It is very important to receive all scheduled doses. If you miss a dose, you should immediately contact your doctor or the unit supervising the treatment. As this medicine has not been tested in patients with kidney problems, you must immediately inform your doctor. Breast feeding must be discontinued for the duration of irinotecan therapy. Ask your doctor for advice before taking any medicine. Driving and using machines In some cases irinotecan may cause side effects, which affect the ability to drive and use tools and machines. Contact your doctor if you are unsure.

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

Photography instructions for preparation of irinotecan solution for infusion:
1. Protective chamber should be used and protective gloves as well as protective glasses should be worn.
2. Opened containers, like injection vials and infusion bottles and used dilution (etc) has taken place in controlled and validated aseptic conditions prior to use are the responsibility of the user and would immediately. If not used immediately, in-use storage times and conditions by trained personnel in a designated area. Precautions should be taken to avoid contact with the skin and mucous membranes.

Intravenous injection:

Irinotecan belongs to a group of medicines called cytostatics (anti-cancer medicines). Irinotecan is used for the treatment of advanced cancer of the colon and rectum in adults, either in a combination with other medicines or alone.

Do not use irinotecan if you

- are allergic (hypersensitive) to irinotecan hydrochloride trihydrate or any of the other ingredients of irinotecan
- have or had chronic inflammatory bowel disease or bowel obstruction
- are pregnant or breastfeeding or if you think you might be pregnant
- have increased levels of bilirubin in the blood (more than 3 times the upper limit of normal)
- have severe bone marrow failure
- are in a poor general health (evaluated by a international standard)
- are using natural remedy St.John’s Wort (hypericum perforatum)
- have rare hereditary problems of fructose intolerance

Take special care with irinotecan

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 is an anti-cancer medicine it will be administered to you in a special unit and under the supervision of a doctor qualified in the use of anti cancer medicines. The unit’s personnel will explain to you what you need to take special care of during and after the treatment. This leaflet helps you to remember that.

Before treatment with irinotecan tell your doctor if any of the following apply to you:

- You have liver problems or jaundice
- You have kidney problems
- You have asthma
- You have ever received radiation therapy
- You experienced severe diarrhea or fever after being treated with irinotecan before.
- You have heart problems
- You smoke, have high blood pressure or high cholesterol as these can increase the risk of heart problems during

Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for Infusion

The following information is intended for medical or healthcare professionals only:

Instructions for use – Cytotoxic

Handling of irinotecan

As with other nephelic agents, caution should be exercised when handling irinotecan. Solution should be carried out under aseptic conditions by trained personnel in a designated area. Precautions should be taken to avoid contact with the skin and mucous membranes.

Treatment with irinotecan

- You have had or are due to have any vaccinations
- You are taking any other medicines. Please see the section below “Taking other medicines.”

1) The first 24 hours after administration of irinotecan

During administration of irinotecan (30 – 90 min.) and shortly after administration you may experience some of the following symptoms:

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

The medical form 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.

2) From day after treatment with irinotecan until next treatment.

During this period you may experience various symptoms, which may be serious and require immediate treatment and close supervision.

Diarrhoea

If your diarrhoea starts more than 24 hours after administration of irinotecan (“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 anti-diarrhoeal treatment that the doctor has given you, exactly as he/she has told you. The treatment may not be changed without consulting the doctor. Recommended anti diarrhoeal treatment is loperamide (4 mg for the first dose 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 may not be taken for more than 48 hours.
2. Drink large amounts of water and rehydration fluids immediately (i.e a water, soda water, fizzy drink, 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 unit at the hospital supervising the irinotecan treatment. It is very important that they are aware of the diarrhoea.

You must immediately tell the doctor, or the unit supervising the treatment, if:

- You have nausea, vomiting or any fever as well as diarrhoea
- You still have diarrhoea 48 hours after starting the diarrhoea treatment

Note: Do not take any treatment for diarrhoea other than that given by you or your doctor and the fluids described above. Follow the doctor’s instruction. The anti-diarrhoeal treatment should not be used to prevent a further episode of diarrhoea. 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 unit immediately so that they can give you any treatment necessary.

