Applicant: Oethmaan Biosims (Pty) Ltd	**SAHPRA approval date:** 26 November 2024
Product: • Loxat 30 • Loxat 100 • Loxat 300	**Dosage form and strength:** Each vial contains 30,0 mg Paclitaxel Each vial contains 10,0 mg Paclitaxel Each vial contains 300,0 mg Paclitaxel

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

LOXAT 30 (Concentrate solution for infusion)

LOXAT 100 (Concentrate solution for infusion)

LOXAT 300 (Concentrate solution for infusion)

6 mg/ml of Paclitaxel

Contains alcohol (49,7 %)

Sugar free

Read all of this leaflet carefully before you are administered LOXAT.

- 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.
- LOXAT 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 LOXAT is and what it is used for

2. What you need to know before you are administered LOXAT

Initial:	26/11/2024

3. How LOXAT is administered

4. Possible side effects

5. How to store LOXAT

6. Contents of the pack and other information

1. What LOXAT is and what it is used for

LOXAT belongs to the group of medicines called antineoplastics, it interferes with the growth of cancer cells, which are eventually destroyed. LOXAT is used to treat cancer of the ovaries, breast and certain types of lung cancer.

2. What you need to know before you are administered LOXAT

You should not be administered LOXAT:

- If you are allergic (hypersensitive) to paclitaxel or any of the other ingredients (especially polyoxyl 35 castor oil) of LOXAT listed in section 6.
- If your white blood cell counts are abnormal (this is checked by blood tests).
- If you are pregnant or breastfeeding a baby.
- If you a child.

Warnings and precautions

Take special care with LOXAT:

LOXAT should only be administered under the supervision of a doctor with experience in cancer treatment medicines. Some side-effects may require immediate attention by the doctor.

To minimise allergic reactions, you will be given other medicines before you receive LOXAT.

Please tell your doctor if:

- you have, or have previously had liver disease, heart disease or vascular disease.
- you have recently had, or are going to have radiotherapy or chemotherapy.
- you had and infection or have been vaccinated recently.
- you have decreased blood cells and bone marrow function. If you develop a fever, bleeding or think you may be suffering from an infection, please inform your doctor immediately.
- you experience chills, fever, rapid heart rate, difficulty breathing, low blood pressure while receiving LOXAT. You may be having a severe allergic reaction to LOXAT.
- you experience high or low blood pressure or changes in your heart rate.
- you experience tightness or pain in the chest, neck, back or arms, as well as fatigue, lightheadedness, abnormal heartbeat and anxiety.
- you have numbness or weakness of the arms and legs (signs of peripheral neuropathy).
- you notice any reactions at the injection site, as the infusion has to be immediately stopped.
- you develop severe or persistent diarrhoea, with fever and stomach pain, during or shortly after the treatment with LOXAT. Your colon could be inflamed (pseudomembranous colitis).
- you have a dry cough with shortness of breath either at rest or after exertion.
- you are sexually active, you and your partner are advised to use effective birth control to prevent pregnancy during treatment and for 6 months after treatment discontinuation with

LOXAT, as there is a risk that use of LOXAT during pregnancy may cause birth defects in your child. Men who would like to father a child during the treatment or in the 6 months following treatment, should seek advice from their doctor or pharmacist. You may want to seek counselling on sperm storage before starting your therapy.

- if you experience any changes in your vision.

Children and adolescents

Safety and efficacy in children have not been established and therefore they must not receive treatment.

