PART III: CONSUMER INFORMATION

[Pr]Irinotecan Hydrochloride Injection USP

(Irinotecan hydrochloride trihydrate)

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

This leaflet provides some useful information about your medicine. Please read it carefully before you start your treatment with Irinotecan Hydrochloride Injection USP.

It is important to remember that other physicians, pharmacists or nurses with whom you come into contact may not be fully familiar with your condition or with all of the side effects of the treatments that you will be receiving. For this reason, it is important that you keep this information with you and share it with your family doctor, home-care nurse, emergency room physician, or other medical personnel who may be assisting you.

ABOUT THIS MEDICATION

What the medication is used for:
Irinotecan Hydrochloride Injection USP is a chemotherapy drug (drug used to treat cancer), used:

- in combination with other drugs to treat cancers of the colon and rectum that have spread to other areas of the body;
- alone to treat cancers of the colon and rectum that have spread to other areas of the body and were not able to be treated effectively with 5-fluorouracil-based therapy.

What it does:
Irinotecan Hydrochloride Injection USP, like most chemotherapy agents, works by killing rapidly dividing cells, such as cancer cells. In some cancers, chemotherapy can be used to reduce tumour size, or stop them from growing.

When it should not be used:
Do not use Irinotecan Hydrochloride Injection if:

- you are allergic to the product or any of its ingredients (see below);
- you have hereditary fructose intolerance.

Irinotecan Hydrochloride Injection USP should not be used with certain antifungals (eg. ketoconazole, fluconazole, itraconazole).

What the medicinal ingredient is:
Each mL of Irinotecan Hydrochloride Injection USP contains 20 mg of irinotecan hydrochloride trihydrate.

What the important nonmedicinal ingredients are:
Irinotecan Hydrochloride Injection USP also contains the following non-medicinal ingredients: Sorbitol, Lactic Acid, Water For Injection, Sodium Hydroxide and Hydrochloric Acid.

What dosage forms it comes in:
Irinotecan Hydrochloride Injection USP is supplied as a sterile, clear, colourless to pale yellow solution. Irinotecan Hydrochloride Injection USP is available in single use amber glass ONCO-TAIN® vials in 40 mg/2 mL, 100 mg/5 mL and 500 mg/25 mL formats (single packs).

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Irinotecan Hydrochloride Injection USP should be given under the supervision of a doctor who is experienced in the use of anti-cancer drugs. Serious side effects with the use of Irinotecan Hydrochloride Injection USP include:

- Severe early and late forms of diarrhea that can be life-threatening as they may lead to dehydration (fluid loss) and electrolyte (salt) imbalance.
- Bowel inflammation (typhlitis and colitis), lack of bowel movement (ileus), or a hole in the wall of the small intestine or large bowel (intestinal perforation).
- Decreased production of blood cells resulting in neutropenia (low blood level of immune cells).
- Cases of bacterial, fungal and viral infections, sometimes fatal and/or life-threatening.

BEFORE you use Irinotecan Hydrochloride Injection USP talk to your doctor or pharmacist if any of the following applies to you:

- If you have low blood cell counts due to a decreased ability of the bone marrow to produce blood cells.
- If you have liver or lung disease.
- If you have a heart disease, recent heart attack or irregular heartbeat.
- If you are taking other drugs (including laxatives, diuretics/fluid pills) or have been previously treated with Irinotecan Hydrochloride Injection USP or other anti-cancer drugs.
- If you are taking antibiotics, antifungals (eg. ketoconazole), heart medications (calcium channel blockers), anticonvulsants (eg. phenytoin, phenobarbital, carbamazepine), atazanavir sulfate (an anti-HIV medication), or natural health products (eg. St. John's Wort).
- If you have diarrhea, constipation, or trouble eating and drinking.
- If there is any possibility that you may become pregnant, ask your physician about using birth control to prevent pregnancy during your treatment with Irinotecan Hydrochloride Injection USP. Tell your physician right away if you become pregnant during treatment. Irinotecan

Hydrochloride Injection UP can be harmful to an unborn child.
- If you have been nursing, you should stop before starting treatment with Irinotecan Hydrochloride Injection USP. Ask your baby's physician to recommend a formula that would be best for your baby.
- If you wish to have a baby in the future.
- If you have colitis (bowel inflammation) / ileus (lack of bowel movement).
- If you are undergoing or have previously undergone radiation treatment.
- If you have diabetes.

Men undergoing treatment with Irinotecan Hydrochloride Injection USP should discuss effective contraceptive methods with their doctor.

