

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

ONIVYDE®

Irinotecan Liposome for Injection

Read this carefully before you start taking ONIVYDE and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about ONIVYDE.

Serious Warnings and Precautions

ONIVYDE administration must be supervised by a doctor with experience in the use of cancer chemotherapeutic medicines.

ONIVYDE is not the same as other medicines containing irinotecan. It should not be substituted for other medicines that contain irinotecan.

ONIVYDE can cause severe side effects which include:

- **Diarrhea** that can happen right after you receive ONIVYDE or more than 24 hours after you receive it (late onset). Late onset diarrhea can be life-threatening.
- **Neutropenia** which is a low level of white blood cells. This increases your risk of getting an infection.

What is ONIVYDE used for?

ONIVYDE is used to treat adult patients with metastatic pancreatic cancer (cancer of the pancreas that has already spread elsewhere in the body)

It is used:

- in patients who had their cancer progress after receiving another medicine called gemcitabine, and
- in combination with other cancer medicines called 5-fluorouracil (5-FU) and leucovorin (LV).

How does ONIVYDE work?

ONIVYDE belongs to a group of medicines called “topoisomerase inhibitors”. It is used in combination with other medicines to treat cancer. It blocks an enzyme that is involved in the division of cancer cells. This prevents these cells from multiplying and growing and they eventually die.

The medicine in ONIVYDE is held within small fatty particles called liposomes. The liposomes build up in the tumor and release the medicine slowly over time, which allows it to act for a longer period.

What are the ingredients in ONIVYDE?

Medicinal ingredients:

- Irinotecan (as sucrose octasulfate salt)

Non-medicinal ingredients:

- N-(carbonyl-methoxypolyethylene glycol-2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG-2000-DSPE)
- 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
- cholesterol
- 2-[4-(2-hydroxyl)piperazin-y1]ethanesulfonic acid (HEPES)
- sodium chloride
- sucrose octasulfate
- water for injection

ONVYDE comes in the following dosage forms:

As a sterile 4.3 mg / mL suspension in a single use vial

Do not use ONVYDE if you:

- had a severe allergic reaction to any medicine containing irinotecan in the past
- are allergic to any of the ingredients contained in ONVYDE
- are allergic to any component of the ONVYDE container
- are breast feeding

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ONVYDE. Talk about any health conditions or problems you may have, including if you:

- have previously been given any medicine that contains irinotecan in any form as it acts differently when contained in liposomes than when it is given in its free form and it is unknown if ONVYDE provides a benefit in people who have previously received other medicines containing irinotecan
- have had genetic testing done and been told that you are homozygous for the UGT1A1*28 allele since this could increase your risk of getting neutropenia (decreased white blood cells)
- have or have had liver problems
- have or have had jaundice (yellowing of the skin or eyes)
- have or have had kidney problems
- have or have had lung disease
- are taking medicines to increase your white blood cell count called colony stimulating factors
- have ever received radiation therapy
- are going to receive any vaccine
- are underweight or have been told that you have a low body mass index (less than 18.5 kg / m²)
- have had surgery on your pancreas known as a Whipple procedure
- have a bowel obstruction
- are pregnant, or you and your partner are planning a pregnancy
- are under 18 years of age
- are 75 years of age or older

Other warnings you should know about:**Diarrhea**

If you get diarrhea (loose or watery and frequent stools) contact your healthcare professional immediately. Drink a lot of clear liquids (e.g. water, apple juice, broth, sports drinks, non-fizzy soft drinks) to prevent dehydration (loss of body fluid). Your

healthcare professional may give you a medicine which contains loperamide but it must not be used for longer than 48 hours. If your diarrhea does not go away, contact your healthcare professional. The diarrhea that you get with ONIVYDE can be life-threatening. You must tell your healthcare professional right away if you experience it.

Blood clots

Onivyde has caused blood clots (thrombosis) in some patients. These clots can be in the lung (pulmonary embolism), the veins (venous thrombosis) or the arteries (arterial thromboembolism). Contact your healthcare professional right away if you develop any sign or symptom of a blood clot including:

- swelling, pain, muscle spasms, tenderness or discolouration in the leg or arms
- chest pain, difficulty breathing, shortness of breath, coughing up blood
- slurred speech, face drooping to one side
- weakness, dizziness, headache

Pregnancy and breast-feeding

You should not receive ONIVYDE if you are pregnant as it may harm your baby. You must tell your healthcare professional if you are or think you may be pregnant. Your healthcare professional may give you a pregnancy test before you receive ONIVYDE. Ask your healthcare professional for advice if you are planning to have a baby. If you are receiving ONIVYDE you should not breastfeed until one month after your last dose.

Birth control in men and women

Women:

During your ONIVYDE treatment and for one month after you receive your last dose, you should not become pregnant. Use an effective birth control method during this time. Talk to your healthcare professional for advice on effective methods of birth control.

Men:

Use condoms if you have sex while receiving ONIVYDE and for at least four months after your last dose.

