trouble

breathing, water retention in the face, increase or decrease of blood pressure, rash, back pain, chest pain, chills, fever, changes in the way your heart beats, indigestion, nausea, dizziness, sweating.

DOXOLIP is considered to be an irritant, take care when you receive **DOXOLIP** and be alert for symptoms of burning or a sensation of tightness at the infusion site.

DOXOLIP must not be given by the intramuscular or subcutaneous route.

Other medicines and DOXOLIP:

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

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

- Cyclophosphamide or taxanes (used in the treatment of certain cancers).
- 6-mercaptopurine (used to treat leukemia and inflammatory bowel disease).
- Other cytotoxic medicines (used to treat arthritis and related conditions).
- Cardiotoxic medicines (medicines that damage the functioning of
- the heart) such as daunorubicin, cyclophosphamide and idarubicin.
- Stavudine (used for HIV/AIDS treatment).
- Bone marrow depressants.
- Medicines that may cause blood abnormalities.
- Vaccines.

DOXOLIP with food or drink:

DOXOLIP can be administered with or without food.

Pregnancy, breastfeeding and fertility:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before receiving **DOXOLIP**.

You should not be given **DOXOLIP** if you are pregnant or breastfeeding.

Do not use **DOXOLIP** if you are pregnant, planning to become pregnant or breastfeeding.

Driving and using machines:

DOXOLIP may cause dizziness or drowsiness. Take care if you feel dizzy, tired or drowsy while receiving **DOXOLIP**.

3. HOW TO RECEIVE DOXOLIP

DOXOLIP should only be administered under the supervision of a doctor who specialises in the treatment of cancer.

DOXOLIP is an injection that goes straight into your vein and it will be given by your doctor every 2 to 3 weeks.

The dose that is used may depend on a number of factors:

- What **DOXOLIP** is being prescribed for.
- The size of the patient (body weight and height).
- Whether or not other medicines are also being taken.

The dose of **DOXOLIP** will be different for different patients. Your doctor will determine the correct dose for you according to your condition.

While you are being treated with **DOXOLIP**, your doctor may want you to drink extra fluids so that you will pass more urine. This will help prevent kidney problems.

The usual dosage for breast and ovarian cancer is 50 mg/m^2 once every four weeks, and for AIDS-KS it is 20 mg/m^2.

If you are being treated for multiple myeloma, the usual dose of **DOXOLIP** is 30 mg/m^2 on the 4^{th} day of the bortezomib 3 week regimen, immediately after the bortezomib infusion. The dose is repeated as long as you respond satisfactorily and tolerate treatment.

If more DOXOLIP is administered to you than you should receive:

Since your doctor will administer **DOXOLIP**, he/she will control the dosage. However, in the event of overdosage, your doctor will manage the overdosage.

If you missed a dose of DOXOLIP:

Your doctor will make sure you receive **DOXOLIP** at the right time. If you think you might have missed a dose of **DOXOLIP**, please inform your doctor.

4. POSSIBLE SIDE EFFECTS

DOXOLIP can have side effects.

Not all side effects reported for **DOXOLIP** are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while receiving **DOXOLIP**, please consult your doctor, pharmacist or other healthcare professional for advice.

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

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.
- Rash or itching.
- Fainting.

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

- Yellowing of the skin and eyes, also called jaundice.
- Liver damage (nausea, vomiting, pain in your stomach area, jaundice, weakness or weight loss).
- Chest pain.
- Changes in the way your heart beats, for example, if you notice it beating faster.
- Heart problems or heart failure.

- Difficulty breathing coughing or shortness of breath, possibly accompanied by fever, that is not brought on by physical activity (Interstitial lung disease)
- Pneumonia (cough, fever and difficulty breathing).
- Signs of recurrent infections such as fever, chills or sore throat.
- Bone marrow suppression (bruising easily, nose bleeds, bleeding gums, tiny red spots on the skin, fever and chills, rash, diarrhoea, tiredness, paleness of skin, lips and nail beds, increased heart rate or shortness of breath).
- Thrombocytopenia (an abnormal drop in the number of blood cells involved in forming blood clots).
- Infection affecting your whole body (sepsis) with symptoms such as high fever, flushed skin, fast heartbeat, confusion and swelling.
- Nerve damage (weakness, numbness or pain) or nerve pain.
- Formation of blood clots in your veins (pain, redness or inflammation of the area affected).
- Hand-foot syndrome, including blistering, peeling, redness of the palms, hands and feet. May include numbness, pain or tingling.
- Severe, blistering skin rash or peeling of your skin.
- Kidney damage (changes in the amount of urine normal for you, blood in your urine, weakness, tiredness or confusion).
- Painful or difficult urination.
- Bladder infection (pain or burning when urinating).
- Less urine than is normal for you.
- Shingles (sensitive, painful, blistering skin rash affecting only one side of your body).