Before you use Irinotecan Hydrochloride Injection USP, talk to your physician to understand what kind of tests will be needed before and during treatment. Your doctor will order blood tests to check your blood count (white blood cells, red blood cells, and platelets), heart and liver function, X-rays or other tests. These tests will help your physician determine your condition before and during treatment.

Will I be able to work?
Some people work full time, while others work part time or wait until their chemotherapy treatments are finished before returning to work. It depends on the type of job you have and the side effects you experience.

Will I be able to drive and use machines?
Many of the side effects of Irinotecan Hydrochloride Injection USP such as fatigue and changes in vision could affect your ability to drive and operate machinery. Pay attention to how you are affected by the medication and avoid driving, using machines or doing any other activity that would require you to be alert or have accurate vision.

What happens after treatment?
After you have completed all your chemotherapy treatments, your doctor will check you regularly to make sure the cancer has not returned.

INTERACTIONS WITH THIS MEDICATION

Some drugs (prescription and over-the-counter), herbal medicines and foods can increase the severity of side effects caused by Irinotecan Hydrochloride Injection USP or can decrease the efficacy of Irinotecan Hydrochloride Injection USP.

Talk to your doctor about these or any other medications you take before you start treatment with Irinotecan Hydrochloride Injection USP:
- antibiotics (eg. ciprofloxacin, norfloxacin, clarithromycin, erythromycin, azithromycin, rifampin);
- antifungals (eg. ketoconazole, fluconazole, itraconazole);
- heart medications (eg. calcium channel blockers, such as verapamil, diltiazem, nifedipine);
- anticonvulsant (antiepileptic) drugs (eg. phenytoin, phenobarbital and carbamazepine);
- Atazanavir sulfate (an anti-HIV medication).

Some herbal medicines/supplements, such as St. John's Wort, could potentially make Irinotecan Hydrochloride Injection USP less effective in treating your cancer. Talk to your doctor about any herbal medicine/supplement you are taking.

Do not drink grapefruit juice when on Irinotecan Hydrochloride Injection USP.

PROPER USE OF THIS MEDICATION

Usual dose:
Your physician will determine your dose and the length of your treatment based on your treatment goals, the medicines you receive, and how your body responds to those medicines.

Chemotherapy is usually given in cycles that include rest periods between treatments. The rest periods give your body a chance to build healthy new cells and regain your strength before your next treatment. You may receive one dose of Irinotecan Hydrochloride Injection USP every week for four weeks (on Day 1, 8, 15, 22 of the cycle) followed by a 2-week rest. Or, you may receive Irinotecan Hydrochloride Injection USP once every 2 weeks (on Day 1, 15, 29 of the cycle) followed by a 1-week rest. Or, you may receive Irinotecan Hydrochloride Injection USP once every 3 weeks. Your treatment cycle will depend on your medical condition and the other chemotherapy medicines you are getting. Do not skip doses or make changes in your treatment on your own.

It is very important to always go to your medical or laboratory appointments, as indicated by your physician or nurse.

How is Irinotecan Hydrochloride Injection USP given?
You receive Irinotecan Hydrochloride Injection USP through a vein in the arm ("intravenously" or "IV"), usually in the hospital, outpatient department or clinic. To administer Irinotecan Hydrochloride Injection USP, your physician or nurse will insert a thin needle or plastic tube (IV) in a vein which allows fluid to drip into your vein from a plastic bag.

If you are getting many treatments over several weeks or months, for your convenience, your physician may insert a catheter (thin tube) or port into a large vein in your body that is placed there as long as it is needed. Medicines get injected through the catheter or port rather than directly into a vein.

It usually takes about 90 minutes to inject Irinotecan Hydrochloride Injection USP. However, you may get other medicines before or after Irinotecan Hydrochloride Injection USP, so your entire treatment may last longer. If you are getting a medicine to prevent nausea, you will probably take that

medicine first. Then you will get the rest of your intravenous medicines, including Irinotecan Hydrochloride Injection USP, one at a time.

Overdose:

In case of overdose, you may experience increased side effects. If you suspect an overdose, talk to your doctor or nurse immediately, or contact the nearest hospital emergency room or poison control centre.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, Irinotecan Hydrochloride Injection USP may cause side effects. Everyone reacts differently to chemotherapy and not all people will experience every side effect.

Chemotherapy medicines work by killing the fastest growing cells in the body, which include cancer cells and some normal cells. Normal cells that grow very rapidly are in your bone marrow, lining of the mouth, stomach, and hair follicles. Since these fast-growing cells can be affected by chemotherapy medicines, this can lead to side effects such as diarrhea. The most common side effects are: low white cell count (increasing the risk of infection), low red cell count (anemia), nausea and vomiting, and hair loss. These side effects usually disappear after treatment ends. Before your next cycle of chemotherapy, your white blood cells count normally increases and new cells grow back. After your chemotherapy is completely finished, your hair will begin to grow back.