Other medicines and LOXAT

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

If you are using any of the following medicines, please tell your doctor:

Medicines that may increase the effect of LOXAT:

- Cisplatin (anticancer medicine)
- Ketoconazole (medicine to treat a fungal infection)
- Doxorubicin (antineoplastics)
- Erythromycin (an antibiotic)
- Fluoxetine (an antidepressant)
- Gemfibrozil (a medicine used in the treatment of high cholesterol)
- Clopidogrel (a medicine used to prevent blood clots)

- Cimetidine (a stomach acid reducer)
- Ritonavir, saquinavir, indinavir and nelfinavir (antiviral medicines used to treat HIV)

Medicines that reduce the effect of LOXAT:

- Rifampicin (an antibiotic used for several infections, including tuberculosis (TB)
- Carbamazepine, phenytoin (medicines used to prevent and control seizures);

While you are being treated with LOXAT, and after you stop treatment with it, *do not have any immunizations (vaccinations) without your doctor's approval.*

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 health care provider for advice before taking LOXAT.

LOXAT should not be used during pregnancy or by women who plan to become pregnant.

LOXAT may cause birth defects in your baby, therefore, you and your partner should use effective contraception during treatment and for at least 6 months after treatment with LOXAT.

Check with your doctor immediately if you think you have become pregnant while taking this medicine.

LOXAT should not be used during breastfeeding.

LOXAT can cause infertility in men. If you are a male patient, speak to your doctor about freezing and storing your sperm before treatment with LOXAT.

Driving and using machines

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

LOXAT contains alcohol. Do not drive or operate any machinery until you know how this medicine affects you.

LOXAT contains polyoxyl castor oil and ethanol

LOXAT contains polyoxyl castor oil which may cause severe allergic reactions.

LOXAT also contains 393 mg of alcohol (ethanol) in each ml (49,7 % v/v). The amount per dose of this medicine is equivalent to 650 ml beer or 260 ml wine. Harmful for those suffering from alcoholism.

To be taken into account in pregnant or breastfeeding women, children and high-risk groups such as patients with liver disease, or epilepsy.

3. How LOXAT is administered

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

You will not be expected to give yourself LOXAT. It will be given to you by a person who is qualified to do so and under carefully controlled conditions.

LOXAT will be administered intravenously by your doctor or under his/her supervision. Your doctor will determine the exact dose and how many doses that you will need.

The dosage may vary according to the type of cancer that you have.

Your doctor may order that you receive premedication medicines (usually corticosteroids, antihistamines, and H_2 antagonists) prior to LOXAT administration.

You will be given LOXAT as an intravenous infusion (slow injection via a drip) into your vein. Tell your doctor or nurse at once if you notice any pain at the injection site during or shortly after treatment.

If you have the impression that the effect of LOXAT is too strong or too weak, talk to your doctor.

If you are given more LOXAT than you should

In the event of overdosage consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

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

If you miss a dose of LOXAT:

Since a healthcare professional will administer LOXAT, it is unlikely that the dose will be missed.

4. POSSIBLE SIDE EFFECTS:

LOXAT can have side effects.

Not all side effects reported for LOXAT are included in this leaflet. Should your general health worsen while taking LOXAT, please consult your doctor, pharmacist or other health care professional for advice.

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

- Severe allergic reaction (anaphylactic reaction): you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint

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

- Fever or infection: if you have a temperature of 38 ºC or greater, sweating or other signs of infection (since you might have less white blood cells than normal).
- Bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising since you might have less platelets than normal.
- Severe liver, kidney or heart damage from a condition called Tumour Lysis Syndrome, caused by harmful amounts of substances from the cancer cells getting into the blood

stream, has been seen sometimes when LOXAT is taken along with other medicines used to treat cancer.

- Irregular heart rate.
- Severe chest pains possibly radiating to the jaw or arm, sweating, breathlessness and nausea (heart attack).
- Blood clots in the veins (thrombosis) and inflammation of the veins associated with blood clots (thrombophlebitis) – this may present as pain and/or swelling in your arms or legs.
- Shortness of breath, cough, coughing up blood or pain in the chest or shoulder (e.g. pulmonary embolism). Some of these effects may not occur immediately (lung fibrosis), respiratory failure.
- Abdominal pain caused by inflammation in your bowel, bowel obstruction or perforation of the wall of your bowel.
- Persistent diarrhoea.
- Inflammation of your pancreas (pancreatitis). Symptoms include upper abdominal pain, nausea and vomiting.
- Damage to the liver which may be severe (hepatic necrosis). This may have an effect on brain function (hepatic encephalopathy). This can sometimes be fatal.
- Severe skin rash with flushing, fever, blisters or ulcers (Stevens - Johnson syndrome).
- Severe rash with reddening, peeling and swelling of the skin that looks like a burn (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:

