

Package leaflet: Information for the user

Irinotecan 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 medac is and what it is used for
2. What you need to know before you are given Irinotecan medac
3. How Irinotecan medac will be given to you
4. Possible side effects
5. How to store Irinotecan medac
6. Contents of the pack and other information

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

Irinotecan medac belongs to a group of medicines called cytostatics (anticancer medicines).

Irinotecan medac may be used alone or in combination with a number of other medicines used to treat cancer. These combinations may be used to treat cancers of the large intestine (colon or rectum) where the disease is at an advanced stage.

Your doctor may use a combination of Irinotecan medac with 5-fluorouracil/folinic acid (5-FU/FA) and bevacizumab to treat your cancer of the large intestine (colon or rectum).

Your doctor may use a combination of Irinotecan medac with cetuximab to treat a particular type of cancer of the large intestine, which expresses a protein called EGFR.

If you need any further information on your condition, please ask your doctor.

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

You will not be given Irinotecan medac

- if you are allergic to irinotecan hydrochloride trihydrate or any of the other ingredients of this medicine (listed in section 6).
- if you have any other bowel disease or a history of bowel obstruction.
- if you are breast-feeding.
- if you have increased levels of bilirubin in the blood (more than 3 times the upper limit of the normal range).
- if you have an imbalance of your blood cells (severe bone marrow failure).
- if you are in a poor general health (evaluated by an international standard).
- if you are using the natural remedy St. John's wort (*Hypericum perforatum*).

For additional contraindications of cetuximab or bevacizumab which may be used in combination with Irinotecan medac, please refer to the product information for these medicines.

Warnings and precautions

Talk to your doctor or pharmacist before you are given Irinotecan medac.

This medicine is intended for adults only.

Check with your doctor if this medicine has been prescribed for use in a child.

Special care is also needed in elderly patients.

As Irinotecan medac is an anticancer medicine it will be administered to you in a special unit and under the supervision of a doctor qualified in the use of anticancer medicines. The unit's personnel will explain to you what you need to take special care of during and after the treatment. This leaflet may help you to remember that.

If you receive Irinotecan medac in combination with cetuximab or bevacizumab, please make sure that you also read the package leaflet for these medicines.

During administration of Irinotecan medac (30 – 90 minutes) and up to 24 hours after administration you may experience some of the following signs and symptoms:

- Diarrhoea
- Sweating
- Abdominal pain
- Visual disturbance
- Excessive mouth watering

The medical term for these symptoms is “**acute cholinergic syndrome**” which can be treated (with atropine). If you have any of these symptoms, **immediately tell your doctor** who will give you any treatment necessary.

From the day after treatment with Irinotecan medac until next treatment you may experience various symptoms, which may be serious and require immediate treatment and close supervision. These can be:

Diarrhoea

If your diarrhoea starts more than 24 hours after administration of Irinotecan medac (“delayed diarrhoea”) it may be serious. It is often seen about 5 days after administration. The diarrhoea should be treated immediately and kept under close supervision. Immediately after the first liquid stools do the following:

1. Take any antidiarrhoeal treatment that the doctor has given you, exactly as he/she has told you. The treatment must not be changed without consulting the doctor. Recommended antidiarrhoeal treatment is loperamide (4 mg for the first intake and then 2 mg every 2 hours, also during the night). This should be continued for at least 12 hours after the last liquid stools. The recommended dosage of loperamide must not be taken for more than 48 hours.
2. Drink large amounts of water and rehydration fluids, immediately (i.e. water, soda water, fizzy drinks, soup or oral rehydration therapy).
3. Immediately inform your doctor who is supervising the treatment, and tell him/her about the diarrhoea. If you are not able to reach the doctor, contact the hospital unit supervising the Irinotecan medac treatment. It is very important that they are aware of the diarrhoea.

Hospitalisation is recommended for the management of the diarrhoea, in the following cases:

- You have diarrhoea as well as fever (over 38 °C).
- You have severe diarrhoea (and vomiting) with excessive loss of water requiring intravenous hydration.
- You still have diarrhoea 48 hours after starting the diarrhoea treatment.

