PART III: CONSUMER INFORMATION

PrYONDELIS®
trabectedin for Injection

This leaflet is a summary and will not tell you everything about YONDELIS®. Contact your doctor or pharmacist if you have any questions about the drug. This leaflet is Part III of a three-part "Product Monograph" published when YONDELIS® was approved for sale in Canada and is designed specifically for Consumers.

ABOUT THIS MEDICATION

What the medication is used for:

YONDELIS® (trabectedin) is used for the treatment of patients with metastatic liposarcoma or leiomyosarcoma (forms of soft tissue sarcoma) when previous medicines have been unsuccessful. YONDELIS® has been shown to slow growth of liposarcoma or leiomyosarcoma but it is not known if YONDELIS® prolongs overall survival or improves quality of life of patients with these sarcomas.

YONDELIS® in combination with CAELYX® (pegylated liposomal doxorubicin hydrochloride) (another anti-cancer medicine) is used for the treatment of patients with platinum-sensitive ovarian cancer after one previous therapy. YONDELIS® has been shown to slow growth of ovarian cancer but it is not known if YONDELIS® prolongs overall survival or improves quality of life of patients with ovarian cancer.

What it does:
YONDELIS® is an anticancer medicine that works by preventing the tumour cells from multiplying.

When it should not be used:
- If you are allergic (hypersensitive) to trabectedin or to any ingredient in the formulation or component of the container of YONDELIS®.
- If you are breast-feeding.
- If you have an active serious or uncontrolled infection.

What the medicinal ingredient is:
trabectedin

What the nonmedicinal ingredients are:
phosphoric acid, potassium dihydrogen phosphate, potassium hydroxide, sucrose

What dosage forms it comes in:
YONDELIS® is a powder for injection. The powder is reconstituted in sterile water and further diluted in a sterile salt solution or sugar solution before it is infused. YONDELIS® is available in a vial that contains 1 mg trabectedin.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

YONDELIS® should be prescribed and managed only by a doctor experienced in anticancer drugs.

In order to avoid irritation at the site of injection, YONDELIS® must be given to you through a central venous line.

YONDELIS® or its combination with CAELYX® must not be used if you have increased blood bilirubin levels.

Serious side effects which have been reported with the use of YONDELIS® include:
- Increase in liver enzymes which can be monitored by lab tests
- Severe muscle pain or weakness (rhabdomyolysis)
- Decrease in white blood cells which may lead to infection
- Blood clots in the lung
- Severe reaction at site of injection

BEFORE you use YONDELIS® talk to your doctor or pharmacist if:
- you have a history of myelosuppression (a decrease in the production of blood cells);
- you have any problems with your kidneys;
- you have any problems with your liver;
- you are pregnant, planning to become pregnant or breast-feeding.

YONDELIS® is not recommended in children or adolescents under 18 years of age.

Contraception and Pregnancy:
Both men and women must use effective contraception while receiving YONDELIS®, and for 3 months after treatment for women and 5 months after treatment for men. You must make sure that you do not become pregnant while receiving YONDELIS®, but if you do, inform your doctor immediately. YONDELIS® may harm your fetus. You should not take YONDELIS® if you are pregnant.

Genetic counselling is 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®.

Breast-Feeding:
YONDELIS® must not be given to patients who are breast-feeding. Therefore you must stop breast-feeding before you start your treatment and you must not begin breast-feeding again until your doctor has confirmed that it is safe to do so.

Driving and using machines:

Tiredness and weakness have been reported in patients receiving YONDELIS®. Do not drive or operate any dangerous tools or machines if you experience such side effects. Even if you have not felt these effects, you must still be cautious.

INTERACTIONS WITH THIS MEDICATION

Inform your doctor, medical health personnel or pharmacist about all medicines you are taking, whether prescribed for you or bought without a prescription.

The following medications may lower the effect of YONDELIS®:
- Rifampin for bacterial infection
- Phenobarbital for epilepsy
- St. John's Wort, an herbal medicine for depression

The following medicines may increase the effect of YONDELIS®:
- Ketoconazole for fungal infections
- Ritonavir for HIV infection
- Clarithomycin for bacterial infections
- Cyclosporine an immune-suppressive medicine
- Verapamil for high blood pressure or heart condition

The following medicines may increase risks of muscle or liver damage (rhabdomyolysis):
- Statins for lowering cholesterol levels

Alcohol must be avoided during treatment with YONDELIS®.

PROPER USE OF THIS MEDICATION

Usual dose:
The dose will be calculated from your height and weight.

For the treatment of metastatic liposarcoma or leiomyosarcoma, the usual dose is 1.5 mg/m^2 body surface area as a 24-hour intravenous infusion.