Other, more rare, side effects could be heart attack, stroke or blood clot (thromboembolism). The kinds of side effects, how often they occur, and how bad they may be, could be related to the dose of chemotherapy, or the regimen used. If you are having a problem with side effects, call your doctor or nurse. They can suggest medicines or other ways to prevent or relieve your discomfort.

Tell your physician, oncology pharmacist or nurse right away if you feel any of the following symptoms *during your treatment or a few hours after treatment:*

- Runny nose, watery eyes, more saliva in your mouth.
- Diarrhea and/or stomach cramps.
- Nausea or vomiting.
- Sweating.
- Flushing (your face and neck may feel hot and look red).
- Visual disturbances.
- Pain or burning during the injection.

Don't wait until your treatment is finished. Your physician may give you a medicine to relieve these symptoms. You may also get medicine before or after future treatments to prevent these symptoms.

Tell your physician, oncology pharmacist or nurse right away if any of the following occur *any time after receiving Irinotecan Hydrochloride Injection USP:*

- Diarrhea for the first time during your treatment.
- Black or bloody stools.
- Symptoms of dehydration (fluid loss), such as lightheadedness, dizziness, or fainting. Your skin may appear flushed, dry, and pale; you may not urinate very much; you may feel irritable or confused. If you are having diarrhea or are vomiting often, you may become dehydrated.
- Shortness of breath along with fluid build-up (for example, swelling in the ankles).
- Fever over 38 ºC (100 ºF), or other signs of infection.
- Difficulty speaking, change in voice and/or tingling or numbness of the mouth or tongue.
- You cannot take liquids by mouth due to nausea or vomiting, have been vomiting for more than 12 hours, or are still having nausea or vomiting although you've taken medicine to control it.
- You cannot get the diarrhea under control within 24 hours.
- You have taken loperamide for 24 hours and still have diarrhea.
- You bleed or bruise easily.
- You have a new skin rash or itching.
- You have pain where Irinotecan Hydrochloride Injection USP was injected.

DIARRHEA

Diarrhea is a common side effect of the chemotherapy you are receiving. Irinotecan Hydrochloride Injection USP can cause both an early and late form of diarrhea. Early diarrhea occurs during or shortly after you have been given Irinotecan Hydrochloride Injection USP. Late diarrhea occurs more than 24 hours and can start up to several days after you have been given Irinotecan Hydrochloride Injection USP. Whilst both forms can be severe, late diarrhea can become severe, quite quickly, and can result in loss of body fluid requiring hospitalization or lead to infection. For this reason, it is important that you pay careful attention to each bowel movement and use the medications provided by your doctor, oncology pharmacist or nurse to control diarrhea symptoms.

You have diarrhea if your stools are soft, loose or watery, increased in number or it is hard to control your bowel due to urgency to go to the toilet. Loperamide is a medicine to help control the severity of diarrhea. You should begin to take loperamide immediately at the earliest sign of a loose stool or the earliest onset of bowel movements more frequent than you would normally expect. However, never take loperamide to prevent diarrhea.

You should take the loperamide as follows: 4 mg (2 tablets) at the first onset of loose stools or diarrhea and then 2 mg (1 tablet) every 2 hours until you have been without diarrhea for at least 12 hours. During the night, you may take 4 mg (2 tablets) of loperamide every 4 hours. The above recommended dosage to treat your diarrhea is higher than the usual dosage of loperamide. In addition, you should try to drink lots of clear liquids (eg. water, apple juice, broth, sports drinks, non-fizzy soft drinks) in order to prevent dehydration. You should not use loperamide for more than 48 consecutive hours.

Diarrhea associated with nausea and/or vomiting needs particular attention. In this circumstance, vomiting can prevent you from taking fluids lost due to diarrhea. As a result, you could be in danger of serious dehydration that could result in severe complications or death. Should diarrhea and vomiting persist together for more than 12 hours, you will need evaluation for intravenous fluid replacement since you are unlikely to improve on your own.

Diarrhea in association with fever also needs particular attention. The fever may be a sign of infection that could result in severe complications or death. If you have a fever in association with diarrhea, you will need prompt evaluation for intravenous antibiotic therapy.

Diarrhea lasting for more than 24 hours while using loperamide is also a concern, even if you do not have nausea, vomiting, or fever. Prolonged diarrhea can put you at risk for dehydration or infection and may require that you receive intravenous fluids and antibiotics. If you have diarrhea lasting for 24 hours, you will need evaluation. Depending upon the circumstances, your physician may request that you begin to take an antibiotic for several days in order to prevent infection that could be seen in association with the diarrhea. Alternatively, your physician may wish to have you seen in the clinic or emergency room.

