Acativs Logo

Package leaflet: Information for the user
Irinotecan Hydrochloride 20mg/ml concentrate for solution for infusion
Irinotecan hydrochloride trihydrate

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

What is in this leaflet:

1. What Irinotecan is and what it is used for

Your medicine is called Irinotecan. Irinotecan belongs to a group of medicines called cytostatics (anti-cancer medicines).
Irinotecan 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 with **5-fluorouracil/folinic acid (5FU/FA)** and **bevacizumab** to treat your **cancer of the large intestine (colon or rectum)**.

Your doctor may use a combination of Irinotecan with **capecitabine** with or without **bevacizumab** to treat your **cancer of the colon and rectum**.

Your doctor may use a combination of Irinotecan with **cetuximab** to treat a particular type of **cancer of the large intestine (KRAS wild-type)** which expresses a protein called **EGFR**.

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

- **You should not be given Irinotecan if any of the following apply to you:**If you are **allergic to irinotecan hydrochloride trihydrate** or any of the other ingredients of this medicine (listed in section 6)
- If you have or have had **chronic inflammatory bowel disease** or **bowel obstruction**
- If you are **pregnant** or **breast feeding** or if you think you might be pregnant
- If you have **severe liver disease**
- If you have **severe bone marrow failure**
- If your gerneal health status does not allow you to carry out general activities of daily living

- If you are taking **St John's Wort** (a herbal supplement)

Warnings and precautions
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 diarrhoea** 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 treatment with Irinotecan
- You have had or are due to have any **vaccinations**
- You are taking any other medicines. Please see the section below '**Other medicines and Irinotecan**'.

As with all anti-cancer medicines the use of Irinotecan is associated with a number of side-effects which may be serious. These side-effects require special management to minimise the risk of complications.

You will be treated by a specialist team experienced in using these kinds of treatments and managing their side effects, which are usually temporary.
However, it is essential that you read the section '**Possible side effects**' and follow the instructions carefully if you get any of the symptoms described.

2

Children
Irinotecan should not be used in children.

Other medicines and Irinotecan
Tell your doctor if you are taking, have recently taken or might take any other medicines.

If you receive Irinotecan in combination with either capecitabine, cetuximab or bevacizumab, please make sure that you also read the patient information leaflet for each medicine.

Some medicines, when taken at the same time as Irinotecan, may affect the way Irinotecan works or Irinotecan may affect the way they work. Tell your doctor if you are taking any of the following medicines:

- **St John's Wort** (a herbal supplement)
- **Ketoconazole** (an antibiotic)
- **Rifampicin** (an antibiotic)
- **Carbamazepine** (used to treat seizures)
- **Phenobarbital** (used to treat seizures)
- **Phenytoin** (used to treat epilepsy)
- **Warfarin** (an anticoagulant used to thin the blood)
- **Atazanavir** (used to treat HIV)
- **Ciclosporin** or **Tacromilus** (used to dampen down your body's immune system)

If you go into hospital to have an operation, tell the anaesthetist and the medical staff that you are being treated with Irinotecan and any other medicines you are taking.
Pregnancy, breast-feeding and fertility
You must **not use Irinotecan if you are pregnant as it may harm your unborn baby**.

You should also **avoid becoming pregnant** while you are being treated with Irinotecan.

Men and women should use adequate contraception while being treated with Irinotecan and for:

- **up to 1 month after you receive your last dose of Irinotecan if you are female**
- **up to 3 months after your last dose of Irinotecan if you are male.**

If you do become pregnant while being treated with Irinotecan you must inform your doctor **IMMEDIATELY**.

Because Irinotecan may be harmful to nursing infants, women **must not breast- feed** while being treated with Irinotecan.
Driving and using machines
Irinotecan may make you feel dizzy or cause visual disturbances. If this happens to you **do not drive or operate machinery** until this resolves.

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

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium free'.

3. How you will be given Irinotecan

If you are prescribed Irinotecan it will only be given to you by doctors or nurses experienced in giving chemotherapy.

Method of administration

Irinotecan will be given as an infusion into your veins over a period of 30 to 90 minutes.

If you receive Irinotecan in combination with **cetuximab,** Irinotecan must not be administered earlier than 1 hour after the end of the **cetuximab** infusion.