For the treatment of ovarian cancer, the usual starting dose is 1.1 mg/m^2 body surface area as a 3-hour intravenous infusion after CAELYX® 30 mg/m^2 body surface areas, as a 90-minute intravenous infusion.

The infusion is given every 3 weeks, although occasionally your doctor may recommend dose delays to ensure that you receive the most appropriate dosage of YONDELIS®.

You must be premedicated with corticosteroids such as dexamethasone 20 mg IV, 30 minutes before each YONDELIS® infusion; not only to prevent vomiting, but also because it appears to protect the liver.
Before YONDELIS® is given to you, it is reconstituted and diluted and then put into a drip bag for intravenous use.

In order to avoid irritation at the site of injection, YONDELIS® must be given to you through a central venous line.
During the treatment period, your doctor will carefully monitor you and decide the most appropriate dosage of YONDELIS® to give you. The length of your whole treatment period will depend on your progress and how well you feel. Your doctor will tell you how long your treatment lasts.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed dose:
If you think that you have missed a dose of YONDELIS®, tell your healthcare provider immediately.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, YONDELIS® or its combination with CAELYX® can cause side effects, although not everyone gets them.

Side effects caused by YONDELIS® treatment:
Very common (may affect more than 1 in 10 people) side effects are that you may:
- feel tired
- feel shortness of breath
- bruise more easily
- have nose bleeds
- have a decrease in white blood cells or platelets which may lead to infection or unexpected bruising or bleeding
- have blood infections (neutropenic infection and neutropenic sepsis). Your doctor will order regular blood tests to detect any abnormalities in the blood.
- experience headache and a loss of strength
- 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.
- have diarrhea, 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
- 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 swollen and violaceous. The lesions may either dry out and desquamate, or blister with ulceration.
- increase in blood bilirubin levels which may lead to yellow eyes or skin, dark urine
- lose hair (alopecia)
- low levels of potassium
- sleep disorder (insomnia)

- pain, redness or swelling of the skin at the site of injection

Your doctor may require blood tests in certain situations in order to avoid developing muscle damage to the muscles (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.

Some other common (may affect up to 1 in 10 people) side effects that you may have are:

- a higher skin pigmentation and rash
- coughing
- dizziness, low blood pressure and flushing
- fever. If you have a raised temperature you should seek medical attention immediately
- 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
- a syncope also called fainting
- 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 build up of fluid in the lungs, which leads to swelling (pulmonary oedema)
- pain in your back, muscles and joints
- damage to your nerves which may result in tingling, numbness, and burning sensation in the extremities
- general swelling or swelling of the limbs

In uncommon (may affect up to 1 in 100 people) cases 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, and sleepiness. These signs could mean that your liver is not working properly. If you experience any of these symptoms you should seek medical attention immediately.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Very Common *(may affect more than 1 in 10 people)*			
Decrease in white blood cells or platelets in blood which may lead to infection or unexpected bruising or bleeding		√	
Nausea, vomiting	√		
Fatigue	√		
Loss of appetite	√		
Increase in blood bilirubin levels which may lead to yellow eyes or skin, dark urine		√	
Reddening painful skin on hands and feet		√	
Increase in blood creatine phosphokinase which may lead to muscle pain, weakness, muscle spasms		√	
Mouth ulceration, mucosal inflammation	√		
Common *(may affect up to 1 in 10 people)*			
Fever		√	
Heart muscle problems, including heart failure that may be present as new chest pain, shortness of breath, tiredness, swelling in your legs, ankles or feet, or heart palpitations		√	
Rare *(may affect up to 1 in 1000 people)*			
Allergic reaction (hypersensitivity) that may present as fever, difficulty breathing, redness or flushing of the skin or a rash, feeling sick (nausea) or being sick (vomiting)		√	
Unknown			
Capillary leak syndrome, the symptoms of which may include sudden swelling (edema) of the arms, legs and other parts of the body, occurring with or without sudden drop in blood pressure		√	

This is not a complete list of side effects. For any unexpected effects while taking YONDELIS®, contact your doctor or pharmacist.

HOW TO STORE IT

YONDELIS® should be stored in the refrigerator (2ºC – 8ºC).

The reconstituted solution should not be stored longer than 24 hours at 2ºC to 8ºC.

The total hold time between initial reconstitution and end of treatment should not be longer than 30 hours.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 1908C
    Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect® Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For questions, concerns, or the full Product Monograph go to: www.janssen.com/canada or contact the manufacturer, Janssen Inc., at:
1-800-567-3331 or 1-800-387-8781.

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