Package leaflet: Information for the user

Irinotecan Hydrochloride medac 20 mg/mL, concentrate for solution for infusion

irinotecan hydrochloride trihydrate

Read all of this leaflet carefully before you are given 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 or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

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

Irinotecan Hydrochloride medac interferes with the growth and spread of cancer cells in the body.

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

Irinotecan Hydrochloride medac may be used alone in patients with metastatic cancer of the colon or rectum whose disease has recurred or progressed following initial 5-fluorouracil-based therapy.

2. What you need to know before you are given Irinotecan Hydrochloride medac

You will not be given Irinotecan Hydrochloride medac
- if you have chronic inflammatory bowel disease and/or a 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 medac contains”).
- if you are a breast-feeding woman (see section 2).
- if blood tests show very high bilirubin levels in your blood.
- 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 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 Irinotecan Hydrochloride medac 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 medac
- 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 medac. The use of Irinotecan Hydrochloride medac 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 medac 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 this 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 immediately if you have diarrhoea, 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 suffer from 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.

Chronic intestinal inflammation and/or intestinal blockage
Call your doctor if you have pain in your belly and if you have problems with bowel movement, 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 Irinotecan Hydrochloride medac.

Kidney function
Occurrences of kidney dysfunction have been reported, which can be detected in blood tests performed by your doctor.

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 medac is rarely associated with blood flow disorders (blood clots in the vessels of your legs, which can travel to other parts of the body such as the lungs or the brain) that may occur rarely in patients with multiple risks factors. Talk to your doctor right away if you have any symptoms such as chest pain, shortness of breath, swelling, pain, redness, or warmth in an arm or leg.

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 in 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 medicines.

Other medicines and Irinotecan Hydrochloride medac
Irinotecan Hydrochloride medac 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 (clarithromycin, erythromycin and telithromycin)
- 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 medac 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 medac 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 medac. 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 received 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 receiving this medicine.

Breast-feeding
Irinotecan and its metabolite were detected 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 receiving this medicine.

Fertility
No studies have been done, nevertheless, this medicine may affect fertility. Prior to receiving 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 received this medicine. Do not drive or operate machinery if you have any of these side effects.

Irinotecan Hydrochloride medac 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, 675 mg/15 mL, 1,125 mg/25 mL and 2,250 mg/50 mL.

Irinotecan Hydrochloride medac contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially ‘sodium-free’.

3. How to use Irinotecan Hydrochloride medac

Irinotecan Hydrochloride medac will be given to you by healthcare professionals.

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

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

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

You may be given other medicines to prevent nausea, vomiting, diarrhoea, and other side effects while you are receiving Irinotecan Hydrochloride medac. You may need to keep using these medicines for at least a day after your Irinotecan Hydrochloride medac injection.

If the medicine escapes from the vein it can cause tissue damage. If you experience burning, pain or notice redness or swelling at the injection site while you are receiving Irinotecan Hydrochloride medac, alert your healthcare professional immediately.

There are currently several treatment schedules recommended for Irinotecan Hydrochloride medac. It is usually given either once every 3 weeks (Irinotecan Hydrochloride medac given alone) or once every 2 weeks (Irinotecan Hydrochloride medac given in combination with 5-FU/FA chemotherapy). The dose will depend on a number of factors, including the treatment schedule, your height and weight, your age and general health, your blood counts, how well your liver is working, whether you have had radiation therapy 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 are given more Irinotecan Hydrochloride medac than you should
Seek emergency medical attention. Overdose symptoms may include some of the serious side effects listed in this package leaflet.

If you forget to use Irinotecan Hydrochloride medac
Call your doctor for instructions if you miss an appointment for your Irinotecan Hydrochloride medac injection.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

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

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty 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 such as a runny nose, increased salivation, watery eyes, sweating, flushing, abdominal cramping. (This can occur while the medicine is being administered. If this happens, alert your healthcare professional promptly. Medicines can be given to stop and/or lessen this early side effect).
- Late diarrhoea: Occurring more than 24 hours after 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, medication and diet modifications advice.

Talk to your doctor or nurse if you experience any of the symptoms in the following table or in the list of symptoms with frequency “not known” 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 of 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 also section "Warnings and precautions"**)**	Very common	Very common
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 (*Clostridioides 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 medac

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 vial and on the carton after EXP. The expiry date refers to the last day of that month.

Storage conditions
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

For single use only.

Shelf life
Before dilution: 3 years.