Driving and using machines

ONIVYDE may affect your ability to drive or use machines. Before doing tasks which require special attention like driving, wait until you are feeling well again.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ONIVYDE:

- medicines used to treat seizures like phenytoin, phenobarbital or carbamazepine
- rifampicin, which is a medicine used to treat tuberculosis
- medicines used to treat fungal infections like ketoconazole, fluconazole, itraconazole or voriconazole
- antibiotics like azithromycin, clarithromycin, erythromycin, ciprofloxacin, or norfloxacin
- medicines used to treat HIV infection like indinavir, atazanavir, lopinavir, nelfinavir, ritonavir or saquinavir
- gemfibrozil a medicine used to treat high fat levels in the blood
- an herbal medicine called St. John's wort.
- grapefruit juice - Do NOT drink grapefruit juice while receiving ONIVYDE

How to take ONIVYDE:

- ONIVYDE will be given to you by a healthcare professional with experience in the use of cancer chemotherapeutic medicines
- It will be infused directly into your vein.
- Follow all instructions given to you by your healthcare professional.

Your healthcare professional will decide how much ONIVYDE you will receive. ONIVYDE will be infused into your vein, typically over a period of 90 minutes. This will be followed by the infusion of two other cancer medicines, LV and 5-FU.

This treatment will be repeated every two weeks. Your healthcare professional may give you a lower dose of ONIVYDE, delay, or stop treatment.

You healthcare professional may give you other medicines to prevent nausea, vomiting, diarrhea or allergic reactions.

Overdose:

If you think you have received too much ONIVYDE, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using ONIVYDE?

These are not all the possible side effects you may feel when taking ONIVYDE. If you experience any side effects not listed here, contact your healthcare professional.

Side effects that may resolve on their own after treatment with ONIVYDE is finished include:

- hair loss

If this affects you severely, tell your healthcare professional.

ONIVYDE may cause abnormal blood test results. Your doctor will perform blood tests before you receive ONIVYDE and while you are receiving it. Your doctor may change how much ONIVYDE you get, delay treatment, or stop your treatment based on the results of these tests.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Neutropenia (decreased white blood cells): aches, feeling tired, fever, flu-like symptoms, infections.		X	
Anemia (decreased red blood cells): dizziness, feeling tired and weak, loss of energy, shortness of breath.		X	
Thrombocytopenia (decreased platelets in the blood); bleeding, bruising, fatigue, weakness.		X	
Diarrhea (loose or watery and frequent stools)		X	
Nausea	X		
Vomiting	X		
Stomatitis (mouth sores and swelling): burning sensation and pain in the mouth, difficulty eating, swelling or sores in the mouth.		X	
Weight loss	X		
Loss of appetite	X		
Hypokalemia (low level of potassium in the blood): generally feeling unwell, irregular heartbeat, muscle cramps, paralysis, twitches or weakness.		X	
Feeling tired	X		
Fever (increase in body temperature)		X	
COMMON			

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Sepsis and septic shock (life-threatening complication of an infection): chills, high or very low body temperature, little or no urine, low blood pressure, palpitations, rapid breathing, rapid heartbeat.		X	
Gastroenteritis (inflammation of the stomach and intestines): abdominal pain, diarrhea, nausea, vomiting.		X	
Diarrhea followed by a stuffy and runny nose, sneezing, post-nasal drip, increased salivation, flushing, slowing of heartbeat, constriction of pupils, watery eyes and production of tears, sweating, abdominal cramping.		X	
Dehydration (loss of body fluid): confusion, dizziness, dry mouth, fainting, feeling thirsty, headache, irritability, urinating less than normal.		X	
Hypomagnesemia (low level of magnesium in the blood): feeling tired, loss of appetite, muscle spasms, shaking, vomiting, weakness.		X	
Thrombotic events (blood clot in a blood vessel): pain, swelling or redness in one part of the body.			X
Infection or allergic reaction at injection site: pain, redness or swelling.		X	
Acute kidney failure (fast decline in proper functioning of the kidney): confusion, feeling weak, nausea, loss of appetite, personality changes, vomiting.		X	
Pneumonia (infection of the lungs): cough, difficult or painful breathing, fever, shortness of breath, wheezing.		X	
UNCOMMON			
Arterial thromboembolism and venous thrombosis (blood clots in arteries and veins): swelling, pain, muscle spasms, tenderness or discoloration in the legs or arms, chest pain, shortness of breath. slurred speech, face drooping to one side, weakness, dizziness, headache			X
Stroke (loss of blood to the brain): confusion, feeling dizzy, numbness or weakness in an arm or leg or the face, loss of coordination, muscle weakness, trouble seeing or speaking, sudden severe headache.			X

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Heart attack (loss of blood supply to the heart): sudden chest pain, pressure or discomfort, feeling faint, feeling anxious, shortness of breath, irregular heartbeat, nausea, sudden heavy sweating.			X
Pulmonary embolism (blood clot in the lungs): coughing up of blood, difficulty breathing, sharp pain in the chest, sudden shortness of breath.			X

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Refrigerate ONIVYDE at 2°C to 8°C (36°F to 46°F). Do not freeze. Protect from light.

ONIVYDE is a cytotoxic drug. All applicable special handling and disposable procedures must be followed.

If you want more information about ONIVYDE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada.html>), the manufacturer’s website www.servier.ca or by calling 1-800-363-6093.

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