Dosage and frequency of administration
The amount of Irinotecan 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 three weeks.**

- **If you have not had previous chemotherapy you will normally receive 180 mg/m2 Irinotecan every two weeks. This will be followed by folinic acid and 5-fluorouracil.**

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

Duration of treatment
The number of infusions that you receive will depend on how you are responding to treatment. Your doctor will discuss this with you.

Blood monitoring
Whilst you are being given Irinotecan and/or other similar medicines you will have regular blood tests to monitor your treatment and to ensure that there are no untoward adverse effects.

4. Possible side effects

Medicines like Irinotecan will cause unwanted side-effects 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.

Please read the following instructions carefully and follow them if you have any of the side-effects listed.

Diarrhoea
Irinotecan may cause you to have diarrhoea. There are two types of diarrhoea, which can be distinguished by when they start. “Early” diarrhoea starts less than 24 hours after the infusion and “delayed” diarrhoea starts more than 24 hours after the infusion. If you have **ANY DIARRHOEA** it is **IMPORTANT** that you follow these instructions carefully.

Early diarrhoea
- **if your diarrhoea starts less than 24 hours** after the infusion (“early diarrhoea”) you should contact your doctor or nurse **IMMEDIATELY** and they will give you a suitable treatment.

This “early diarrhoea” may be accompanied by other symptoms such as
- sweating
- chills
- abdominal cramps
- watering eyes
- stuffy nose
- visual disturbance
- dizziness
- low blood pressure
- feeling unwell
- feeling weak
- excessive mouth watering
- pupils of the eye get smaller

Tell your doctor or nurse about all your symptoms.

Do not use any anti-diarrhoeal treatment that your doctor has given you for "delayed diarrhoea".

Delayed diarrhoea
- **if your diarrhoea starts more than 24 hours** after the infusion ("delayed diarrhoea") **you should IMMEDIATELY take any anti-diarrhoeal treatment that the doctor has given you EXACTLY as he has told you. If you are unsure of what this is, ask your doctor or nurse.**

Drink large amounts of rehydration fluids, **IMMEDIATELY** (i.e. water, soda water, fizzy drinks, soup or oral rehydration therapy).

You must tell your doctor if
- you have nausea and vomiting as well as diarrhoea
- you have any fever as well as the diarrhoea
- you still have diarrhoea 48 hours after starting the diarrhoea treatment

Do not take any treatment for diarrhoea other than that given to you by your doctor or nurse and only drink the fluids described above.

Decrease in white blood cells
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**. Your doctor will probably arrange for you to have regular blood tests to monitor these white blood cells.

If you have any fever this may be an indication of infection associated with this **neutropenia** and requires immediate treatment.

If you have any **fever**, and particularly if you also have **diarrhoea**, contact your doctor or nurse **IMMEDIATELY** so that they can give you necessary treatment.

Nausea and vomiting
If you have nausea and/or vomiting contact your doctor or nurse **IMMEDIATELY**.

Breathing difficulties
If you have breathing difficulties contact your doctor or nurse **IMMEDIATELY**.

Other side effects
Very few patients who become dehydrated as a result of diarrhoea, vomiting or infection may develop kidney problems, low blood pressure or circulatory failure.
In rare cases, there have been reports of blockage, perforation, bleeding or inflammation of the intestines, or inflammation of the pancreas. If you have severe stomach pain or if you develop such symptoms as passing black or bloodstained bowel movements or vomit blood contact your doctor **IMMEDIATELY**.

All medicines can cause allergic reactions. Any sudden wheeziness, difficulty in breathing, swelling, rash or itching (especially affecting the whole body) should be reported to a doctor **IMMEDIATELY**.

Irinotecan may cause changes in laboratory tests carried out by your doctor.

If you receive Irinotecan in combination with **cetuximab**, some of the side effects you may experience can also be related to this combination. Such side effects may include a acne-like rash.

If you receive Irinotecan in combination with **capecitabine**, some of the side effects you may experience can also be related to this combination. Such side effects may include: very common blood clots, common allergic reactions, heart attack and fever in patients with a low white blood cell count.

If you receive Irinotecan in combination with **capecitabine** and **bevacizumab**, some of the side effects you may experience can also be related to this combination. Such side effects include: low white blood cell count, blood clots, high blood pressure and heart attack.

If you receive **bevacizumab** in combination with Irinotecan, **5-fluorouracil and folinic acid**, some of the side effects you may experience can also be related to this combination. Such side effects include: hypertension, diarrhoea and leukopenia (decrease in the number of white blood cells).