Frequent side effects

- Infection – usually of the urinary tract or upper respiratory tract. This may be associated with low blood cell count resulting from receiving paclitaxel. This can sometimes be fatal.
- Decreased production of blood cells and platelets (myelosuppression), low haemoglobin level (anaemia), low white blood cells, low platelet count, bleeding.
- Mild allergic reactions (mainly flushing and rash).
- Nerve problems – these may appear as pins and needles in the hands and feet (can persist beyond 6 months of paclitaxel discontinuation).
- Abnormal ECG, slow heart rate.
- Low blood pressure.
- Nausea, vomiting, diarrhoea, sores in the mouth or lips.
- Hair loss, temporary mild changes to the nails and skin.
- Pain in the muscle or joints.
- Injection site reactions (local swelling, pain, redness, hardening of tissues, death of skin tissue, extravasation (leaking of drug outside the vein) resulting in cellulitis (painful swelling and redness).
- Changes in blood tests that show how your liver is working.

Less frequent side effects

- Shock due to infections (known as 'septic shock'), pneumonia, peritonitis, blood poisoning (sepsis).
- Shortage of white blood cells with fever and increased risk of infection (febrile neutropenia).

- Sudden disorder in blood forming cells (acute myeloid leukaemia), myelodysplastic syndrome.
- Significant allergic reactions causing low or high blood pressure, breathing problems, severe itching, back pain, chest pain, rapid beating of the heart, abdominal (tummy) pain, pain around hands and feet, and sweating).
- Serious and potentially fatal hypersensitivity reactions (anaphylactic reaction): you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint. Should this occur, seek medical attention urgently.
- Serious and potentially fatal hypersensitivity reactions with shock (anaphylactic shock).
- Loss of appetite (anorexia), dehydration.
- Confusional state.
- Effect on nerves that control the muscles, resulting in muscle weakness in arms and legs (motor neuropathy), seizures ('fits'), convulsions, effect on the brain (encephalopathy), dizziness, headache, ataxia (irregular muscle contraction).
- Optic nerve and/or visual disturbances (scintillating scotomata).
- Loss of hearing (ototoxicity), or ringing in the ears (tinnitus), vertigo.
- Irregular heartbeat (may be caused by irregular impulse conduction), pain in the middle of your chest which may be caused by heart disease, pain or weakness in heart muscles (heart muscle degeneration), increased frequency of heartbeat, severe chest pains possibly radiating to the jaw or arm, sweating, breathlessness and nausea (heart attack).

- High blood pressure (may give you headaches), blood clots in the veins (thrombosis) and inflammation of the veins associated with blood clots (thrombophlebitis)- this may present as pain and/or swelling in your arms or legs or inflammation of the vein, shock.
- Problems with your lungs such as inflammation or accumulation of fluids, which may make it difficult to breathe, cough.
- Abdominal pain which may be caused by accumulation of fluid in the abdomen (ascites), inflammation of colon sometimes with persistent severe diarrhoea (pseudomembranous colitis), bowel obstruction, blood clot in the blood vessels to your bowel or perforation of the wall of your bowel, constipation.
- Damage to the liver which may be severe (hepatic necrosis). This may have an effect on brain function (hepatic encephalopathy).
- Itching, skin rash/redness, rapid formation of a rash followed by the appearance of skin lesions on the soles of the feet and palms and ulcers in the mouth (erythema multiforme, Stevens-Johnson syndrome, epidermal necrolysis), severe skin peeling (exfoliative dermatitis), nettle rash (urticaria), loosening of finger or toenails (you are advised to wear protection on your hands and feet when exposed to the sun).
- Fever (pyrexia), feeling weak (asthenia), oedema, feeling unwell (malaise).
- Laboratory tests may show that your kidney function has been affected.

