Package leaflet: Information for the user

Irinotecan Hydrochloride 20 mg/mL concentrate for solution for infusion
irinotecan hydrochloride, trihydrate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Irinotecan Hydrochloride is and what it is used for

Irinotecan Hydrochloride is an anticancer medicine containing the active substance irinotecan hydrochloride, trihydrate.

Irinotecan hydrochloride, trihydrate interferes with the growth and spread of cancer cells in the body.

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

Irinotecan Hydrochloride 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 Irinotecan Hydrochloride

Do not use Irinotecan Hydrochloride:
- if you have chronic inflammatory bowel disease and/or bowel obstruction
- if you are allergic to irinotecan hydrochloride trihydrate or any of the other ingredients of this medicine (listed in section 6 “What Irinotecan Hydrochloride contains”)
- if you are a breast-feeding woman (see section 2)
- 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 (WHO performance status higher than 2)
- if you are taking or have recently taken St John’s Wort (a herbal extract containing *Hypericum*)
- 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 Irinotecan Hydrochloride 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 Irinotecan Hydrochloride.

- If you have Gilbert's syndrome, an inherited condition that can cause elevated bilirubin levels and jaundice (yellow skin and eyes)

Take special care with Irinotecan Hydrochloride. The use of Irinotecan Hydrochloride should be confined to units specialised in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a physician qualified in the use of anticancer chemotherapy.

Diarrhoea
Irinotecan Hydrochloride can cause diarrhoea, 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 if you still have diarrhoea, 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 diarrhoea. 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 Irinotecan Hydrochloride.

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 to high fat content) can be reduced.

Vascular disorders
Irinotecan Hydrochloride 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.

For contraception and breast-feeding information, refer to the information provided below under section Contraception, pregnancy, breast-feeding and fertility.

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

If used in combination with other anticancer medicines for your condition please make sure that you also read the leaflets for the other medicine.

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

Other medicines and Irinotecan Hydrochloride
Irinotecan Hydrochloride 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 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 (clarithromycine, erythromycin and telithromycine)
- Medicines used to treat tuberculosis (rifampicin and rifabutin)
- St. John's Wort (a herbal dietary supplement)
- 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 used 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 Irinotecan Hydrochloride if you are already having, or have recently had chemotherapy (and radiotherapy).

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

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

There may be more medicines that interact with Irinotecan Hydrochloride. 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

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.

Pregnancy

This medicine may cause problems with the foetus 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.

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.

This medicine contains sorbitol
This medicine contains a sugar (sorbitol). Sorbitol is a source of fructose. If you (or your child) have hereditary fructose intolerance (HFI), a rare genetic disorder, you (or your child) 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 (or your child) have HFI or if your child can no longer take sweet foods or drinks because they feel sick, vomit or get unpleasant effects such as bloating, stomach cramps or diarrhoea.

This medicine contains 45 mg sorbitol in each mL which is equivalent to 90 mg/2 mL, 225 mg/5 mL and 1125 mg/25 mL.

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

3. How to use Irinotecan Hydrochloride

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

Irinotecan Hydrochloride will be given to you by healthcare professionals.

Your doctor may recommend a DNA test before your first dose of Irinotecan Hydrochloride.

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

The amount of Irinotecan Hydrochloride 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.

Irinotecan Hydrochloride is injected into a vein through an intravenous route (IV). You will receive this injection in a clinic or hospital setting. Irinotecan Hydrochloride 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, diarrhoea, and other side effects while you are receiving Irinotecan Hydrochloride. You may need to keep using these medicines for at least a day after your Irinotecan Hydrochloride injection.

Tell your care givers if you feel any burning, pain, or swelling around the IV needle when Irinotecan Hydrochloride is injected. If the medicine escapes from the vein it can cause tissue damage. If you experience pain or notice redness or swelling at the IV site while you are receiving Irinotecan Hydrochloride, alert your healthcare professional immediately.

There are currently several treatment schedules recommended for Irinotecan Hydrochloride. It is usually given either once every 3 weeks (Irinotecan Hydrochloride given alone) or once every 2 weeks (Irinotecan Hydrochloride 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 diarrhoea.

Only your doctor may assess the duration of treatment.

If you use more Irinotecan Hydrochloride 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 Irinotecan Hydrochloride
Call your doctor for instructions if you miss an appointment for your Irinotecan Hydrochloride injection.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effects 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.

