



Package Leaflet: Information For The User Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for Infusion

Initiation hydrochloride trihydrate The name of your medicine is 'Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for Infusion' but in the rest of the leaflet it will be called "Irinotecan

Injection". Read all of this leaflet carefully before you start using this medicine.

medicine. Keep this leaflet. You may need to read it again. If you have any further questions, ask your doctor. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet: 1. What Irinotecan Injection is and what it is used for 2. What you need to know before you are given Irinotecan Injection 3. How you will be given Irinotecan Injection 4. Possible side effects

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5. How to store Irinotecan Injection 6. Contents of the pack and other information

1. What Irinotecan Injection is and what it is used for linotecan 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. Your doctor may use a combination of Irinotecan with 5-fluorouracil/folinic acid (SFU/FA) and bevacizumab to treat your cancer of the large intestine (colon or rectum).

or rectum). Your doctor may use a combination of Irinotecan with capacitabine 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. or rectum)

. What you need to know before you are given Iring

You should not be given Irinotecan Injection if you are allergic to Irinotecan Injection or any of the other ingredients of this medicine (listed in section 6) have or have had chronic inflammatory bowel disease or have betruction

are breast feeding have severe liver disease

It is very important to receive all scheduled doses. If you miss a dose, contact your doctor promptly. 4. Possible side effects

4. Possible side effects Like all medicines, Irinotecan Injection 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 "Warnings and precautions" If you experience any of the following side effects after you have been efficient were medicine to fill work.

have been given your medicine, tell your doctor immediately. If you are not in hospital, you MUST GO straight away. Allergic reactions. If you have wheeziness, difficulty in doctor immediately. If you are not in hospital, you MUST GO straight away. Allergic reactions. If you have wheeziness, difficulty in breathing, swelling, rash or itching (especially affecting the whole body) contact your doctor or nurse immediately. Severe allergic reactions (anaphylactic/anaphylactoid reactions) may occur most often in the minutes following injection of the product: skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and you may feel you are going to faint. Very commo (may affect more than 1 in 10 people) Blood disorder: neutropenia (decreased number of some white blood cells), thrombocytopenia Delayed diarhoea Nausea and vomiting

(lecteased number of block platers), anderna Delayed diarrhoea Nausea and vomiting Hair loss (the hair grows again after end of treatment) In combination therapy transient increase in the levels of liver enzymes or bilirubin Common (may affect up to 1 in 10 people) Acute cholinergic syndrome: the main symptoms are early diarhoea and other symptoms such as abdominal pain; red, sore, itching and weeping eyes (conjunctivitis); running nose (rhinitis); low blood pressure; widening of the blood vessels; sweating, chilis; a feeling of general discomfort and illness, dizziness; visual disturbance, small puplis; watering eyes and increased salivation, occurring during or within the first 24 hours after the infusion of Irinotecan Injection.

Injection. Fever, infections (including sepsis) Fever associated with a severe decrease in the number of white blood cells Dehydration, commonly associated with diarrhoea and/or

vomiting. Constipation Fatigue Consupation Fatigue Increased level of liver enzymes and creatinine in the blood. Uncommon (may affect up to 1 in 100 people) Allergic reactions. If you have wheeziness, difficulty in breathing, swelling, rash or itching (especially affecting the whole body) contact your doctor or nurse immediately. Mild skin reactions; mild reactions at the infusion site Difficulty breathing Lung disease (interstitial pulmonary disease) Intestinal blockage Abdominal pain and inflammation, causing diarrhoea (a condition known as

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.

have severe bone marrow failure are in poor general health (evaluated by an international have severe come memory tomos are in poor general health (evaluated by an international standard) are using the natural remedy St John's Wort (hypericum perforatum) Warnings and precautions Special care is needed in elderly patients. As Innotecan Injection 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 Intotecan Injectiontell your doctor if any of the following apply to you: You have kidney problems You have eastma You have ever received radiation therapy You experienced severe diarthoea or fever after being You have asthria You have extracted radiation therapy You experienced severe diarthoea or fever after being treated with lrinotecan Injection 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 lrinotecan InjectionYou have had or are due to have any vaccinations You are taking any other medicines. Please see the section elow "Other medicines and irinotecan². 1) The first 24 hours after administration of Irinotecan Injection During administration of Irinotecan Injection (30 – 90 min.) and shortly after administration you may experience some of the following symptoms: All should also a some of the following symptoms: Diarrhoea Watering eyes Sweating Visual disturbance Abdominal pain 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. 2) From the day after treatment with Irinotecan Injectionuntil next treatment. xt treatment next treatment. During this period you may experience various symptoms, which may be serious and require immediate treatment and close supervision.

immediate treatment and uses Gapen... Diarrhoea If your diarrhoea starts more than 24 hours after administration of Irinotecan Injection ("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 stool do the following:

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 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 stool. The recommended dosage of loperamide may not be taken for

recommended dosage of loperamide may not be taken for more than 48 hours.

