Package leaflet: Information for the user

Treosulfan

Powder for Solution for Injection or Infusion 5 g
Treosulfan

Read all of this leaflet carefully before you are given 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 or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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2. What you need to know before you are given Treosulfan Powder for Solution for Injection or Infusion 5 g
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1. What Treosulfan Powder for Solution for Injection or Infusion 5 g is and what it is used for

Treosulfan belongs to the group of anticancer medicines called bifunctional alkylating agents. These agents inhibit tumour growth.

Treosulfan has been prescribed by your doctor for the treatment of ovarian cancer.

2. What you need to know before you are given Treosulfan Powder for Solution for Injection or Infusion 5 g

You are not given Treosulfan Powder for Solution for Injection or Infusion 5 g
- if you are allergic to treosulfan.
- if you do not have enough blood cells (severe bone marrow depression).

Before each administration, you will have blood tests to check that you have enough blood cells to receive treosulfan.

Warnings and precautions
Talk to your doctor or pharmacist before using Treosulfan Powder for Solution for Injection or Infusion 5 g,
- if you experience reduction in blood cells as this may become worse with ongoing treatment. Blood tests will be performed at shorter intervals starting with the third course of treatment. This is especially important if combined with other forms of therapy that suppress the bone marrow function such as radiotherapy.
- if you develop inflammation of the lungs which causes shortness of breath (allergic alveolitis or pulmonary fibrosis); treatment with treosulfan should then be stopped.

Be also aware of the following:
- the risk of getting different types of infections is increased.
- different types of blood cancer may occur after long-term treatment
- as treosulfan is excreted via your kidney your blood counts should be carefully monitored and your dose adjusted accordingly if you suffer from impaired kidney function.
- treatment with anticancer medicines may increase the risk of generalised infection after some vaccinations. Therefore, you should not receive vaccination with live vaccines.
- because of the possible development of bladder inflammation with pain, more frequent or urgent urination with or without bloody urine (haemorrhagic cystitis) you are advised to drink more fluids than usual for up to 24 hours after your treosulfan infusion.
- when treosulfan is not carefully given into a blood vessel, painful inflammation of the surrounding tissue may occur.

Other medicines and Treosulfan Powder for Solution for Injection or Infusion 5 g
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
The effect of ibuprofen/chloroquine treatment may be reduced when given in combination with treosulfan.

It is not advisable to use any medicines without telling your doctor as there may be interactions between treosulfan and other medicines.

Pregnancy and breastfeeding
Do not use treosulfan if you are pregnant or breast-feeding unless your doctor considers it as absolutely necessary.
You must use effective contraception during therapy, e.g. birth control pill.

If you are planning to become pregnant or thinking of breastfeeding discuss it with your doctor first.

Fertility
No data available.

Driving and using machines
Your ability to drive or operate machines may be influenced in case of nausea and vomiting. If you are affected in this way do not drive or operate machines.

3. How you are given Treosulfan Powder for Solution for Injection or Infusion 5 g

The use of treosulfan will be confined to hospital units specialised in the administration of cytotoxic chemotherapy and will only be administered under the supervision of a qualified oncologist.

Treosulfan will be given to you by a drip given into a vein over 15 to 30 minutes (intravenous infusion) in a dose which is fixed by a doctor individually for you.

Your doctor will calculate your treosulfan dose on the basis of your blood counts measured. Your doctor will reduce the dose if other anticancer medicines or radiotherapy have been given. The dose you are given also depends on your size and varies with your body surface area (BSA). Technically, this is measured in square metres (m^2), but actually is worked out from your height and weight. Usual doses for treosulfan alone are 6-8 g/m^2 BSA. In combination with cisplatin, treosulfan is usually dosed at 5 g/m^2 BSA.

During the course of treosulfan therapy the infusions will usually be given every 3 to 4 weeks. In general, 6 courses of treatment are given.

Your doctor may change the dose and frequency of dosing depending on your blood tests, your general condition, further therapies and your response to treosulfan. If you have any questions about your treatment, ask your doctor, nurse or hospital pharmacist.

If you experience pain at the site of injection, please tell your doctor or nurse immediately.

Use in children
This medicine is not recommended for use in children.

If you are given more Treosulfan Powder for Solution for Injection or Infusion 5 g than you should
If too much of this medicine has been given to you, you may get sick or your blood cells may be reduced. Your doctor may give you a blood transfusion and will undertake other measures if necessary.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor will discuss these with you and will explain the risks and benefits of your treatment.

