1.3.2 Patient Information Leaflet

SCHEDULING STATUS

S4

PATIENT INFORMATION LEAFLET

INOTRIX 40 mg/2 mL concentrate for solution for infusion

INOTRIX 100 mg/5 mL concentrate for solution for infusion

INOTRIX 300 mg/15 mL concentrate for solution for infusion

(Irinotecan hydrochloride trihydrate)

(Contains Sorbitol)

Read all of this leaflet carefully before INOTRIX is administered to you

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist, nurse or other health care provider.

What is in this leaflet:

1. What INOTRIX is and what it is used for

INOTRIX belongs to a group of medicines called cytostatics (anti-cancer medicines).

INOTRIX is used to treat cancer of the lower bowel, alone or in combination with two other medicines (5-fluorouracil and folinic acid)

2. What you need to know before INOTRIX is administered to you

INOTRIX should not be administered to you:

- If you are hypersensitive (allergic) to irinotecan hydrochloride trihydrate or any of the ingredients of INOTRIX (listed in section 6).
- If you are pregnant or breastfeeding or if you think you may be pregnant.
- If you have severe bone marrow failure.
- If your WHO performance status > 2 (i.e. if your general health status does not allow you to carry out general activities of daily living).
- If you have a disease involving frequent inflammation of the intestine (chronic inflammatory bowel disease) or blockage of the intestine (ileus).
- If your bilirubin (breakdown product of red blood cells) level is high.
- If you are a child or adolescent.
- If you are taking azole antifungal medication (used to treat fungal infections).
- If you are taking St John's Wort (a herbal supplement).
- If you are having any live attenuated vaccinations. Speak to your healthcare provider before any vaccination.

Warnings and precautions

Tell your doctor or healthcare professional before being given the INOTRIX concentrate for solution for infusion if:

- you have impaired liver function you are at greater risk of developing severe decrease in white blood cells or fever.
- you experience nausea and vomiting. If you experience vomiting together with delayed diarrhoea, you should be hospitalised for treatment.
- you experience early diarrhoea together with a group of symptoms such as sweating, abdominal cramping, watery eyes and salivation. If this occurs, inform your doctor as a specific medication is required in order for these symptoms to disappear.
- you are an elderly patient, the dose may have to be adjusted accordingly.
- If you have recently had or are due to have vaccinations
- If you have previously received pelvic/abdominal radiotherapy you may be at increased risk of developing bone marrow suppression
- if you suffer/suffered from heart disease 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.
- If you have a type of lung disease that causes scarring of lungs

INOTRIX should only be administered under the supervision of a qualified medical doctor in units specialised in the administration of chemotherapy. It is recommended that INOTRIX be administered only in healthcare institutions with adequately equipped facilities, including an intensive care unit.

Some people will need special care from their doctors when they are on INOTRIX. It is especially important that your doctor explains the need for sufficiently prolonged antidiarrhoeal treatment and abundant fluid intake if you require it.

You may develop diarrhoea soon after treatment or delayed diarrhoea, which if not properly treated can be life-threatening. As soon as the first liquid stool occurs please consult your doctor or healthcare professional immediately for appropriate treatment. You may need an antibiotic or hospitalisation.

Your blood cell count should be monitored weekly as infection may occur due to a decrease in white blood cells. Fever together with a decrease in white blood cells should be urgently treated in hospital. The INOTRIX dose should be delayed or reduced accordingly.

INOTRIX is rarely associated with blood flow disorders (blood clots in the vessels of your legs and lungs) and it may occur rarely in patients with multiple risks factors.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before being given INOTRIX.

Children and adolescents

INOTRIX has not been studied in children or adolescents and therefore should not be used in this patient population.

Other medicine and INOTRIX:

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines).

The use of INOTRIX with these medicines may cause undesirable interactions.

In particular tell your doctor if you are using medicines containing the following active substances:

- Medicines used to cause muscle paralysis/anaesthesia during surgery (neuromuscular blocking medicines). The effect of these medicines may be prolonged when administered together with INOTRIX.