Nausea and vomiting

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

Neutropenia

Irinotecan 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 and is reversible. Your doctor should arrange for you to have regular blood tests to monitor these while blood cells. Neutropenia is serious and should be treated immediately and carefully monitored.

Breathtaking difficulties

If you have any breathing difficulties contact your doctor immediately.

Impaired liver function

Before treatment with irinotecan is started and before every following treatment cycle the liver function should be monitored (by blood tests). If the blood tests show signs of damage to the liver you should immediately contact the doctor or the unit supervising the irinotecan treatment.

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 problem.

Radiation therapy

Before treatment with irinotecan, tell your doctor, if you have ever received radiation therapy.

Vaccinations

Before treatment with irinotecan, tell your doctor, if you have had or are due to have any vaccinations.

Using other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This is also valid for herbal medicines, strong vitamins and minerals. If you receive irinotecan in combination with other capcitabine, oesultam or bevacizumab, please make sure that you also read the patient information leaflet for each medicine. Some medicines may alter the effects of irinotecan e.g. ketoconazole (for the treatment of fungal infections). Cyproheptadine (for the treatment of tuberculosish), warfarin (an anticoagulant used to thin the blood), Rifampicin used to treat HIV), Clozapin or Tacrolimus (used to dampen down your body’s immune system) and some medicines for the treatment of epilepsy can cause a decrease in the number of blood cells. The herbal medicine St John’s Wort (Hypericum perforatum) may not be used concurrent with irinotecan and not between treatments, as it may decrease the effect of irinotecan.

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

Pregnancy and breast-feeding

Irinotecan must not be used during pregnancy. Irinotecan can cause birth defects.

Women of child-bearing age should avoid becoming pregnant. Contraceptive measures must be taken by both male and female patients during and for at least three months (by males) and one month (by females) after cessation of therapy. Still, if you become pregnant during this period you must immediately inform your doctor.

Breast feeding must be discontinued for the duration of irinotecan therapy.

Ask your doctor for advice before taking any medicine.

Driving and using machines

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

During the first 24 hours after administration of irinotecan you may feel dizzy or have visual disturbances. If this happens to you do not drive or use any tools or machines.
Important information about some of the ingredients of irinotecan

Irinotecan contains sorbitol. If you suffer from intolerance to some sugars, tell your doctor before you are given this medicinal product.

3. How to use irinotecan

Irinotecan will be given as an infusion into your veins over a period of 30 to 90 minutes. The amount of infusion you are given will depend on your age, size 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 meters (m²):

- If you have previously been treated with 5-fluorouracil you will normally be treated with irinotecan alone starting with a dose of 350 mg/m² every 3 weeks.
- If you have not had previous chemotherapy you will normally receive 180 mg/m² irinotecan every 2 weeks. This will be followed by toleic acid 5-fluorouracil every 2 weeks.
- If you are treated with irinotecan in combination with cetuximab you will receive the same dose of irinotecan as administered in the last cycles of the prior irinotecan containing regimen. Irinotecan must be administered earlier than 1 hour after the end of the cetuximab infusion.

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

If you receive more irinotecan than you should

It is unlikely that you will be given too much irinotecan. However in the event that this occurs you may have some severe blood disorders and diarrhoea. Maximum supportive care should be taken to prevent dehydration due to diarrhoea and to treat any infectious complications. You should talk to the doctor administering your medicine.

If you miss a dose of irinotecan

It is very important to receive all scheduled doses. If you miss a dose, contact your doctor promptly.

If you stop using irinotecan

Do not stop medicine without doctor or pharmacist approval.

If you have any further questions on the use of this product, ask your doctor.

4. Possible side effects

Like all medicines, irinotecan 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. See also information in section “Take special care with irinotecan.”