Note! Do not take any treatment for diarrhoea other than that given to you by your doctor and the fluids described above. Follow the doctor's instructions. The antidiarrhoeal treatment should not be used preventive, even though you have experienced delayed diarrhoea at previous cycles.

Fever

If the body temperature increases over 38 °C it may be a sign of infection, especially if you also have diarrhoea. If you have any fever (over 38 °C) contact your doctor or the hospital unit immediately so that they can give you any treatment necessary.

Nausea (feeling sick) and vomiting

If you have nausea and/or vomiting contact your doctor or the hospital unit immediately.

Neutropenia

Irinotecan medac may cause a decrease in the number of some of your white blood cells, which play an important role in fighting infections. This is called neutropenia. Neutropenia is often seen during treatment with Irinotecan medac and is reversible. Your doctor should arrange for you to have regular blood tests to monitor these white blood cells. Neutropenia is serious and should be treated immediately and carefully monitored.

Breathing difficulties

If you have any breathing difficulties contact your doctor immediately.

Impaired liver function

Before treatment with Irinotecan medac is started and before every following treatment cycle your doctor will monitor your liver function (by blood tests).

Impaired kidney function

As this medicine has not been tested in patients with kidney problems, please check with your doctor if you have any kidney problems.

Accidental injection beside the blood vessel (extravasation)

If accidental injection beside the blood vessel occurs, the infusion site should be monitored for signs of inflammation. Your doctor will flush the site and may also treat it with ice.

Heart problems

Myocardial ischaemia (a painful heart condition caused by lack of blood flow to the heart) has been observed following treatment with Irinotecan medac. If you have any heart disease, known risk factors for heart disease, or previous treatment with anti-cancer medicines your doctor will monitor you closely. Action should be taken to try to minimise all modifiable risk factors for heart problems (e.g. smoking, high blood pressure, and high level of fat in the blood).

Infections

You might get serious infections or face reduced response to vaccinations during therapy with Irinotecan medac. Your doctor will try to avoid vaccinations during therapy with Irinotecan medac. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

If you have one or more of the symptoms mentioned, after you have returned home from the hospital, you should immediately contact the doctor or the hospital unit supervising the Irinotecan medac treatment.

Other medicines and Irinotecan medac

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is also valid for herbal medicines.

Medicines known to alter the effects of Irinotecan medac or vice versa:

- ketoconazole (for the treatment of fungal infections)
- rifampicin (for the treatment of tuberculosis)
- carbamazepine, phenobarbital and phenytoin (medicines for the treatment of epilepsy)
- atazanavir (for the treatment of HIV infection)
- anticoagulants (medicines to prevent blood clotting)
- yellow fever vaccine and other live vaccines. Tell your doctor if you have had or are due to have any vaccinations.
- cyclosporine and tacrolimus (used to dampen down your body's immune system)
- The herbal medicine St. John's wort (*Hypericum perforatum*) must not be used during treatment with Irinotecan medac and not between treatments, as it may decrease the effect of irinotecan.

If you require an operation, please tell your doctor or anaesthetist that you are using this medicine, as it may alter the effect of some medicines used during surgery.

Pregnancy, breast-feeding and fertility

Pregnancy

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

You should not be given Irinotecan medac if you are pregnant. If you or your partner is being treated with Irinotecan medac, you must avoid becoming pregnant during treatment and for at least three months after cessation of therapy. Still, if you become pregnant during this period you must immediately inform your doctor.

Breast-feeding

You must discontinue breast-feeding for the duration of Irinotecan medac therapy.

Fertility

There are no human data on the effect of irinotecan on fertility. In treated animals the fertility of offspring was decreased. If you plan to become pregnant or father a child, please talk to your doctor.

Driving and using machines

In some cases Irinotecan medac may cause side effects which affect the ability to drive and use tools and machines. Contact your doctor or pharmacist if you are unsure.

During the first 24 hours after administration of Irinotecan medac you may feel dizzy or have visual disturbances. If this happens to you do not drive or use any tools or machines.

Irinotecan medac contains sorbitol

Irinotecan medac contains sorbitol. If you have been told by your doctor that you have an intolerance to some sugars (e.g. fructose intolerance), contact your doctor or pharmacist before you are given this medicine.

