1.3.2.1 Patient Information Leaflet

SCHEDULING STATUS

S4

YONDELIS® 1 mg (powder for concentrate for solution for infusion)

Trabectedin, 1 mg

Sucrose 400 mg per vial

Read all of this leaflet carefully before you are given YONDELIS

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

2. What you need to know before you are given YONDELIS.

3. How to take YONDELIS.

4. Possible side effects.

5. How to store YONDELIS.

6. Contents of the pack and other information.

1. What YONDELIS is and what it is used for

YONDELIS is an anti-cancer medicine that works by preventing the tumour cells from multiplying.

- YONDELIS is used for the treatment of patients with advanced liposarcoma and leiomyosarcoma, (*malignant diseases that start in deep soft tissue such as fat cells, muscles and other tissues*) when previous medicines have been unsuccessful, or the patients are unsuited to receive them.

- YONDELIS in combination with pegylated liposomal doxorubicin (PLD: another anti-cancer medicine) is used for the treatment of patients with ovarian cancer that has come back after at least 1 previous therapy. It is suitable for platinum sensitive ovarian tumours in patients who may not be suitable for platinum-based chemotherapy. It is not suitable for all ovarian tumours.

2. What you need to know before you are given YONDELIS

YONDELIS should not be administered to you:

- if you are allergic (hypersensitive) to trabectedin or any of the other ingredients of YONDELIS,
- if you have any serious infections,
- if you are pregnant or breastfeeding,
- if you will receive yellow fever vaccine,

- If you have severe liver or kidney damage. Tell your doctor if you know or suspect that you have any liver or kidney problems before starting the treatment with YONDELIS.

Warnings and precautions

Special care should be taken with YONDELIS:

You should seek medical attention immediately if any of the following conditions appear:

- If you develop a fever**,** as YONDELIS may cause side effects affecting your blood and liver.
- If you still feel sick, vomit or are unable to drink fluids and therefore pass less urine despite being given anti-sickness medicines.
- If you experience severe muscle pain or weakness as it could be a sign of damage to your muscles, (rhabdomyolysis, *see POSSIBLE SIDE EFFECTS*).
- If you notice that YONDELIS infusion leaks out of your vein while you are being given it. It could lead to damage and death of your tissue cells around the injection site (tissue necrosis, *see also POSSIBLE SIDE EFFECTS*) which may require surgery.
- If you have an allergic reaction (hypersensitivity). In this case you may experience one or more of the following signs: fever, difficulty in breathing, redness or flushing of the skin or a rash, feeling sick (nausea) or being sick (vomiting: *see POSSIBLE SIDE EFFECTS*).

YONDELIS should not be used in children below 18 years of age with paediatric sarcomas.

Other medicines and YONDELIS:

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

Tell your doctor if you are taking any of the following medicines:
You must not use YONDELIS if you are to receive the yellow fever vaccine and it is not recommended that you use YONDELIS if you will receive a vaccine containing live virus particles. The effect of medicines containing phenytoin (for epilepsy) may be decreased if given together with YONDELIS and this is therefore not recommended.

If you use other medicines, you may need to be closely monitored as the effects of YONDELIS might be:

- decreased (examples are medicines containing rifampicin (for bacterial infections), phenobarbitone (for epilepsy) or St. John's Wort (*Hypericum perforatum*, an herbal medicine for depression)) or
- increased (examples are medicines containing ketoconazole or fluconazole (for fungal infections), ritonavir (for HIV infection), clarithromycin (for bacterial infections), aprepitant (to prevent nausea and vomiting), ciclosporin (inhibit the defensive system of the body) or verapamil (for high blood pressure and heart conditions)) as a result.

If you are given YONDELIS or the combination YONDELIS + PLD together with a medicine that might cause damage to the liver or to the muscles (rhabdomyolysis), you may need to be closely monitored when using YONDELIS together with this medicine, as there could be an increased risk of damage. Medicines containing statins (for lowering

cholesterol levels and preventing cardiovascular disease) is an example of medicines that may cause muscle damage.

YONDELIS with food and drink:

Alcohol consumption must be avoided during treatment with YONDELIS as this may harm the liver.

Pregnancy and breastfeeding and fertility:

Pregnancy

You should not use YONDELIS if you are pregnant or if you are trying to become pregnant as YONDELIS may harm the unborn baby.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking this medicine.

Adequate contraceptive precautions must be used by men of a fertile age and women of childbearing potential when receiving YONDELIS and for 8 months following the end of treatment for women and 5 months following the end of treatment for men. If a pregnancy should occur you must tell your doctor immediately and genetic counselling is recommended since YONDELIS can cause genetic damage.

