

Applicant/PHRC: **Hetero Drugs South Africa (Pty) Ltd**

Product proprietary name: **CAROHET 40 mg/2 mL, 100 mg/5 mL & 300 mg/15 mL**

Dosage form and strength: **Injection, Each mL contains irinotecan hydrochloride trihydrate 20 mg**

FINAL PATIENT INFORMATION LEAFLET FOR CAROHET

SCHEDULING STATUS

S4

CAROHET 40 mg/2 mL solution for injection

CAROHET 100 mg/5 mL solution for injection

CAROHET 300 mg/15 mL solution for injection

Irinotecan hydrochloride trihydrate

Contains sugar “sorbitol”

Read all of this leaflet carefully before you are given CAROHET:

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

What is in this leaflet

1.What CAROHET is and what it is used for

2.What you need to know before you use CAROHET

3.How to use CAROHET

4.Possible side effects

5.How to store CAROHET

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6. Contents of the pack and other information.

1. What CAROHET is and what it is used for

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

CAROHET 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 colon and rectum.

2. What you need to know before you use CAROHET

CAROHET should not be administered to you:

- If you are hypersensitive (allergic) to irinotecan hydrochloride trihydrate (active ingredient) or any of the other ingredients of CAROHET.
- If you are pregnant or breastfeeding.
- 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.
- If you are taking azole antifungal medication (used to treat fungal infections) or St John's Wort (a herbal supplement).

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- If you are the administration of live or live-attenuated vaccines.

Warnings and precautions

Tell your doctor or health care provider before being given the injection:

Special care should be taken with CAROHET:

- If you have impaired liver function you are at greater risk of developing severe decrease in white blood cells or fever.
- If you experience nausea and vomiting. If you experience vomiting together with delayed diarrhoea, you should be hospitalised for treatment.
- If 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.
- If you are an elderly patient, the dose may have to be adjusted accordingly.

Contraceptive measures must be taken during and for at least 3 months after stopping therapy.

Avoid vaccination with live vaccines.

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

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Some people will need special care from their doctors when they are on CAROHET. 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 CAROHET dose should be delayed or reduced accordingly.

The safety and efficacy of CAROHET in children have not been established.

Other medicines and CAROHET

If you are taking other medicines on a regular basis, including complementary, traditional or herbal medicines (e.g., St. John's Wort), the use of CAROHET with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or health care professional for advice.

CAROHET may interact with the following medicines:

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

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- Other medicines used for cancer therapy (antineoplastic medicines). When administered together with CAROHET, 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 CAROHET, dexamethasone may enhance 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 CAROHET, can result in dehydration.
- Medicines used to treat epilepsy (i.e., anticonvulsants e.g., carbamazepine, phenobarbitone or phenytoin) decrease the effect of CAROHET.
- Medicines used to treat fungal infection, known as azole antifungals (e.g., ketoconazole), as these may increase the effect of CAROHET.
- A HIV medicine known as atazanavir may increase the effects of CAROHET.
- A cancer medicine known bevacizumab may increase the effects of CAROHET.
- St. John's Wort (a herbal medication used to treat depression).
- When administered together with CAROHET, the effect of CAROHET is reduced.
- Other bone marrow depressants medication.
- Loperamide should not be taken in advance for the treatment of the diarrhoea side effect.

Pregnancy, breastfeeding and fertility

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CAROHET should not be used if you are pregnant or breastfeeding your baby. Women of childbearing age receiving CAROHET should be advised to avoid becoming pregnant and to inform the treating doctor immediately should this occur.

Contraceptive measures must be taken during and for at least three months after cessation of therapy.

Driving and using machines

There is potential for dizziness or visual disturbances, and it is advised not to drive or operate machinery if these symptoms occur.

CAROHET contains sorbitol

Since CAROHET contains sorbitol, it is unsuitable for use in hereditary fructose intolerance.

3.How to use CAROHET

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

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

The amount of CAROHET 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).

Your doctor will tell you how long your treatment with CAROHET will last. If you have the impression that CAROHET is too strong or too weak, tell your doctor or pharmacist.

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If you receive more CAROHET than you should

Since a healthcare professional will administer CAROHET, he / she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to use CAROHET

Since a healthcare professional will administer CAROHET, it is unlikely that the dose will be missed.

4. Possible side effects

CAROHET can have side effects.

Not all side effects reported for CAROHET are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving CAROHET, please consult your health care provider for advice.

If any of the following happens, stop treatment with CAROHET and tell your doctor immediately

- allergic skin reactions
- inflammation at the injection site
- inflammation of the lining of the mouth
- swelling of feet and hands, headache, increased sweating, flushing

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

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

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- Diarrhoea.

CAROHET 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 your 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 CAROHET. 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)

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- 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.

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Do not take any treatment for diarrhoea other than that given to you by your doctor.

- **Decrease in white blood cells** (*Frequent*)

CAROHET 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.

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 IMMEDIATELY.

Other side effects.

If you experience any of the following conditions please report it to a doctor IMMEDIATELY:

Frequent:

- 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

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- 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

Less frequent:

- Extravasation which is leakage of medicine from the vein into the surrounding tissue, sign and symptoms include stinging burning sensation and oedema around the injection site
- Tumour-lysis syndrome which is when a large number of cancer cells die within a short period releasing their contents in the blood, sign and symptoms include nausea with or without vomiting, lack of appetite, fatigue, dark urine

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

Frequent:

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

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- 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 or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via “**6.04 Adverse Drug Reactions Form**”, found online under SAHPRA’s publications:

<https://www.sahpra.org.za/publications/Index/8/>. By reporting side effects, you can help provide more Information on the safety of **CAROHET**.

5.How to store CAROHET

Store at or below 25 °C and store in original package, protect from light and moisture as well as do not freeze.

KEEP OUT OF REACH OF CHILDREN.

In-use storage conditions

CAROHET are subjected to 0,9 % NaCl (0,12 mg/ml Concentration), 0,9 % NaCl (2,8 mg/ml Concentration), 5 % Glucose (0,12mg/ml concentration), 5 % Glucose (2,8 mg/ml Concentration) for 24 Hrs at 2-8 °C, 3 days at 25 °C and 28 days at 5 °C.

6. Contents of the pack and other information

What CAROHET contains

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- The active substance is irinotecan hydrochloride trihydrate

The other ingredients are:

- Sorbitol
- Lactic acid
- Sodium hydroxide
- Hydrochloric acid

What CAROHET looks like and contents of the pack

CAROHET 40 mg/2 mL

5 ml Fiolax amber tubular glass vials, type I with 13 mm neck with 13 mm serum rubber GBB stopper with a golden yellow flip off seal.

Pack size: 1 x 10 mL

CAROHET 100 mg/5 mL

5 ml Fiolax amber tubular glass vials, type I with 13 mm neck with 13 mm serum rubber GBB stopper with a rust flip off seal.

Pack size: 1 x 10 mL

CAROHET 300 mg/15 mL

20 mL/mm Tubular type I vials with 20 mm rubber GBB stopper with a purplement flip off seal.

Pack size: 1 x 20 mL

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HOLDER OF CERTIFICATE OF REGISTRATION

Hetero Drugs South Africa (Pty) Ltd

Waterfall Corporate

Campus, Building No.2,

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REGISTRATION NUMBER(S)

CAROHET 40 mg/2 mL: 56/26/0832.829

CAROHET 100 mg/5 mL: 56/26/0833.830

CAROHET 300 mg/15 mL: 56/26/0834.831

DATE OF FIRST AUTHORISATION/ RENEWAL OF AUTHORISATION

11 July 2023

DATE OF REVISION OF THE TEXT

N/A