- Other medicines used for cancer therapy (antineoplastic medicines). When administered together with INOTRIX, these medicines may worsen diarrhoea and blood disorders that may be experienced.
- A cortisone medicine known as dexamethasone used to treat inflammation and also cancer. When administered together with INOTRIX, dexamethasone may enhance (increase) the chances of experiencing a decrease in a type of white blood cells (a blood disorder known as lymphocytopenia).
- Laxatives, as these can worsen the incidence or severity of diarrhoea.
- Medicines that increase urination (diuretics) as this, together with the vomiting and diarrhoea that may be experienced with INOTRIX, can result in dehydration.
- Medicines used to treat epilepsy (i.e. anticonvulsants e.g. carbemazepine, phenobarbitone or phenytoin) which may decrease the effect of INOTRIX.
- Medicines used to treat fungal infection, known as azole antifungals (e.g. ketoconazole), as these may increase the effect of INOTRIX.
- A HIV medicine known as atazanavir may increase the effects of INOTRIX.
- A cancer medicine known as bevacizumab may increase the effects of INOTRIX.
- St. John's Wort (a herbal medication used to treat depression). When administered together with INOTRIX, the effect of INOTRIX is reduced.

- Ciclosporin or tacrolimus which are immunosuppressants (used to dampen down your body's immune system)
- A medicine which works against vitamin K , as this may increase your risk of bleeding. You may need to have more frequent checks.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before being administered INOTRIX.

You should not be administered with INOTRIX if you are pregnant or breastfeeding your baby. It could harm your baby.

Women of childbearing age as well as men who have been administered with INOTRIX, must use contraceptive measures during the period of treatment and for at least 3 months after
stopping treatment.

Driving and using machines

INOTRIX might cause dizziness or blurred vision. Do not drive or operate tools or machines if you experience such side effects.
It is not always possible to predict to what extent INOTRIX may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which INOTRIX affects them.

INOTRIX contains sorbitol (a sugar), If your doctor has told you that you have an intolerance to some sugars, talk to your doctor before you receive INOTRIX.
INOTRIX contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How INOTRIX will be administered

You will not be expected to give yourself INOTRIX. It will be given to you by a person who is qualified to do so.

Your doctor will calculate the exact dosage for you based on your weight and height.

When INOTRIX is administered on it's own, the usual dose is 350 mg/m^2 given as an intravenous infusion over 30 to 90 minutes every three weeks.

When INOTRIX is to be used together with 5-fluorouracil and folinic acid, the usual dose is 80 mg/m^2 given as an intravenous infusion over 30 to 90 minutes, followed by an infusion of folinic acid and the 5-fluorouracil over six weeks. After this period there will be one weeks rest.

The usual dose will be adjusted or delayed if you have neutropenia (very low blood count of a type of white blood cells), severe diarrhoea, vomiting or if you are elderly.

Your doctor will tell you how long your treatment with INOTRIX will last. Do not stop any treatment unless your doctor tells you to do so.

If you have the impression that the effect of INOTRIX is too strong or too weak, tell your doctor.

If you are administered more INOTRIX than you should

Since a healthcare professional will administer INOTRIX, he/she will control the dosage.

However, in the event of overdosage, your doctor will manage the overdosage.

If your dose of INOTRIX is missed

Your doctor will administer INOTRIX so this should not happen. In the event a dose is missed, your doctor will not give you a double dose to make up for the missed doses.

Do not miss your doctor's appointments. Your doctor will tell you when treatment is to be stopped.

4. Possible side effects

INOTRIX can have side effects.

Not all side effects reported for INOTRIX are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking INOTRIX, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling around the eyes or face or tongue, (which may rarely be a serious allergic reaction)

- Swelling in the ankles, wrists, arms and legs
- Difficulty breathing
- Severe nausea, vomiting
- Fever
- Severe diarrhoea

These are all very serious side effects. If you have them, you may have had a serious reaction to INOTRIX. You may need urgent medical attention or hospitalisation.

A frequent side-effect with INOTRIX is diarrhoea. Please take note of the following important information:

Diarrhoea

INOTRIX 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 tell your doctor or healthcare professional immediately.

Patients with an increased risk of diarrhoea are those who had a previous abdominal/pelvic radiotherapy and initial raised white blood cells.

Early diarrhoea (Frequent)

• if diarrhoea starts less than 24 hours after the infusion ("early diarrhoea") you should contact your doctor IMMEDIATELY.

This "early diarrhoea" may be accompanied by a group of other symptoms listed below. This is known as acute cholinergic syndrome occurring during or within the first 24 hours after the infusion of INOTRIX. The symptoms may be:

Frequent:

• abdominal pain/cramping

Less frequent:

• chills

• lacrimation (watery eyes)

• rhinitis (irritation and inflammation inside the nose which may result in stuffy nose, runny nose and/or post-nasal drip)

• dizziness

• hypotension (low blood pressure)

• malaise (lack of well being)

• increased salivation (mouth watering)

• myosis (constriction to the pupil of the eyes)

Frequency unknown:

• sweating

• visual disturbances

• conjunctivitis (inflammation of the eye)

• vasodilation (widening of blood vessels)

Delayed diarrhoea (Frequent)

• if your diarrhoea starts more than 24 hours after the infusion (“delayed diarrhoea”)

you should IMMEDIATELY contact your doctor.