Rare (may affect up to 1 in 1,000 people) Severe allergic reactions (anaphylactic/anaphylactoid reactions) may occur most often in the minutes following injection of the product: skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and you may feel you are going to faint. If this happens you should tell your doctor immediately

lappens you should lear your doctor mediately Early effects such as muscular contraction or cramps and umbness (paraesthesia). Gastrointestinal biedding and inflammation of the colon cluding the appendix Intestinal perforation; anorexia; abdominal pain; nflammation of pancreas Inflammation of pancreas Increased blood pressure during and following dministration.

Decreased levels of potassium and sodium in the blood, nostly related to diarrhoea and

Working Ventual of diameters and the voniting 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 and fats. Not known (frequency cannot be estimated from the available

ation of the liver with concurrent fat accu

liver If you receive Irinotecan Injection in combination with celuximab, some of the side effects you may experience can also be related to this combination. Such side effects may include an accne- like rash. Therefore, please make sure that you also read the package

effects may include an acne-like rash. Therefore, please make sure that you also read the package leaflet for cetuximab. If you receive Irinotecan Injection 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. Therefore, please make sure that you also read the package leaflet for capecitabine. If you receive Irinotecan Injection 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 cells, high blood pressure and heart attack. Therefore, please make sure that you also read the package leaflet for capecitabine and bevacizumab.

bevacizumab. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please

effects not listed in this leaflet, please tell your doctor or pharmacist. 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 the national reporting system (see contact details below). By reporting side effects you can help provide more information on the safety of this medicine.

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5. How to store Irinotecan Injection Keep out of the reach and sight of children. Do not freeze.

2. Drink large amounts of water and rehydration fluids immediately (i.e. water, soda water, fizzy $% \left(\frac{1}{2}\right) =0$

Rare (may affect up to 1 in 1,000 people) Severe allergic reactions (anaphylactic/

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data) Infla

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 instruction. The anti-diarrhoeal treatment should not be used to prevent a further episode of diarrhoea even though you have experienced delayed diarrhoea at prevents cycles. previous cycles. Fever If the body temperature increases over 38 C it may be a sign of infection, especially if you also have diarhoea. 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 womting If you have nausea and/or vomiting contact your doctor or the unit immediately. iting ea and/or vomiting contact your doctor or the If you have nauses and/or vomiting contact your doctor or th unit immediately. Neutropenia Irinotecan Injection 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 Injection 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. If you have any example, immediately. Impaired liver function Before treatment with linotecan Injection is started and before every following treatment cycle the liver function should be monitored (by blood tests). Other medicines and innotecan Other medicines and innotecan

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 linitotecan Injection 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

diarrhoea You still have diarrhoea 48 hours after starting the diarrh treatment

Other medicines and innotecan Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This includes herbal medicines, strong vitamins and

If you receive Irinotecan Injection in combination with capecitabine, cetuximab or bevacizumab, please make sure that you also read the patient information please make sure that you also read the patient information leaflet for each medicine. Some medicines may alter the effects of Irinotecan Injection e.g. ketoconazole (for the treatment of fungal infections), rifampicin (for the treatment of tuberculosis), warfarin (an anticoagulant used to thin the blood), atazanavir (used to treat HIV), ciclosporin or tacrolimus (used to dampen down your body's immune system) and some medicines for the treatment of enilensy (carabanzeoine.

obuy s minitare system; of epilepsy (carbamazepine, phenobarbital and phenytoin). The herbal medicine St John's Wort (hypericum perforatum) phenous The hert The herbal medicine SI John's Wort (hypericum perforatum) may not be used concurrently with Irinotecan Injection and not between treatments, as it may decrease the effect of Irinotecan Injection. If you require an operation, please tell your doctor or anesthetist that you are being treated with irinotecan, as it may alter the effect of some medicines used

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

6. Contents of the pack and other information What Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for Infusion contains The active substance is innotecan hydrochloride trihydrate. 1 ml of concentrate contains 20 mg irinotecan hydrochloride trihydrate equivalent to 17.33 mg or irinotecan for the substance is a substantial to the substantial substanti

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

One 25 mi Viai contenno coc ..., trihydrate The other ingredients are sorbitol (E420), lactic acid, sodium hydroxide, hydrochloric acid and water for ingretions. What Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for Infusion looks like and

Contents of the pack Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution for Infusion is a clear, pale yellow coloured solution.