<u>Frequency unknown</u>:

- Disseminated intravascular coagulation, or "DIC," has been reported. This concerns a serious condition that makes people bleed too easily, get blood clots too easily, or both.

- Narrowing of your airway that usually comes and goes (bronchospasm). It may make it hard for you to breathe.
- Tumour lysis syndrome (complications of substances released from treated cancer cells entering the blood).
- A swelling of part of the back of your eye (macular oedema), visual disturbances such as seeing flashes of light (photopsia) or floaters.
- Inflammation of a vein (phlebitis).
- Redness and swelling of the palms of your hands or soles of your feet which may cause your skin to peel (Palmar-plantar erythrodyesthesia syndrome).
- An autoimmune disorder that may affect your skin, joints, kidneys, brain, and other organs (systemic lupus erythematosus).
- Infertility.
- Inflammation of the lungs caused by radiation therapy to the chest (radiation pneumonitis).
- Radiation recall (a skin rash like severe sunburn) which can occur on skin that has previously been exposed to radiotherapy.

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

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 LOXAT.

5. How to store LOXAT

- Store at room temperature not exceeding 30 °C.
- After first use any unused concentrate may be stored at room temperature not exceeding 25 °C for up to 28 days.
- The concentrate for infusion is stable for 48 hours when diluted with 0,9 % sodium chloride or 5 % glucose solution to concentrations of 0,3 mg/ ml or 1,2 g/ ml when stored below 25 °C.
- To be kept in outer container until required.
- Store all medicines out of reach of children. Do not use the concentrate for infusion after the expiry date printed on the container or label.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What LOXAT contains

The active substance is:

Each vial of LOXAT 30 contains 30 mg paclitaxel per 5 ml, as the active ingredient.

Each vial of LOXAT 100 contains 100 mg paclitaxel per 16,67 ml, as the active ingredient.

Each vial of LOXAT 300 contains 300 mg paclitaxel per 50 ml, as the active ingredient.

The other ingredients are citric acid anhydrous, polyoxyl 35 castor oil and ethanol anhydrous (49,7 %).

What LOXAT looks like and contents of the pack

LOXAT 30: Clear colourless to pale yellow solution, practically free from visible particles.

LOXAT 100: Clear colourless to pale yellow solution, practically free from visible particles.

LOXAT 300: Clear colourless to pale yellow solution, practically free from visible particles.

LOXAT are packed in:

LOXAT 30: Single 10 ml amber glass vial in a cardboard carton.

LOXAT 100: Single 20 ml amber glass vial in a cardboard carton.

LOXAT 300: Single 50 ml amber glass vial in a cardboard carton.

Holder of Certificate of Registration

Oethmaan Biosims (Pty) Ltd

207A Sherwood House

Greenacres Office Park

c/o Victory and Rustenburg Roads

Victory Park

Johannesburg

2195

Tel. No.: +27 11 433 0602

Applicant: Oethmaan Biosims (Pty) Ltd	**SAHPRA approval date:** 26 November 2024
Product: • Loxat 30 • Loxat 100 • Loxat 300	**Dosage form and strength:** Each vial contains 30,0 mg Paclitaxel Each vial contains 10,0 mg Paclitaxel Each vial contains 300,0 mg Paclitaxel

This leaflet was last revised in

26 November 2024

Registration number

LOXAT 30: 41/26/1095

LOXAT 100: 41/26/1096

LOXAT 300: 41/26/1097

Access to the corresponding Professional Information

www.oethmaan.co.za

Telephone number: 011 433 0602

Email: info@oethmaan.co.za

Initial:	26/11/2024