

Alvinotec®

Irinotecan Hydrochloride

Concentrate for Solution for Infusion

Read this leaflet carefully before you start taking Alvinotec®. This leaflet provides answers to the most common questions. If you have any further questions, ask your doctor or pharmacist. This medicine has been prescribed for your current illness only. Do not take it in similar conditions and do not pass it on to others. The information in this leaflet was last updated on the date listed on the bottom of the page. More recent information on the medicine may be available. You should ensure that you speak to your doctor or pharmacist to obtain the most up-to-date scientific information on the medicine. The latest version of this leaflet is available on www.nanoalvand.com.

What is in this leaflet

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1. What Alvinotec® is and what it is used for

Alvinotec® is an anticancer medicine containing the active substance irinotecan hydrochloride trihydrate. This medicine interferes with the growth and spread of cancer cells in the body.

Alvinotec® is indicated in combination with other medicines for the treatment of patients with advanced or metastatic cancer of the colon or rectum.

Alvinotec® may be used alone in patients with metastatic cancer of the colon or rectum whose disease has recurred or progressed following initial fluorouracil-based therapy.

2. What you need to know before you use Alvinotec®

Do not use Alvinotec®

- if you are allergic to irinotecan hydrochloride trihydrate or any of the other ingredients of this medicine (listed in section 6 "What Alvinotec® contains").
- if you have chronic inflammatory bowel disease and/or bowel obstruction.
- if you are breast-feeding.
- if your bilirubin level is higher than 3 times the upper limit of the normal range.
- if you have severe bone marrow failure.
- if you are in poor general condition.
- if you are taking or have recently taken St. John's Wort (a herbal extract containing Hypericum perforatum).
- if you are to take or have recently taken live attenuated vaccines (vaccines against yellow fever, chicken pox, shingles, measles, mumps, rubella, tuberculosis, rotavirus, influenza) and during the 6 months after stopping chemotherapy.

If you receive Alvinotec® in combination with other medicines, please make sure that you also read the package leaflet of the other medicines regarding additional contraindications.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Alvinotec®, if you have Gilbert's syndrome, an inherited condition that can cause elevated bilirubin levels and jaundice (yellow skin and eyes)

Diarrhea

Alvinotec® can cause diarrhea, which in some cases may be severe. This may start a few hours or a couple of days after the medicine infusion. If left untreated, it could lead to dehydration and serious chemical imbalances, which can be life-threatening. Your doctor will prescribe medicine to help prevent or control this side effect. Make sure you get the medicine right away, so that you will have it at home when you need it.

- Take the medicine as prescribed at the first sign of loose or frequent bowel movements.
- Drink large amounts of water and (or) salty drinks (fizzy water, soda or soup).
- Call your doctor or nurse know if you still have diarrhea, especially if it lasts more than 24 hours, or if you get lightheaded, dizzy, or faint.

Neutropenia (decrease in some white blood cells)

This medicine can lower your white blood cell count, mainly in the weeks after the medicine is given. This can increase the risk of getting an infection. Be sure to let your doctor or nurse know right away if you have any signs of infection, such as fever (38°C or higher), chills, pain when passing urine, a new cough, or bringing up sputum. Avoid being near people who are sick or have infections. Tell your doctor at once if you develop signs of infection.

Blood monitoring

Your doctor will likely test your blood before and during your treatment, to check for effects of the medicine on blood counts or on blood chemistry. Based on the test results, you may need medicines to help treat the effects. Your doctor may also need to reduce or delay your next dose of this medicine, or even stop it altogether. Keep all your appointments for doctor visits and lab tests.

This medicine may lower your platelet count in the weeks after it is given, which can increase your risk of bleeding. Speak with your doctor before taking any medicines or supplements that might affect your body's ability to stop bleeding, such as aspirin or aspirin-containing medicines, warfarin, or vitamin E. Tell your doctor right away if you have unusual bruising, or bleeding such as nosebleeds, bleeding gums when you brush your teeth, or black, tarry stools.