NAUSEA AND VOMITING
The amount of nausea and vomiting varies widely from person to person. Some have mild nausea and vomiting, while others may have severe nausea and vomiting for a short time after treatment. Nausea and vomiting may start right after a chemotherapy treatment or several hours later, and may last several days. As noted above, vomiting can become quite severe, and you can lose body fluid for which you may need intravenous fluids or hospitalization. In addition, vomiting may make it difficult for you to take medications (such as loperamide for diarrhea).

Your physician can give you medicine to prevent nausea or reduce its severity.
Here are some tips that may help reduce nausea.

- Eat small meals or snacks throughout the day instead of 2 or 3 large meals.
- Eat foods that are cold or at room temperature.
- Cut out foods that are fried, spicy, fatty or sweet.
- Stay away from odours that may bother you such as cooking smells, cigarette smoke, car exhaust or perfume.
- Sit upright in a chair after eating – don't lie flat for at least 2 hours.
- Wear loose-fitting clothes, especially around the waist.
- You can also try drinking clear fluids (water, diluted soft drinks, apple juice, and broth) or sucking on popsicles, ice chips, mints or sour candy (but avoid sour candy if you have mouth sores).
- Eat something light a few hours before your chemotherapy treatment.

If these suggestions and the medications you are taking do not work, or if nausea and vomiting become so severe you cannot take anti-nausea or other medications, you should contact your physician or seek help at the emergency room.

OTHER BOWEL PROBLEMS
Cases of colitis, which may be accompanied by abdominal pain and/or presence of blood in the stools, have been observed. Rarely ileus has also been reported. If you experience either of these, please consult your physician.

INFECTION
A week or two after a chemotherapy cycle, your white blood cell count may be low. This is the most dangerous time for getting an infection. White blood cells defend your body against infections. When there are very few white blood cells, there may not be enough to fight off an infection. It's important to know the signs of infection so that you can get treatment before the infection becomes serious. The signs of infection include:

- fever over 38 ºC (100 ºF),
- chills or sweating,
- sore throat or coughing,
- redness or swelling around a cut, wound or a catheter site,
- a burning feeling when you urinate,
- unusual vaginal itching or discharge.

Infections and infestations such as bacterial, fungal and viral infections have been observed during Irinotecan Hydrochloride Injection USP treatment. If you experience any of the signs of infections above during or after your treatment with Irinotecan Hydrochloride Injection USP, notify your health care professional immediately.

Your physician may prescribe oral antibiotics to help prevent infection during chemotherapy. Your physician may also give you a medicine to help increase the number of your white blood cells. If there is evidence of an infection, your physician may need to admit you to the hospital for a short period of time to receive intravenous antibiotics.

The following tips can help you prevent infections.

- Wash your hands often. Use lotion afterwards to prevent your skin from becoming dry and cracked.
- Bathe or shower every 1 to 2 days.
- Be careful not to cut yourself when you use a knife, scissors, razor or other sharp objects.
- Stay away from people who are sick.
- Have someone else clean cat litter boxes, birdcages or fish tanks.
- Eat well-balanced meals.

HEART ATTACKS, STROKES, OR BLOOD CLOT
Although these types of serious medical conditions are uncommon during Irinotecan Hydrochloride Injection USP therapy, they may occur both in patients with known risk factors for heart disease or blood clots and in patients without known risk factors for these conditions. These conditions can be life-

threatening or fatal. The signs of heart attacks, strokes or blood clot include:

- Worsening of pre-existing angina chest pain.
- New onset of chest pains and/or shortness of breath.
- Sudden loss of vision, difficulty speaking, or loss of muscular function or loss of sensation on one side of your body.
- Swelling in one of your legs (this may be evidence of a blood clot in the legs that could put you at risk for more serious complications).
- If you have a central venous catheter and you develop swelling in the arm or neck on the side of the catheter (possible evidence of a blood clot).

You should seek medical attention immediately if you experience any of these symptoms.

ANEMIA

Chemotherapy medicines affect the bone marrow, which is where red blood cells are formed. Red blood cells carry oxygen to the muscles and other tissues in your body. When there are too few red blood cells, your muscles, and other body tissues can't get enough oxygen to do their work, and you feel exhausted. If your red blood cell count drops very low, you may also feel weak or dizzy, or may have shortness of breath. These are all symptoms of anemia. If you have these symptoms, tell your physician or nurse. Your physician may give you medicine to treat anemia that is caused by chemotherapy. Do not start taking iron tablets on your own - they may not work for anemia caused by chemotherapy medicines and can make your nausea worse.