After dilution: Once the concentrate has been diluted for infusion the solution can be kept for 6 hours at room temperature (15 °C – 25 °C) or for 24 hours in a refrigerator (2 °C – 8 °C).

Do not use Irinotecan Hydrochloride medac if you notice any precipitate in the vials or after dilution.

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 medac contains

- The active substance is irinotecan hydrochloride trihydrate. Each millilitre of the concentrate for solution for infusion contains 20 mg irinotecan hydrochloride trihydrate, equivalent to 17.33 mg irinotecan.
  Each vial of 2 mL contains 40 mg of irinotecan hydrochloride trihydrate (40 mg/2 mL).
  Each vial of 5 mL contains 100 mg of irinotecan hydrochloride trihydrate (100 mg/5 mL).
  Each vial of 15 mL contains 300 mg of irinotecan hydrochloride trihydrate (300 mg/15 mL).
  Each vial of 25 mL contains 500 mg of irinotecan hydrochloride trihydrate (500 mg/25 mL).
  Each vial of 50 mL contains 1000 mg of irinotecan hydrochloride trihydrate (1000 mg/50 mL).

- The other ingredients are sorbitol (E 420), lactic acid, sodium hydroxide (to adjust to pH 3.5) and water for injections.

What Irinotecan Hydrochloride medac looks like and contents of the pack
Irinotecan Hydrochloride medac 20 mg/mL, concentrate for solution for infusion is a clear yellow solution.

Irinotecan Hydrochloride medac 40 mg: One 2 mL vial.
Irinotecan Hydrochloride medac 100 mg: One 5 mL vial.
Irinotecan Hydrochloride medac 300 mg: One 15 mL vial.
Irinotecan Hydrochloride medac 500 mg: One 25 mL vial.
Irinotecan Hydrochloride medac 1000 mg: One 50 mL vial.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

medac
Gesellschaft für klinische
Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

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

Finland:
Irinotecan medac

France:
IRINOTECAN MEDAC

Germany:
Irinomedac

United Kingdom (Northern Ireland):
Irinotecan Hydrochloride medac

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The following information is intended for healthcare professionals only:

Instruction for personnel regarding safe handling of Irinotecan Hydrochloride medac

Like all antineoplastic agents, Irinotecan Hydrochloride medac must be prepared and handled carefully. The use of protective glasses, mask and gloves is required.

If Irinotecan Hydrochloride medac concentrate for solution for infusion or the prepared solution for infusion should come into contact with your skin, wash it off immediately and thoroughly with soap and water. If Irinotecan Hydrochloride medac concentrate for solution for infusion or the prepared solution for infusion should come into contact with the mucous membranes, wash it off immediately and thoroughly with water.

As with all injectable medicinal products, Irinotecan Hydrochloride medac must be prepared under aseptic conditions.

If a clouding or condensation 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

As with any other injectable medicinal products, Irinotecan Hydrochloride medac solution for infusion must be prepared aseptically.

If you observe any precipitate in the vial or solution for infusion, discard the product according to standard procedures for cytotoxic agents.

Aseptically withdraw the calculated amount of Irinotecan Hydrochloride medac concentrate for solution for infusion from the vial with a calibrated syringe and inject into a 250 mL infusion bag or bottle containing either 0.9% sodium chloride solution or 5% glucose solution. Mix the solution for infusion in the infusion bag or bottle thoroughly by manual rotation.

Do not mix with other medicines.

Shelf life

After dilution, the irinotecan solution for infusion should be infused into a peripheral or central vein. Irinotecan Hydrochloride medac should not be delivered as an intravenous bolus or an intravenous infusion shorter than 30 minutes or longer than 90 minutes.

After dilution in 0.9% sodium chloride solution or 5% glucose solution, chemical and physical in-use stability has been demonstrated for up to 6 hours at room temperature (approximately 25 °C) and ambient lighting or 48 hours if stored at refrigerated temperatures (approximately 2 °C – 8 °C).

From a microbiological point of view, the solution for infusion should be used immediately. If the product is not used immediately after dilution, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 6 hours at room temperature or 24 hours if stored at 2 °C – 8 °C unless dilution has taken place in controlled conditions.

Warnings against some visible signs of deterioration

Do not use Irinotecan Hydrochloride medac if you notice a precipitate in the vials or the diluted solution. In this case, the product should be discarded according to the standard procedures for disposal of cytotoxic waste. Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Administration

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

Disposal

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