Nausea and vomiting

You may have nausea and vomiting on the day you receive this medicine or in the first few days after. Your doctor may give you medicine before your treatment to help prevent nausea and vomiting. Your doctor will likely prescribe anti-nausea medicines that you can take at home. Have these medicines on hand for when you need them. Call your doctor if you are unable to take fluids by mouth due to nausea and vomiting.

Acute cholinergic syndrome

This medicine may affect part of your nervous system that controls body secretions, leading to what is known as cholinergic syndrome. Symptoms can include runny nose, increased saliva, excess tears in the eyes, sweating, flushing, abdominal cramps, and diarrhea. Let your doctor or nurse know right away if you notice any of these symptoms, as there are medicines that can help control them.

Lung disorders

Rarely, people on this medicine have serious lung problems. Tell your doctor right away if you have new or worsening cough, trouble breathing, and fever. Your doctor may need to stop your treatment to manage this problem. This medicine may increase your risk of major blood clots in the veins of the legs or lungs, which can travel to other parts of the body such as the lungs or brain. Tell your doctor right away if you notice chest pain, shortness of breath, or swelling, pain, redness, or warmth in an arm or leg.

Chronic intestinal inflammation and/or intestinal blockage

Call your doctor if you have pain in your belly and you cannot move your bowels, especially if you also have bloating and loss of appetite.

Irradiation therapy

If you recently received treatment with pelvic or abdominal radiotherapy, you may be at increased risk of developing bone marrow suppression. Please talk to your doctor before starting the Alvinotec®.

Kidney function

Occurrences of kidney dysfunction have been reported.

Cardiac disorders

Inform your doctor if you suffer/suffered from heart disease or if you previously received anticancer medicines. Your doctor will monitor you closely and discuss with you how risk factors (for example smoking, high blood pressure and high fat content) can be reduced.

Vascular disorders

Alvinotec® is rarely associated with blood flow disorders (blood clots in the vessels of your legs and lungs) and it may occur rarely in patients with multiple risks factors.

Others

This medicine may cause sores in the mouth or on the lips, often within the first few weeks after starting treatment. This can cause mouth pain, bleeding, or even trouble eating. Your doctor or nurse can suggest ways to reduce this, such as changing the way you eat or how you brush your teeth. If needed, your doctor can prescribe medicine to help with the pain.

Tell your doctor or dentist that you are on this medicine if you are planning to have surgery or any procedure.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Other medicines and Alvinotec®

Alvinotec® can interact with a number of medicines and supplements, which may either raise or lower the level of the medicine in your blood. Tell your doctor, nurse or pharmacist if you are using, have recently used or might use any of the following:

- medicines used to treat seizure (carbamazepine, phenobarbital, phenytoin and fosphenytoin)
- medicines used to treat fungal infection (ketoconazole, itraconazole, voriconazole and posaconazole)
- medicines used to treat bacterial infection (clarithromycin, erythromycin and telithromycin)
- medicines used to treat tuberculosis (rifampicin and rifabutin)
- St. John's Wort (Hypericum perforatum)
- live attenuated vaccines
- medicines used to treat HIV (indinavir, ritonavir, amprenavir, fosamprenavir, nelfinavir, atazanavir, and others)
- medicines used to suppress your body's immune system to prevent transplant rejection (cyclosporine and tacrolimus)
- medicines used to treat cancer (regorafenib, crizotinib, idelalisib and apalutamide)
- vitamin K antagonists (common blood thinner such as warfarin)
- medicines used to relax muscles during general anaesthesia and surgery (suxamethonium)
- 5-fluorouracil/folinic acid
- bevacizumab (a blood vessel growth inhibitor)
- cetuximab (an EGF receptor inhibitor)

Tell your doctor, pharmacist or nurse before being given Alvinotec® if you are already having, or have recently had chemotherapy (and radiotherapy).

Don't start or stop taking any medicines while you are on Alvinotec® without talking with your doctor first.

This medicine can cause serious diarrhea. Try to avoid laxatives and stool softeners while taking this medicine.

There may be more medicines that interact with Alvinotec®. Check with your doctor, pharmacist or nurse about your other medicines, herbs, and supplements, and whether alcohol can cause problems with this medicine.