Very common side effects (more than 1 in 10 patients):

- Blood disorder: Neutropenia (decreased number of some white blood cells), thrombocytopenia (decreased number of blood platelets), anaemia.
- Diarrhoea.
- Nausea and vomiting.
- Hair loss (the hair grows again after end of treatment).

In combination therapy transient serum levels of some enzymes (ALT, AST, alkaline phosphatase) or bilirubin.

Common side effects (less than 1 in 10 patients):

- Acute cholestatic syndrome: The main symptoms are defined as early diarrhoea and various other symptoms such as abdominal pain, red stools, itching and weeping eyes (conjunctivitis); running nose (rhinitis); low blood pressure; widening of the blood vessels, sweating, chills.
- Feeling of general discomfort and illness, dizziness, visual disturbance, pupil contraction; watering eyes and increased salivation, occurring during or within the first 24 hours after the infusion of irinotecan.
- Fever, infections (including sepsis).
- Fever associated with a severe decrease in the number of some white blood cells.
- Dehydration, commonly associated with diarrhoea and/or vomiting.
- Constipation.
- Fatigue.
- Increased level of liver enzymes and creatinine in the blood.

Uncommon side effects (less than 1 in 100 patients):

- Allergic reactions.
- Mild skin reactions: mild reactions at the infusion site.
- Early effects such as breathing difficulties.
- Lung disease (interstitial pulmonary disease).
- Intrahepatic bleeding.
- Abdominal pain and inflammation, causing diarrhoea (a condition known as pseudomembranous colitis).
- Infrequent cases of renal insufficiency. Low blood pressure or cardio-circulatory failure have been observed in patients who experienced episodes of dehydration associated with diarrhoea and/or vomiting or sepsis.

Rare side effects (less than 1 in 1000 patients):

- Severe allergic reactions (anaphylaxis/anaphylactoid reactions). If this happens you should tell your doctor immediately.
- Early effects such as nausea and vomiting.
- Increased levels of bilirubin in the blood (more than 3 times the normal level).

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

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

5. How to store irinotecan

Keep out of the reach and sight of children.

Do not freeze.

For single use only.

Store below 25°C. Store in the original package in order to protect from light.

Do not use this medicinal product after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

The product should be diluted and used immediately after opening. If prepared aseptically, the diluted solution can be stored for 24 hours at temperatures up to 15-25°C and for 48 hours at 2-8°C (e.g. in a fridge).

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

6. Further information

What irinotecan hydrochloride 20 mg/ml Concentrate for Solution for infusion contains:

The active substance is irinotecan hydrochloride Trihydrate.

- 1 ml of concentrate contains 20 mg irinotecan hydrochloride trihydrate equivalent to 17.33 mg of irinotecan.
- One 2 ml vial contains 40 mg irinotecan hydrochloride trihydrate.
- One 5 ml vial contains 100 mg irinotecan hydrochloride trihydrate.
- One 15 ml vial contains 300 mg irinotecan hydrochloride trihydrate.
- One 25 ml vial contains 500 mg irinotecan hydrochloride trihydrate.
- The other ingredients are sorbitol (E420), lactose acid, sodium hydroxide, hydrochloric acid and water for injections.

What irinotecan hydrochloride 20 mg/ml Concentrate for Solution for infusion looks like and is contained of the pack

Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for infusion is a clear, pale yellow coloured solution.

Packing size:

1 x 2 ml vial of 1 or 5 ml vial or 1 x 15 ml vial or 1 x 25 ml vial

Not all pack sizes may be marketed.

Marketing authorisation holder:

Accord Healthcare Limited.

Sage House, 319 Pinner Road, North Harrow, HA1 4HF, UK.

Manufacturers:

Accord Healthcare Limited.
Sage House, 319 Pinner Road, North Harrow, HA1 4HF, UK.

Cemelog BRS Limited, 2040 Budaörs, Vasút u. 2., Hungary.

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