- Diarrhoea (see section 2)
  - Early diarrhoea: 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 diarrhoea: Occurring greater than 24 hours of receiving this medicine. Because of concerns of dehydration and electrolyte imbalances with diarrhoea 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:

Symptoms	**Frequency[*] of occurrence in Monotherapy**	**Frequency[†] of occurrence in Combination Therapy**
Abnormally low number of white blood cells which could put you at increased risk for infection	Very common	Very common
Low number of red blood cells causing tiredness and shortness of breath	Very common	Very common
Decreased appetite	Very common	Very common
Cholinergic syndrome (see Take special care with Irinotecan Hydrochloride)	Very common	Very common

Symptoms	**Frequency[*] of occurrence in Monotherapy**	**Frequency[†] of occurrence in Combination Therapy**
Vomiting	Very common	Very common
Nausea	Very common	Very common
Abdominal pain	Very common	Common
Hair loss (reversible)	Very common	Very common
Inflammation of mucous membranes	Very common	Very common
Fever	Very common	Common
Feeling weak and having no energy	Very common	Very common
Low number of platelets (blood cells that help with clotting) which may cause bruising or bleeding	Common	Very common
Abnormal liver function test values	Common	Very common
Infection	Common	Common
Low number of white blood cells with fever	Common	Common
Difficulty in passing stools	Common	Common
Abnormal kidney function test values	Common	Not reported

[*] Very common: may affect more than 1 in 10 people

[†] Common: may affect up to 1 in 10 people

Not known: frequency cannot be estimated from the available data

- Severe, persistent or bloody diarrhoea (which may be associated with stomach pain or fever) caused by bacteria called (*Clostridium difficile*)
- Blood infection
- Dehydration (due to diarrhoea and vomiting)
- Dizziness, rapid heartbeat and pale skin (a condition called hypovolaemia)
- 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 diarrhoea 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 diarrhoea and/or vomiting, or infections of the blood.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Irinotecan Hydrochloride

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month. Shelf life: The shelf life of unopened vials is 3 years. Once opened, vials should be used immediately as they contain no antimicrobial preservatives.
- Concentrate: Keep vials in the outer carton in order to protect from light. Do not freeze.
- Diluted concentrate: For single use only. Unused solution should be discarded
- Following dilution: Chemical and physical in-use stability has been demonstrated in glucose 50 mg/mL (5%) and sodium chloride 9 mg/mL (0.9%) for 72 hours at 2-8 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would

normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine if you notice particles visible in the concentrate or infusion solution.

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 Irinotecan Hydrochloride contains

- The active substance is irinotecan hydrochloride, trihydrate. Each millilitre (mL) of solution contains 20 milligrams (mg) of irinotecan hydrochloride, trihydrate, equivalent to 17.33 mg irinotecan.
- The other ingredients are sorbitol (E420), lactic acid, Water for Injections, and sodium hydroxide and hydrochloric acid (used to adjust pH) (see section 2).

What Irinotecan Hydrochloride looks like and contents of the pack

Irinotecan Hydrochloride is in the form of a concentrate for solution for infusion (a concentrated solution which is diluted to make a solution which is given as a slow infusion via a drip).

The medicine comes in glass containers called vials, containing 2 mL, 5 mL and 25 mL of irinotecan hydrochloride, trihydrate.

The vials are wrapped in a protective plastic to reduce the risk of spillage if the vials break - these are referred to as ONCO-TAIN® vials.

The vials are available in single packs. Not all presentations may be marketed.

Marketing Authorisation Holder
Hospira UK Limited
Walton Oaks
Walton-On-The-Hill
Dorking Road
Tadworth
Surrey
KT20 7NS
UK

Manufacturer

Pfizer Service Company BV
Hoge Wei 10
1930 Zaventem
Belgium

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Spain	Irinotecan Hospira
United Kingdom (Northern Ireland)	Irinotecan Hydrochloride
Portugal	Faultenocan

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The following information is intended for healthcare professionals only:

Instructions for personnel regarding safe handling of Irinotecan Hydrochloride

As with other antineoplastic agents, Irinotecan Hydrochloride infusions must be prepared and handled with caution. The use of glasses, mask and gloves is required.

Pregnant women should not handle cytotoxics.

If Irinotecan Hydrochloride concentrate or infusion solutions should come into contact with the skin, wash immediately and thoroughly with soap and water. If Irinotecan Hydrochloride concentrate or infusion solutions should come into contact with the mucous membranes, wash immediately with water.

Preparation of the solution for infusion
As with any other infusion, Irinotecan Hydrochloride infusion must be prepared aseptically.

Aseptically withdraw the required amount of Irinotecan Hydrochloride concentrate from the vial with a calibrated syringe and inject into a 250 mL infusion bag or bottle containing either 9 mg/mL (0.9%) sodium chloride solution or 50 mg/mL (5%) glucose solution only. The infusion should then be thoroughly mixed by manual rotation. Do not mix with any other medicines.

Shelf life
Once opened, vials of Irinotecan Hydrochloride should be used immediately as they contain no antimicrobial preservatives.

Stability after dilution:
Chemical and physical in-use stability has been demonstrated in glucose 50 mg/mL (5%) and in sodium chloride 9 mg/mL (0.9%) for 72 hours at 2 to 8 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Warnings against some visible signs of deterioration
If any precipitate is observed in the vials or in the infusion solution, the product must be discarded according to standard procedures for cytotoxic agents.

Administration
For information on administration, please read the Summary of Product Characteristics for Irinotecan Hydrochloride.

Disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.