Genetic counselling is also recommended for patients wishing to have children after therapy. Male patients should seek advice on sperm conservation prior to treatment because of the risk of irreversible infertility due to therapy with YONDELIS.

Breastfeeding

YONDELIS must not be given to patients who are breastfeeding. Therefore, you must stop breastfeeding before you start your treatment and you must not begin breastfeeding again until your doctor has confirmed that it is safe to do so.

Driving and using machinery:

During your treatment with YONDELIS you may feel tired and experience a loss of strength. Do not drive or use any tools or machines if you are experiencing any of these side effects.

YONDELIS contains potassium and sucrose:

YONDELIS contains potassium, less than 1 mmol (39 mg) per vial and can therefore be considered as essentially “potassium-free”.

YONDELIS contains sucrose which may have an effect on the control of your blood sugar if you have diabetes mellitus. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking YONDELIS.

3. HOW TO RECEIVE YONDELIS

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

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

YONDELIS is given to you under the supervision of a medical practitioner experienced in the use of chemotherapy. Its use should be confined to qualified oncologists or other health professionals specialised in the administration of cytotoxic medicines.

Your doctor will prescribe an appropriate dose for you**.**

If you receive more YONDELIS than you should:

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 missed a dose of YONDELIS

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

4. POSSIBLE SIDE EFFECTS

YONDELIS or its combination with PLD can have side effects.

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

Side effects caused by the single treatment with YONDELIS*:*

Frequent

- You may:

- feel tired,
- feel short of breath (dyspnoea),
- bruise more easily,
- have nose bleeds,
- be more prone to infections like chest infection (pneumonia), catheter site infection and infection in the blood (sepsis). An infection could also give you a raised temperature (fever).

If you develop any of these symptoms you should seek medical attention immediately.

- Your doctor may require blood tests in certain situations in order to avoid that you develop muscle damage (rhabdomyolysis). In very severe cases this could lead to kidney failure. If you experience severe muscle pain or weakness, you should seek medical attention immediately.
- You could have increased levels of the yellow pigment bilirubin in the blood which might cause jaundice (a yellowing of the skin, mucous membranes and eyes).
- You may experience headache and a loss of strength.
- You may also lose your appetite, feel sick (nausea) or vomit, and become constipated. If you still feel sick, vomit or are unable to drink fluids and therefore pass less urine, despite being given anti-sickness medication, you should immediately seek medical help.
- Your doctor will order regular blood tests to detect any abnormalities in the blood.
- You may have fever. If you have a raised temperature you should seek medical attention immediately.

- You could also feel pain in your back, muscles and joints. There could be damage to your nerves which may result in muscle pain, weakness and numbness. You could experience general swelling or swelling of the limbs and a sensation of creeping on the skin.
- You may experience diarrhoea, loss of water from the body, inflammation of the mouth (stomatitis), pain in the abdomen, weight loss, digestive discomfort and a change in your sense of taste.
- You may lose hair (alopecia).
- You could also experience dizziness, sleeping problems, low blood pressure and flushing.
- You may have a reaction at the site of injection. YONDELIS infusion may leak out of your vein while you are being given it, leading to damage and death of your tissue cells around the injection site (tissue necrosis, *see also TAKE SPECIAL CARE WITH YONDELIS*), which may require surgery.

Less frequent

- You may experience difficulty in breathing, irregular heartbeat, decreased urine output, abrupt change in mental status, areas of mottled skin, extremely low blood pressure associated with abnormal laboratory tests results (decrease in platelet count). If you get any of the above symptoms or signs, seek medical care immediately.
- You may experience yellowing of your skin and eyeballs (jaundice), pain in the upper right area of your abdomen, nausea, vomiting, a general sense of not feeling well, difficulty in concentrating, disorientation or confusion, sleepiness. These signs could be indicative of the inability of the liver to perform its normal

function. If you get any of the previous described symptoms or signs, seek medical care immediately.

- You may experience fever, difficulty in breathing, redness or flushing of the skin or a rash, feeling sick (nausea) or being sick (vomiting)
- You may notice that YONDELIS infusion leaks out of your vein (extravasation) while you are being given it. Then you will notice some redness, swelling, itchiness and discomfort at the injection site. If you get any of these symptoms or signs, tell your nurse or doctor immediately.

  It could lead to damage and death of your tissue cells around the injection site (tissue necrosis) which may require surgery.