Contraception, pregnancy, breast-feeding and fertility

Pregnancy

This medicine may cause problems with the fetus if taken at the time of conception or during pregnancy. Before initiating treatment, your doctor will ensure that you are not pregnant.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Contraception

If you are a woman of childbearing age, then you have to use effective contraception during and up to 6 months after stopping treatment.

As a man, you have to use effective contraception during and up to 3 months after stopping treatment. It is important to check with your doctor about what kinds of birth control can be used with this medicine.

Breast-feeding

Irinotecan and its metabolite were measured in human milk. Breast-feeding should be discontinued for the duration of your treatment with this medicine.

If you are breast-feeding, ask your doctor or pharmacist for advice before taking this medicine.

Fertility

No studies have been done, nevertheless, this medicine may affect fertility. Prior to taking this medicine talk with your doctor about the possible risk with this medicine and the options that may preserve your ability to have children.

Driving and using machines

You may notice that you are dizzy and/or have trouble with your vision in the first 24 hours or so after you take this medicine. Do not drive or operate machinery if you have this side effect.

Alvinotec® contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

Alvinotec® contains sorbitol

This medicine contains a sugar (sorbitol). Sorbitol is a source of fructose. If you have hereditary fructose intolerance (HFI), a rare genetic disorder, you must not receive this medicine. Patients with HFI cannot break down fructose, which may cause serious side effects.

You must tell your doctor before receiving this medicine if you have HFI or can no longer take sweet foods or drinks because you feel sick, vomit or get unpleasant effects such as bloating, stomach cramps or diarrhea.

This medicine contains 45 mg sorbitol in each ml which is equivalent to 90 mg/2 ml, 225 mg/5 ml and 675 mg/15 ml.

3. How to use Alvinotec®

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Alvinotec® will be given to you by healthcare professionals.

Your doctor may recommend a DNA test before your first dose of Alvinotec®.

Some people are genetically more likely to have certain side effects from the medicine.

The amount of Alvinotec® that you will receive depends on many factors, including your height and weight, your general health or other health problems, and the type of cancer or condition being treated. Your doctor will determine your dose and schedule.

Alvinotec® is injected into a vein through an intravenous route (IV). You will receive this injection in a clinic or hospital setting. Alvinotec® must be given slowly, and the IV infusion can take up to 90 minutes to complete.

You may be given other medications to prevent nausea, vomiting, diarrhea, and other side effects while you are receiving Alvinotec®. You may need to keep using these medicines for at least a day after your Alvinotec® injection.

Tell your care givers if you feel any burning, pain, or swelling around the IV needle when Alvinotec® is injected. If the medicine escapes from the vein it can cause tissue damage.

Only your doctor may assess the duration of treatment.

There are currently several treatment schedules recommended for Alvinotec®. It is usually given either once every 3 weeks (Alvinotec® given alone) or once every 2 weeks (Alvinotec® given in combination with 5FU/FA chemotherapy). The dose will depend on a number of factors, including the treatment schedule, your body size, your age and general health, your blood counts, how well your liver is working, whether you have had radiation to your abdomen/pelvis, and whether you have any side effects such as diarrhea.

If you use more Alvinotec® than you should

Seek emergency medical attention. Overdose symptoms may include some of the serious side effects listed in this medication guide.

If you forget to use Alvinotec®

Call your doctor for instructions if you miss an appointment for your Alvinotec® injection.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor if you get any side effects, including those not listed in this leaflet.

Some side effect could be serious. You must immediately contact your doctor if you experience any of those following serious side effects (see section 2).

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficult breathing; swelling of your face, lips, tongue, or throat.

Diarrhea

Early diarrhea: Occurring within 24 hours of receiving this medicine, accompanied by symptoms runny nose, increased salivation, watery eyes, sweating, flushing, abdominal cramping. (This can occur while the medicine is being administered. If so, alert your healthcare professional promptly. Medication can be given to stop and/or lessen this early side effect).

Late diarrhea: Occurring greater than 24 hours of receiving this medicine. Because of concerns of dehydration and electrolyte imbalances with diarrhea it is important to be in contact with health care professionals for monitoring, and for medication and diet modifications advice.