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.

Decrease in white blood cells (Frequent)

INOTRIX 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.

If you have any fever, this may be an indication of infection associated with this neutropenia.

Contact your doctor or healthcare provider immediately.

Nausea and vomiting (Frequent)

If you have any fever, and particularly if you also have diarrhoea and/or nausea and/or vomiting contact your doctor or healthcare provider IMMEDIATELY.

Tell your doctor if you notice any of the following IMMEDIATELY:

Frequent side effects:

- difficulty in breathing
- dehydration
- change in kidney function tests
- excessive bilirubin (breakdown product of red blood cells) in the blood
- low blood volume resulting in dizziness or fainting
- inflammation and ulceration of the membranes lining the digestive tract
- infection
- anaemia which is decreased number of red blood cells which may lead to a feeling of weakness, fatigue or poor concentration

- leucopenia which is too few white blood cells which results in greater risk of infection
- thrombocytopenia which is too few platelets in the blood which may result in bleeding into the skin, bruising or prolonged bleeding after injury
- blockage of blood vessels that can result in severe chest pain, stroke, inflammation of a vein with formation of a clot, heart attack, heart arrest, sudden death

Other side-effects have also been reported with INOTRIX

Frequent:

- loss of hair
- lack of appetite
- constipation
- inflammation of the mouth
- decreased weight
- pain
- lack of energy

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get 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 via https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of INOTRIX.

5. How to store INOTRIX

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

INOTRIX will be stored in the pharmacy

Store at or below 25 °C.

After dilution in either 0,9 % sodium chloride or 5 % dextrose, the diluted solution is stable for 24 hours at a temperature at or below 25 ºC for 4 days under refrigeration (between 2 and 8 ºC). Discard any unused portion thereafter. Do not freeze.

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

Do not use after the expiry date stated on the vial and the carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What INOTRIX contains

The active substance is irinotecan hydrochloride trihydrate.

Each mL of solution contains 20 mg irinotecan hydrochloride trihydrate

INOTRIX 40 mg/2 mL concentrate for solution for infusion contains 40 mg irinotecan hydrochloride trihydrate.

Contains 90,0 mg sorbitol.

INOTRIX 100 mg/5 mL concentrate for solution for infusion contains 100 mg irinotecan hydrochloride trihydrate.

Contains 225,0 mg sorbitol.

INOTRIX 300 mg/15 mL concentrate for solution for infusion contains 300 mg irinotecan hydrochloride trihydrate.

Contains 675,0 mg sorbitol.

The other ingredients of INOTRIX are Sorbitol, Lactic acid, and water for injection.

What INOTRIX looks like and contents of the pack

[PRODUCTA NAME] concentrate for solution for infusion is a clear colourless to slightly yellow solution, essentially free from visible particles.

The diluted infusion solution is a pale yellow clear, sterile, pyrogen-free solution, free from visible particles.

INOTRIX 40 mg/2 mL concentrate for solution for infusion is marketed in Type – I, 2 R amber BB tubular glass vial with 13 mm neck stoppered with 13 mm Omniflex plus coated dark grey colour bromobutyl rubber stopper and sealed with cleared lacquered Aluminium seal having red colour PP disc. A single vial is further packed in a pre-printed carton with a package leaflet.

INOTRIX 100 mg/5 mL concentrate for solution for infusion is marketed in Type – I, 6 R amber BB tubular glass vial with 20 mm neck stoppered with 20 mm Omniflex plus coated dark grey colour bromobutyl rubber stopper and sealed with cleared lacquered Aluminium seal having sky blue colour PP disc. A single vial is further packed in a pre-printed carton with a package leaflet.

INOTRIX 300 mg /15 mL concentrate for solution for infusion is marketed in Type – I, 20 R amber BB tubular glass vial with 20 mm neck stoppered with 20 mm Omniflex plus coated dark grey colour bromobutyl rubber stopper and sealed with cleared lacquered Aluminium seal having sky blue colour PP disc. A single vial is further packed in a pre-printed carton with a package leaflet.

Not all packs and pack sizes are necessarily marketed.

NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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This leaflet was last revised in

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