FATIGUE

Feeling tired - or fatigued - is one of the most common side effects of chemotherapy. Many other factors such as stress, diet, sleeping patterns, and your age can also cause fatigue. For some, fatigue may start to improve 2 to 3 months after you complete your chemotherapy treatments. Here's how you can help reduce fatigue.

- Plan your activities. Allow rest between periods of activity.
- List all of the things you have to do, and number them in order of importance. Only do the things on your list that must get done. Leave the other tasks for another day.
- Ask family and friends to help you with driving, housework or other tasks. For example, ask your friend to pick up a few things for you the next time they go to the supermarket.
- Eat a well-balanced diet.
- Do light exercise regularly.

HAIR LOSS

Hair loss is common in chemotherapy. However, the hair loss is temporary, and your hair usually starts to grow back within 2 or 3 months after you've finished your treatments.

Many survivors suggest getting a wig before you start chemotherapy treatment. That way, your stylist can match your current hair color and set it in the same style. While wigs can be expensive, there are organizations such as The Canadian Cancer Society that provide wigs free of charge. In addition to wigs, some people like to wear stylish hats, scarves or turbans to cover their head.

SPEECH DISORDERS

Speech disorders such as difficulty speaking, stuttering and/or slurred speech, sometimes occurring with tingling or numbness of the mouth or tongue, have been observed during or immediately following Irinotecan Hydrochloride Injection USP treatment. In most cases, these symptoms improved within minutes to hours after finishing Irinotecan Hydrochloride Injection USP treatment. If you experience any difficulty speaking, change in voice and/or tingling or numbness of the mouth or tongue during or after your treatment with Irinotecan Hydrochloride Injection USP, notify your health care professional immediately.

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

Symptom / effect	Talk with your physician or pharmacist or nurse	
	Only if severe	In all cases
Common		
Diarrhea with nausea and/or vomiting[1]		√
Diarrhea lasting more than 24 hours[1]		√
Diarrhea with fever[1]		√
Vomiting for more than 12 hours[2]		√
Dehydration manifest by lightheadedness, dizziness, or fainting; dry, flushed or pale skin; irritability or confusion[3]		√
Fever, chills or sweating, sore throat or coughing, redness or swelling around cut, wound or a catheter site, burning feeling when you urinate[4]		√
Uncommon		
Black or bloody stool[5]		√
Bruising, small red hemorrhages into the skin, failure of cuts to stop bleeding or blood in stool		√
Chest Pain in association with shortness of breath and sensation of fullness/ heaviness[6]		√
Sudden loss of vision, difficulty speaking, loss of muscular function or loss of sensation on one side of your body[7]		√
Swelling in one of your legs, arm or neck[8]	√	
Rare		
Progressively increasing shortness of breath	√	

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

Symptom / effect	Talk with your physician or pharmacist or nurse	
	Only if severe	In all cases
Very rare		
Allergic Reaction (skin rash/swelling/difficulty breathing)	√	

[1] See section entitled "DIARRHEA" above.
[2] See section entitled "NAUSEA AND VOMITING" above.
[3] See signs of dehydration under the section entitled "Tell your physician, oncology pharmacist or nurse right away if any of the following occur *any time after receiving Irinotecan Hydrochloride Injection USP* " above.
[4] See section entitled "INFECTION" above.
[5] See section entitled "Tell your physician, oncology pharmacist or nurse right away if any of the following occur *any time after receiving Irinotecan Hydrochloride Injection USP*" above.
[6] See symptoms of heart attack under section entitled "HEART ATTACKS, STROKES, OR BLOOD CLOT" above.
[7] See symptoms of stroke under section entitled "HEART ATTACKS, STROKES, OR BLOOD CLOT" above.
[8] See symptoms of a blood clot (thromboembolism) under section entitled "HEART ATTACKS, STROKES, OR BLOOD CLOT" above.

This is not a complete list of side effects. For any unexpected effects while taking Irinotecan Hydrochloride Injection USP, contact your physician or pharmacist.

HOW TO STORE IT

Store Irinotecan Hydrochloride Injection USP at room temperature (15°C to 30°C). Protect from light and freezing. Avoid excessive heat. It is recommended that the vial remain in the carton until time of use

Keep out of reach and sight of children.

Reporting Suspected 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.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting Pfizer Canada ULC; at: **1-800-463-6001**

This leaflet was prepared by:
Pfizer Canada ULC
Kirkland, Québec H9J 2M5

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