Contact your doctor straight away if you notice any of the following:
- Allergic reactions: if you develop itching, rash, swelling of the face, lips, tongue and/or throat, which may cause difficulties in swallowing or breathing, drop of blood pressure.
- Fever or infection: if you have a body temperature of 38 °C or higher, sweating or other signs of infection (since you might have fewer white blood cells than normal).
- Weakness, becoming easily breathless or if you look pale (since you might have fewer red blood cells than normal).
- Bleedings from gums, mouth or nose, unexpected bruising (since you might have fewer platelets than normal).
- Difficulty in breathing (since you might have an allergic reaction, inflammation or infection of the lung).

Very common (may affect more than 1 in 10 people):
- Reduction in white blood cells (which makes infections more likely), platelets (which may cause bleedings from gums, mouth or nose and unexpected bruising) or red blood cells (which can make the skin pale and cause weakness or breathlessness) – hence the need for regular blood tests.
- Stomach upsets including nausea (feeling sick) with or without vomiting (being sick).
- Mild loss of hair. After your treatment, normal hair growth should return.
- Bronze discolouration of the skin.

Common (may affect up to 1 in 10 people):
- Infections caused by fungi, viruses or bacteria.

Uncommon (may affect up to 1 in 100 people):
- Different types of blood cancer (after long-term treatment).

Rare (may affect up to 1 in 1,000 people):
- Allergic reactions (e.g. itching, rash, swelling of the face, lips, tongue and/or throat, with difficulties in swallowing or breathing, drop of blood pressure).

Very rare (may affect up to 1 in 10,000 people):
- Generalised life-threatening infections (sepsis).
- Severe reduction of red blood cells, white blood cells and platelets at the same time which can cause weakness, bruising or make infections more likely (pancytopenia).
- Addison's disease, a condition where the adrenal glands do not work properly, leading to bronzed skin, stomach upset, low blood pressure (feeling faint) and a general feeling of weakness.
- Sweating, trembling and hunger as a result of the decreased amount of glucose in your blood (hypoglycaemia).
- Pins and needles and a feeling of numbness (paraesthesia).
- Weakening of the heart muscle caused by a structural change (cardiomyopathy).
- Difficulty in breathing (inflammation and scarring of the lungs and infection of the lungs).
- Yellow discolouration of the skin and the whites of the eyes (icterus) as signs of impaired liver function also shown by blood tests.
- Urticaria or hives, an itchy rash; inflammation of the skin with or without scale formation (scleroderma and psoriasis).
- Inflammation of the bladder with pain, more frequent and urgent urination and with or without bloody urine (haemorrhagic cystitis).
- Feeling of getting ill (flu-like complaints).
- Painful local redness and swelling at the injection site (in case of leakage of treosulfan solution into the surrounding tissue).

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Treosulfan Powder for Solution for Injection or Infusion 5 g

Keep out of the sight and reach of children.

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

Do not store above 25 °C.

Once brought into solution the injection should be used immediately.

6. Contents of the pack and other information

What Treosulfan Powder for Solution for Injection or Infusion 5 g contains
The active substance is treosulfan.

What Treosulfan Powder for Solution for Injection or Infusion 5 g looks like and contents of the pack
Treosulfan Powder for Solution for Injection or Infusion is a white crystalline odourless powder.
Each vial contains 5 g of treosulfan.

Treosulfan vials are packed in boxes, each containing 5 vials.

Marketing Authorisation Holder and Manufacturer
medac
Gesellschaft für klinische Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

This leaflet was last revised in 04/2017.

The following information is intended for healthcare professionals only:

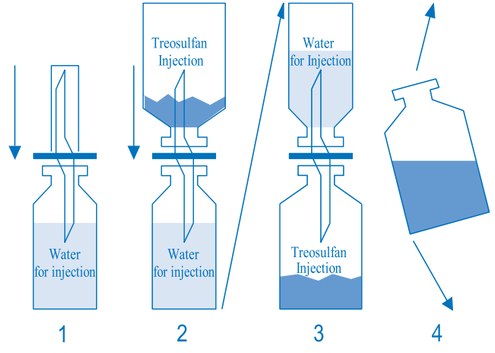
Instructions for reconstitution of Treosulfan Powder for Injection or Infusion

The powder for solution for injection or infusion is mixed with 100 ml water for injection resulting in a 50 mg/ml treosulfan solution.

To avoid solubility problems during reconstitution the following aspects should be regarded.

1. The solvent, water for injection, is warmed to 25 - 30 °C (not higher!) by using a water bath.
2. The treosulfan is carefully removed from the inner surface of the infusion bottle by shaking.
   This procedure is very important, because moistening of powder that sticks to the surface results in caking.
   In case caking occurs the bottle has to be shaken long and vigorously.
3. One side of the double sided cannula is put into the rubber stopper of the water bottle. The treosulfan bottle is then put on the other end of the cannula with the bottom on top.
   The whole construction is converted and the water let run into the lower bottle while the bottle is shaken gently.

Following these instructions, the whole reconstitution procedure should take no longer than 2 minutes.



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