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

Tell your doctor as soon as possible if you notice any of the following:

- Headache, dizziness.
- Nausea, vomiting, diarrhoea, inflammation of the mouth or throat, abdominal pain, constipation.

- Anaemia (tiredness, weakness, pale skin colour, white to pale gums, rapid heartbeat), blood abnormalities.
- Folliculitis (an infection of the hair follicles which can be either bacterial or fungal causing itching or small, white-headed pimples around the pocket from which your hair grows).
- Cold sores (clusters of small, ulcerative blisters on your lips or outer edge of your mouth).
- Upper respiratory tract infection.
- Oral thrush (fungal infection inside your mouth causing pain, burning, inflammation and white patches inside your mouth).
- Anxiety, sleeping disturbances.
- Lacrimation (excessive secretion of tears), pink eyes, inflammation of the retina.
- Blurred vision.
- Nose bleeds.
- Low blood pressure (dizziness or light-headedness) or high blood pressure.
- Sudden drop in your blood pressure if you get up to quickly (light- headedness or dizziness).
- Coughing.
- Mucositis (painful inflammation and ulceration of the mucous membranes lining the digestive tract), stomatitis (inflammation of the mucous membrane of the mouth), pain in your mouth.
- Inflammation of your tongue (red, swollen or painful), or gums (red, swollen, bleeding or painful).
- Taste disturbances.
- Indigestion, dry mouth or difficulty swallowing.
- Flatulence (release of excessive air (break wind)).
- Inflammation of the skin (skin becomes itchy and may develop blisters), skin rash, nail disorder, acne, sweating, hair loss.
- Dry or flaky skin.
- Flushing (redness of your face).

- Muscle weakness.
- Leg cramps, bone pain, back pain, muscle pain or joint pain.
- Breast pain.
- Swelling from excessive accumulation of watery fluid in cells.
- Weight loss, anorexia (severe weight loss) or wasting syndrome (severe loss of weight and muscle, tiredness or loss of appetite).
- Confusion or feeling depressed.
- Abnormal skin sensations (tingling, tickling, itching or burning).
- Drowsiness.
- Redness of your testicles if you are a male.
- Flu-like symptoms (runny nose, sore throat or headache).
- Elevated body temperature.
- Inflammation of your vagina if you are female (discharge, itching or pain).
- Lack of strength or energy, or tiredness.
- Dehydration (excessive loss of water from your body causing increased thirst, little or dark coloured urine or vomiting).
- Low levels of potassium in your blood (muscle weakness, pain or cramps, or changes in your blood pressure).
- High levels of potassium in your blood (weakness, general discomfort or changes in the way your heart beats).
- Low levels of magnesium in your blood (muscle cramps, changes in the way your heart beats, tremors, confusion or disorientation).
- Low sodium levels in your blood (nausea, vomiting, headaches, confusion, restlessness, muscle weakness or tiredness).
- Low levels of calcium in your blood (bruising or small pinpoint bleeds on your skin, tingling sensations, muscle spasms or changes in the way your heart beats).
- Changes in your liver enzymes when tests are done.

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. You can also report side effects to SAHPRA via the 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 **DOXOLIP.**

Suspected adverse reactions can also be reported directly to the Holder of Certificate of Registration (HCR) via email: pharmacovigilance.africasme@sunpharma.com or tel: +27(0) 12 643 2000.

5. HOW TO STORE DOXOLIP

- Store between 2 °C to 8 °C.
- Do not freeze. Keep vials in carton until required for use.
- Discard any unused portion.
- **STORE ALL MEDICINES OUT OF REACH OF CHILDREN.**
- After dilution with dextrose 5 % in water for intravenous infusion, the diluted **DOXOLIP** solution should be used immediately.
- Diluted product not for immediate use should be stored between 2 °C to 8 °C for no longer than 24 hours. Partially used vials should be discarded.
- Please return expired medicine or partially used vials to your pharmacist for safe disposal.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What DOXOLIP contains

The active ingredient is Doxorubicin hydrochloride.

Inactive ingredients:

Ammonium sulphate, cholesterol, ethyl alcohol, histidine, hydrogenated soy phosphatidyl choline, N-(carbonyl-methoxypolyethylene glycol 2 000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt, sucrose, water for injection.

What Doxolip looks like and contents of the pack

DOXOLIP: A translucent red coloured liposomal dispersion.

DOXOLIP is packed in a 10 ml colourless USP type I glass vial with a 20 mm grey bromobutyl rubber stopper, sealed with a 20 mm light blue aluminium flip off seal. One vial is packed per outer carton.

Holder of Certificate of Registration

Ranbaxy Pharmaceuticals (Pty) Ltd

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Registration number

43/26/0018

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Access to the corresponding PIL translation:

The PIL is available in one other language (Afrikaans), a copy is accessible on the company website: https://sunpharma.com/south-africa-products/