Talk to your doctor or nurse if you experience any of the symptoms below:

Very common (may affect more than 1 in 10 people)

- abnormally low number of white blood cells which could put you at increased risk for infection
- low number of red blood cells causing tiredness and shortness of breath
- decreased appetite
- cholinergic syndrome (see "Warnings and precautions")
- vomiting
- nausea
- abdominal pain (Combination Therapy: common)
- hair loss (reversible)
- inflammation of mucous membranes
- fever (Combination Therapy: common)
- feeling weak and having no energy

Common (may affect up to 1 in 10 people)

- low number of platelets which may cause bruising or bleeding (Combination Therapy: very common)
- abnormal liver function test values (Combination Therapy: very common)
- infection
- low number of white blood cells with fever
- difficulty in passing stools
- abnormal kidney function test values

Not known (frequency cannot be estimated from the available data)

- severe, persistent or bloody diarrhea (which may be associated with stomach pain or fever) caused by bacteria called Clostridium difficile
- blood infection
- dehydration (due to diarrhea and vomiting)
- dizziness, rapid heartbeat and pale skin (a condition called hypovolemia)
- allergic reaction
- temporary speech disorders during or shortly after treatment
- pins and needles

- high blood pressure (during or after infusion)
- heart problems*
- lung disease causing wheezing and shortness of breath (see section 2)
- hiccups
- intestinal blockage
- enlarged colon
- bleeding from the bowels
- inflammation of the large intestine
- abnormal lab test results
- hole in the intestine
- fatty liver disease
- skin reactions
- reactions at the site where the medicine was administered
- low level of potassium in the blood
- low level of salt in the blood mostly related with diarrhea and vomiting
- muscle cramps
- kidney problems*
- low blood pressure*
- fungal infections
- viral infections

* Infrequent cases of these events have been observed in patients who experienced episodes of dehydration associated with diarrhea and/or vomiting, or infections of the blood.

5. How to store Alvinotec®

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date.
- Store below 30°C. do not freeze.
- Store in the original package in order to protect from light.
- After dilution, chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C.
- From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.
- Cytotoxic agent. Must be transported, stored and used according to guidelines for handling of cytotoxic compounds.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Alvinotec® contains

The active substance is irinotecan hydrochloride trihydrate 20 mg/ml equivalent to irinotecan 17.33 mg/ml. The other ingredients are sorbitol, lactic acid, sodium hydroxide, hydrochloric acid, and water for injection.

What Alvinotec® looks like and contents of the pack

Alvinotec® is a clear, colorless, and free of particulate matter solution.

Alvinotec® is supplied in three strengths. One vial of Alvinotec® contains 40 mg/2 ml, 100 mg/5 ml, or 300 mg/15 ml of irinotecan hydrochloride trihydrate.

Each vial is packed in a box with a leaflet.

Not all strengths may be marketed.

For medical or healthcare professionals only

Like all anti-neoplastic substances, Alvinotec® must be prepared and handled carefully. The use of protective glasses, mask and gloves is required. If Alvinotec® comes into contact with your skin, wash it off immediately and thoroughly with soap and water. If Alvinotec® comes into contact with your mucous membranes, wash it off immediately and thoroughly with water.

As with all injectable drugs, Alvinotec® must be prepared under aseptic conditions.

If a clouding, condensation or precipitate is visible in the vial or after dilution of the concentrate, the medicine may not be used and must be disposed of.

Preparation of the solution for infusion

Aseptically withdraw the calculated amount of Alvinotec® concentrate for solution for infusion from the vial into a syringe and transfer into a 250 ml infusion bag or bottle containing either 0.9% (w/v) sodium chloride solution or 5% (w/v) dextrose infusion solution. Mix the solution for infusion in the infusion bag or bottle thoroughly by manual rotation.

Do not mix with other medicines.

Shelf life

The diluted solution is physically and chemically stable up to 24 hours as a solution for infusion (9% (w/v) sodium chloride solution and 5% (w/v) dextrose solution) when stored at 2°C to 8°C when protected from light.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

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