3. How Irinotecan medac will be given to you

This medicine is intended for adults only.

Irinotecan medac will be given as an infusion into your veins over a period of 30 to 90 minutes. The amount of Irinotecan medac you are given depends on your age, height, weight and general medical condition. It will also depend on any other treatment you may have received for your cancer. Your doctor will calculate your body surface area in square metres (m²) from your height and weight.

- If you have previously been treated with 5-fluorouracil you will normally be treated with Irinotecan medac alone starting with a dose of 350 mg/m² every three weeks.
- If you have not had previous chemotherapy you will normally receive 180 mg/m² Irinotecan medac every two weeks. This will be followed by folinic acid and 5-fluorouracil.

If you receive Irinotecan medac in combination with cetuximab, Irinotecan medac must not be administered earlier than one hour after the end of the cetuximab infusion. Please follow the advice of your doctor regarding your current treatment.

These dosages may be adjusted by your doctor depending on your condition and any side effects you may have.

If you are given more Irinotecan medac than you should

In case you were given a higher dosage of Irinotecan medac than required the occurring side effects may be more severe. You will get maximum supportive care to prevent dehydration due to diarrhoea and to treat any infectious complication. If you think you have been administered an overdose please contact your doctor.

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. Your doctor will discuss these side effects with you and explain the risks and benefits of your treatment.

Some of these side effects must be treated immediately. These are:

- Diarrhoea
- A decrease in the number of neutrophil granulocytes, a type of white blood cell, which plays an important role in fighting infections.
- Fever
- Nausea and vomiting
- Breathing difficulties (possible symptom of severe allergic reactions)

Please read instructions described in section “**Warnings and precautions**” carefully and follow them if you have any of the side effects listed above.

Other side effects include:

Very common: may affect more than 1 in 10 people

- Blood disorders including abnormally low number of neutrophil granulocytes, a type of white blood cell (neutropenia) and reduction of the quantity of haemoglobin in blood (anaemia)
- In combination therapy, thrombocytopenia (reduction in the number of blood platelets) causing bruises, tendency to bleed and abnormal bleeding
- Delayed severe diarrhoea
- In monotherapy, fever

- In monotherapy, infections
- In monotherapy, severe nausea (feeling sick) and vomiting (being sick)
- Hair loss (the hair grows again after end of treatment)
- In combination therapy, transient and mild to moderate increase in serum levels of liver enzymes (such as transaminases, alkaline phosphatase) or bilirubin

Common: may affect up to 1 in 10 people

- Severe transient acute cholinergic syndrome: The main symptoms are defined as early diarrhoea and various other symptoms such as abdominal pain; red, sore, itching or weeping eyes (conjunctivitis); runny nose (rhinitis); low blood pressure; flushing due to widening of blood vessels (vasodilation); sweating, chills; a feeling of general discomfort and illness; dizziness; visual disturbances, pupil contraction; watering eyes and increased salivation, occurring during or within the first 24 hours after the infusion of Irinotecan medac.
- In monotherapy, thrombocytopenia (reduction in the number of blood platelets) causing bruises, tendency to bleed and abnormal bleeding
- In combination therapy, fever
- In combination therapy, infections
- Infections associated with a severe decrease in the number of some white blood cells (neutropenia) resulting in death in three cases
- In combination therapy, severe nausea (feeling sick) and vomiting (being sick)
- Fever associated with a severe decrease in the number of some white blood cells (febrile neutropenia)
- Loss of water (dehydration), commonly associated with diarrhoea and/or vomiting
- Constipation
- Feeling weak (asthenia)
- Transient and mild to moderate increase of levels of creatinine in the blood
- In monotherapy, transient and mild to moderate increase in serum levels of liver enzymes (such as transaminases, alkaline phosphatase) or bilirubin
- In combination therapy, transient pronounced (grade 3) increase in serum levels of bilirubin