Therefore, if you receive Irinotecan in combination with either **capecitabine, cetuximab, bevacizumab** or **5-fluorouracil and folinic acid,** please make sure that you also read the package leaflet for each medicine.

Other side effects which may occur when you are treated with Irinotecan are:

Very common (may affect more than 1 in 10 people):
- blood disorders: thrombocytopenia (decreased number of blood platelets), anaemia (decrease in the number of red blood cells).
- loss of appetite
- hair loss
- mouth ulcers

fatigue

Common (may affect up to 1 in 10 people):
- infections
- mild stomach pain.
- constipation.
- increased levels of liver enzymes, bilirubin and creatinine in the blood

Side effects where the frequency is not known
- inflammation of the digestive tract, including the mouth (white thrush), or throat infections
- gastrointestinal bleeding and ulcers in the lining of the colon or rectum
- abdominal pain and inflammation, causing diarrhoea (a condition known as pseudomembraneous colitis)
- high blood pressure
- lung disease causing shortness of breath
- mild allergic skin reactions or skin rashes

- temporary speech disorders
- thrombosis (blood clots), heart attack, stroke
- sepsis (blood poisoning)
- liver problems: hepatic steatosis (fat in the liver), steatohepatitis (inflammation of the liver due to buildup of fat in the liver)
- muscular cramps and twitches
- pins and needles
- inflammation at the injection site
- low potassium and sodium (mostly related to diarrhoea and vomiting)
- low levels of magnesium in the blood
- increased amylase and lipase (measures of how well your pancreas is working)
- abnormal gait
- confusion
- headache
- collapse
- flushing
- slower heart beat
- bladder infection
- breast pain
- hiccups

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 Website: 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

Keep this medicine out of the sight and reach of children.
Do not freeze.
For single use only.
Keep the vial in the outer carton in order to protect from light.
Do not use this medicine 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 30°C and for 48 hours at 2-8°C (e.g. in a fridge).

6. Contents of the pack and other information

What Irinotecan 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 2ml vial contains 40 mg irinotecan hydrochloride trihydrate.
- One 5ml vial contains 100 mg irinotecan hydrochloride trihydrate.
- One 15ml vial contains 300 mg irinotecan hydrochloride trihydrate.
- One 25ml vial contains 500 mg irinotecan hydrochloride trihydrate.
- The other ingredients are sorbitol E420, lactic acid, sodium hydroxide, hydrochloric acid and water for injections.

What Irinotecan looks like and contents of the pack
Irinotecan Hydrochloride 20 mg/ml concentrate for solution for infusion is a clear, colourless to slightly yellow solution.

Pack size:
1 x 2 ml vial
1 x 5 ml vial
1 x 15 ml vial
1 x 25 ml vial

Marketing Authorisation Holder
Actavis Group hf.
Reykjavíkurvegi 76-78,
IS-220 Hafnarfjörður
Iceland

Manufacturer
Actavis Nordic A/S
Ørnegårdsvej 16
DK-2820 Gentofte
Denmark
Or
Actavis Italy S.p.A.
Via Pasteur 10,
20014 Nerviano (MI),
Italy

This leaflet was last revised in May 2018

Logo actavis
Actavis, Barnstaple, EX32 8NS, UK

The following information is intended for healthcare professionals only:

Instructions for use / handling, preparation and disposal guide for use with Irinotecan 20 mg/ml concentrate for solution for infusion

Irinotecan Hydrochloride 20 mg/ml concentrate for solution for infusion
Irinotecan hydrochloride trihydrate

Use - Cytotoxic

Handling

As with other antineoplastic agents, Irinotecan must be prepared and handled with caution. The use of glasses, mask and gloves is required.
If Irinotecan solution or infusion solution should come into contact with the skin, wash immediately and thoroughly with soap and water. If Irinotecan solution or infusion solution should come into contact with the mucous membranes, wash immediately with water.

Preparation for the intravenous solution
As with any other injectable drugs, the Irinotecan solution 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 concentrate for solution 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. The infusion should not be thoroughly mixed by manual rotation.

From a microbiological point of view, the product should be used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

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

Irinotecan should **not** be delivered as an intravenous bolus or an intravenous infusion shorter than 30 minutes or longer than 90 minutes.

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

Logo actavis
Actavis, Barnstaple, EX32 8NS, UK