  Some of the symptoms or signs of extravasation may not be visible until several hours after it occurred. There may be blistering, peeling and darkening of the skin over the site. It is possible for it to take a few days before the full extent of tissue damage is visible. If you get any of the previous described symptoms or signs, seek medical care immediately.

Other side effects that may occur with the combination of YONDELIS and PLD:

When YONDELIS is used in combination with PLD some of these side effects are more likely to occur and some may occcur in a more severe way.

Frequent

- You may have the hand and foot syndrome. It may present as red skin of the palms, fingers, and soles of the feet that later may become swelling and violaceous. The lesions may either dry out and desquamate or blister with ulceration.

- You may have a higher skin pigmentation and rash.
- You could have mucosal inflammation as a swelling redness of the inside of the mouth leading to painful ulcers and mouth sores or as an inflammation of the gastrointestinal tract.
- You may also have blood infections (neutropenic infection and neutropenic sepsis). Your doctor will order regular blood tests to detect any abnormalities in the blood.
- You may have syncope also called fainting.
- You could have a weakness in the ventricles, the heart's major pumping chambers (left ventricular dysfunction), sudden blockage in a lung artery (pulmonary embolism) and an abnormal buildup of fluid in the lungs, which leads to swelling (pulmonary oedema).

Less frequent:

- You may experience difficulty in breathing, irregular heartbeat, decreased urine output, abrupt change in mental status, areas of mottled skin, extremely low blood pressure associated with abnormal laboratory tests results (decrease in platelet count). If you get any of the above symptoms or signs, seek medical care immediately.
- You may experience fever, difficulty in breathing, redness or flushing of the skin or a rash, feeling sick (nausea) or being sick (vomiting).
- You may feel severe muscle aches and pains (myalgia), stiffness and muscle weakness. You also may experience a darkening of the urine colour. All of the previously described, could be a sign of damage to your muscles (rhabdomyolysis).

- You may notice that YONDELIS infusion leaks out of your vein (extravasation) while you are being given it. Then you will notice some redness, swelling, itchiness and discomfort at the injection site. If you get any of these symptoms or signs, tell your nurse or doctor immediately.
  It could lead to damage and death of your tissue cells around the injection site (tissue necrosis) which may require surgery.
  Some of the symptoms or signs of extravasation may not be visible until several hours after it occurred. There may be blistering, peeling and darkening of the skin over the site. It is possible for it to take a few days before the full extent of tissue damage is visible. If you get any of the previous described symptoms or signs, seek medical care immediately.

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

5. How to store YONDELIS

Store all medicines out of the reach of children.

Store in a refrigerator (2 ºC – 8 ºC).

Store in the original package / container.

Do not store in a bathroom.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Storage conditions of the reconstituted and diluted medicinal product

After reconstitution, the product can be stored for 30 hours at or below 25 ºC.

It is however recommended that the reconstituted solution should be diluted and used immediately. If not diluted and used immediately, it should not be held for longer than 24 hours at 2 ºC to 8 ºC, unless reconstitution has taken place in controlled and sterile conditions.

After dilution, it can be stored for 30 hours at or below 25 ºC. The total hold time between initial reconstitution and end of treatment should not be longer than 30 hours.

Do not use YONDELIS after the expiry date which is stated on the carton and the vial label after EXP.

The expiry date refers to the last day of that month.

Instructions for storage and disposal

Appropriate procedures for storage and disposal of cytotoxic medicines must be followed. Medical professionals are referred to the full prescribing information for information on in-use stability of the reconstituted and diluted solutions.

6. Contents of the pack and other information

What YONDELIS contains:

- The active substance is trabectedin. Each vial contains 1 mg of trabectedin.
- The other ingredients are sucrose (400 mg per vial), potassium dihydrogen phosphate, phosphoric acid (for pH-adjustment) and potassium hydroxide (for pH-adjustment).

What YONDELIS looks like and contents of the pack

- YONDELIS is provided as a sterile lyophilised white to off-white cake, essentially free of visible contaminants.
- YONDELIS is supplied in a colourless glass vial with a grey rubber stopper and sealed with an aluminium crimp seal with a pink flip-off plastic cap. One vial in packed into a carton.

Holder of Certificate of Registration and Manufacturer

KEY ONCOLOGICS (PTY) LTD

39 Eleventh Avenue

Houghton Estate

Johannesburg

RSA

Tel: +27 11 483 0060

This leaflet was last revised in

- Date on the registration certificate: 01 March 2013.
- Date of the most recently revised patient information leaflet: 29 September 2025

Registration number

43/26/0557