Uncommon: may affect up to 1 in 100 people

- Mild allergic reactions – skin rash including red itchy skin, urticaria, conjunctivitis, rhinitis
- Mild skin reactions
- Mild reactions at the infusion site
- Lung disease presenting as shortness of breath, dry cough and inspiratory crackles (interstitial pulmonary disease), early effects such as breathing difficulties
- Partial or complete blockage of the bowel (intestinal obstruction, ileus), stomach and intestines bleeding
- Bowel inflammation which causes abdominal pain and/or diarrhoea (a condition known as pseudo-membranous colitis)
- Kidney failure, low blood pressure or cardio-circulatory failure as a consequence of dehydration associated with diarrhoea and/or vomiting, or in patients who experienced sepsis

Rare: may affect up to 1 in 1,000 people

- Severe allergic reactions (anaphylactic/anaphylactoid reaction), including swelling of the hands, feet, ankles, face, lips, mouth or throat which may cause difficulty in swallowing or extreme difficulty breathing.
- Muscular contraction or cramps and numbness (paraesthesia)
- Inflammation of the large bowel causing abdominal pain (colitis including typhlitis, ischemic and ulcerative colitis)
- Intestinal perforation; loss of appetite; abdominal pain; inflammation of the mucous membranes

- Inflammation of the pancreas without or with symptoms (mainly abdominal pain)
- High blood pressure during and following administration
- Low levels of potassium and sodium in the blood, mostly related to diarrhoea and vomiting

Very rare: may affect up to 1 in 10,000 people

- Transient speech disorders
- Increase in levels of some digestive enzymes which break down sugars (amylase) and fats (lipase)
- One case of low platelet count in the blood due to antibodies against platelets

If you receive Irinotecan medac in combination with cetuximab, some of the side effects you may experience can also be related to this combination. Such side effects may include an acne-like rash. Therefore, please make sure that you also read the package leaflet for cetuximab.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Irinotecan 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.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

For single use only.

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 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 dispose of medicines no longer required. These measures will help protect the environment.

6. Contents of the pack and other information

What Irinotecan 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 (E420), lactic acid, sodium hydroxide (to adjust to pH 3.5) and water for injections.

What Irinotecan medac looks like and contents of the pack

Irinotecan medac 20 mg/ml, concentrate for solution for infusion is a clear yellow solution.

Irinotecan medac 40 mg: One 2 ml vial.

Irinotecan medac 100 mg: One 5 ml vial.

Irinotecan medac 300 mg: One 15 ml vial.

Irinotecan medac 500 mg: One 25 ml vial.

Irinotecan 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

Local Representative:

Fannin Limited

Fannin House

South Country Business Park

Leopardstown

Dublin 18

Ireland

This medicinal product is authorised in the Member States of the EEA under the following names:

Czech Republic	Irinotecan medac 20 mg/ml, koncentrát pro přípravu infuzního roztoku
Finland	Irinotecan medac 20 mg/ml, Infuusiokonsentraatti, liuosta varten
France	IRINOTECAN MEDAC 20 mg/ml, solution à diluer pour perfusion
Germany	Irinomedac® 20 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Ireland	Irinotecan medac 20 mg/ml, concentrate for solution for infusion
Poland	Irinotecan medac
Portugal	Irinotecano medac 20 mg/ml, Concentrado para solução para perfusão
Slovak Republic	Irinotecan medac 20 mg/ml infúzny koncentrát
United Kingdom	Irinotecan Hydrochloride medac 20 mg/ml, concentrate for solution for infusion

This leaflet was last revised in 01/2016.

The following information is intended for healthcare professionals only:

Instructions for use/handling, preparation and disposal guide for use with Irinotecan medac concentrate for solution for infusion

Use/handling

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

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

Preparation of the intravenous solution

As with any other injectable drugs, the Irinotecan medac solution for infusion must be prepared aseptically.

If any precipitate is observed in the vials or after dilution, the product should be discarded according to standard procedures for cytotoxic agents.

Aseptically withdraw the required amount of Irinotecan 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 % dextrose solution. The solution for infusion should then be thoroughly mixed by manual rotation.

Irinotecan solution for infusion should be infused into a peripheral or central vein.

Irinotecan 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 % dextrose 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 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 6 hours at room temperature or 24 hours if stored at 2 °C – 8 °C unless dilution has taken place in controlled and validated aseptic conditions.

Disposal

All materials used for dilution and administration should be disposed of according to hospital standard procedures applicable to cytotoxic agents.