Pack sizes: 2 ml/ 5 ml/ 15 ml/ 25 ml Not all pack sizes may be marketed

Marketing Authorisation Holder and Manufacturer Marketing Authorisation Holder TA

Manufactured in India by: TAJ PHARMACEUTICALS LTD. Mumbai, India at SURVEY NO.188/1 TO 189/1,190/1 TO 4, ATHIYAWAD, DABHEL, DAMAN- 396210 (INDIA)

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Irinotecan Hydrochloride 20 mg/ml Concentrate for Solution

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 Injection As with other antineoplastic agents, caution should be exercised when handling Irinotecan Injection. Dilution 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. Protection instructions for preparation of Irinotecan solution for infusion

I. Protective chamber should be used and protective gloves as well as protective gown should be worn. If there is no protective chamber available mouth cover and goggles should be used.
2. Opened containers, like injection vials and infusion bottles

 Opened containers, like injection vials and influsion b and used cannulae, syringes, catheters, tubes, and residuals of cytostatics should be considered as hazardous waste and undergo disposal according to local guidelines for the handling of HAZARDOUS WASTE.
Follow the instructions below in case of spillage: the instructions below in case of spillage: ive clothing should be worn

during surgery. Pregnancy, breast-feeding and fertility 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, Irinotecan Injection must not be used during pregnancy. Irinotecan Injection can cause birth defects. must not be used during pregnancy. Irinotecan Injection 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 none 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 Injectiontherapy. Ask your doctor for advice before taking any medicine. Driving and using machines In some cases Irinotecan Injection 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 Injection you may feel dizzy or have visual disturbances. If this happens to you do not drive or use any tools or machines. disturbances. It this happens to you contain tools or machines. Important information about some of the ingredients of Irinotecan Injection ontains sorbitol. If you suffer from Intolecan Injection contains sorbitol. If you suffer from Intolerance to some sugars, tell your doctor before you are given this medicinal product. This medicinal product contains less than 1 mmol sodium per dose, i.e. essentially 'sodium-free'.

3. How you will be given Irinotecan Injection Irinotecan Injection 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 Injection 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 Injection every two weeks. This will be followed by folinic acid and 5-fluorouracil.

If you are treated with irinotecan in combination with tuximab you will normally receive the ame dose of irinotecan as administered in the last cycles of same dose of irinotecan as administered in the last cycles of the prior irinotecan containing regimen. Irinotecan Injection must not be administered less than 1 hour after the end of the cetuximab infusion. These dosages may be adjusted by your doctor depending on your condition and any side effects you may have.

If you receive more Irinotecan Injection than you should It is unlikely that you will be given too much Irinotecan Injection. However in the event that this occurs you may have 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 debte or diministration way mendicine. the doctor administering your medicine. If you miss a dose of Irinotecan Injection

rotation. The pro

broken glass should be collected and placed in the ontainer for HAZARDOUS WASTE. contaminated surfaces should be flushed properly with opious amount of cold water Should be flushed properly with copious amount of cold water the flushed surfaces should then be wiped thoroughly and the materials used as HAZARDOUS WASTE In the event of Irinotecan Injectioncontact with the skin, the area should be rinsed with plenty of running water and then washed with soap and water. In case of contact with mucous membranes, wash the contacted area thoroughly with water. If you have any discomfort, contact doctor.

you have any discomfort, contact doctor. 5. In case of contact of frinotecan Injectionwith eyes wash them thoroughly with Jelenty of water. Contact an ophthalmologist immediately. Preparation for the infusion solution Infotecan concentrate for solution for infusion is intended for intravenous infusion only after diluting prior to administration in the recommended diluents, either 0.9 % Sodium chloride solution for infusion or 5% glucose solution for infusion. Aseptically withdraw the required amount of innotecan concentrate for solution from the vial with a calibrated syringe and inject into a 250 ml infusion bag or botte. The infusion should be thoroughly mixed by manual rotation.

duct should be diluted and used immedia

rotation. The product should be diluted and used immediately after opening. Irinotecan solution is physically and chemically stable with infusion solutions (0.9% (w/v) golucose solution) for up to 28 days when stored in LDPE or PVC containers at 5°C or at 25°C and protected from light. When exposed to light. physico-chemical stability has been demonstrated for up to 3 days. From a microbiological point of view, the diluted solution 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 24 hours at 2 to 8°C, unless reconstitution / dilution (etc) has taken place in controlled and validated aseptic conditions. If any precipitate is observed in the viais or after reconstitution, the product should be discarded according to standard procedure for cytotoxic agents. Irinotecan Injection should not be delivered as an intravenous bolus or an intravenous infusion shorter than 30 minutes or longer than 90 minutes. Disposal All items used for preparation, administration or otherwise

than 30 minutes or longer a Disposal All items used for preparation, administration or otherwise coming into contact with Irinotecan Injection should undergo disposal according to local guidelines for the handling of cytotoxic compounds.

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