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Package leaflet: Information for the user

2091

Treosulfan 5g powder for solution for infusion

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1 What Treosulfan is and what it is used for
2 What you need to know before you are given Treosulfan
3 How you use Treosulfan
4 Possible side effects
5 How to store Treosulfan
6 Contents of the pack and other information

1 What Treosulfan 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 advanced ovarian cancer after at least one line of standard therapy.

2 What you need to know before you are given Treosulfan

Do not use Treosulfan

- 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 nurse before using Treosulfan if you:

- experience a 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;
- develop inflammation of the lungs which causes shortness of breath (allergic alveolitis or pulmonary fibrosis). If this happens to you, treatment with Treosulfan should be stopped.

Also be aware of the following when using Treosulfan :

- the risk of developing certain types of infection is increased;
- different types of blood cancer may occur after long-term treatment;
- as treosulfan is excreted via your kidneys, your blood count 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;
- due to the possible development of bladder inflammation causing pain or 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 treatment with treosulfan;
- when treosulfan is not carefully administered into a blood vessel, painful inflammation of the surrounding tissue may occur.

Other medicines and Treosulfan

Tell your doctor or nurse 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 take any other medicines without consulting your doctor, as there may be interactions between Treosulfan and other medicines.

Pregnancy and breast-feeding

Do not use Treosulfan if you are pregnant or breast-feeding, unless your doctor considers it absolutely necessary. You must also use effective contraception during therapy, e.g. birth control and for the first six months after therapy.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines

If you experience nausea or vomiting, your ability to drive or operate machinery may be impaired. If you are affected in this way, do not drive or operate machines.

3 How to use Treosulfan

Treosulfan will be given to you by a doctor or nurse, as a drip into your vein. This will occur over a period of 15 to 30 minutes (intravenous infusion), at a dose that has been calculated specifically for you by the doctor.

For single use only.

Your doctor will calculate your required dose of Treosulfan, based on your blood count measurements. Your doctor will reduce the dose if another anticancer medicine or radiotherapy treatment has been given to you. The dose that you are given also depends on your body size and varies according to your body surface area (BSA). Technically, this is measured in square metres (m^2), but is actually worked out from your height and weight. The usual dose for treosulfan alone is 6-8g/m^2 BSA. In combination with cisplatin, treosulfan is usually dosed at 5g/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 your treatment depending on your blood test results, your general condition, any further treatments you are undergoing and your response to the treatment with Treosulfan. If you have any questions about your treatment, ask your doctor or nurse.

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 than you should

If you are given too much of this medicine, 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 nurse.

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 explain the risks and benefits of your treatment.

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Information for Healthcare Professionals

Guidelines for the safe handling of antineoplastic agents:

1. Trained personnel should reconstitute the medicinal product.
2. This should be performed in a designated area.
3. Adequate protective gloves, masks and clothing should be worn.
4. Precautions should be taken to avoid the medicinal product accidentally coming into contact with the eyes. In case the solution comes in contact with the skin or the eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat the transient stinging of the skin. Medical advice should be sought if the eyes are affected.
5. Cytotoxic preparations should not be handled by staff who may be pregnant.
6. Adequate care and precautions should be taken in the disposal of items (syringes, needles, etc.) used to reconstitute cytotoxic agents.
7. The work surface should be covered with disposable plastic-backed absorbent paper.
8. Use Luer-lock fittings on all syringes and sets. Large bore needles are recommended to minimise pressure and the possible formation of aerosols. The latter may also be reduced by the use of a venting needle.

Instructions for reconstitution of Treosulfan

To avoid solubility problems during reconstitution, the following aspects should be considered:

1. The solvent, water for injections, 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.

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Product Name	**Treosulfan 5g powder for solution for infusion**	**Sap code :**	**510520044GB01**	**Reference Artwork**	--------
Packaging Material	**Pack Insert Artwork**	**Reason of change :**	**New Development**	**Proof 1**	21.07.2017
Size : Foil Width	------	**Country :**	**UK**	**Proof 2**	24.07.2017
Size : Foil Repeat Length	------	**Pack Size :**	----------	**Proof 3**	25.07.2017
Size : Strip Size	------	**Barcode No. :**	----------	**Proof 4**	24.08.2017
Size : Carton/Label	------	**Pharmacode :**	**2091**	**Proof 5**	22.12.2017
Size : PI - Open Size PI - Close Size	**L. 180 x H. 450 mm** **L. x H. mm**	**No. of colours :**	**1**		
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Tell your doctor or nurse 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 or a drop in blood pressure.
- Fever or infection: if you have a body temperature of 38 °C or higher, experience sweating or notice any other signs of infection (since you might have fewer white blood cells than normal).
- Weakness, becoming short of breath or if your skin turns pale (since you might have fewer red blood cells than normal).
- Bleeding from gums, mouth or nose or if unexpected bruising appears (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 bleeding from gums, mouth or nose and may cause unexpected bruising) or red blood cells (which can make the skin pale and cause weakness or breathlessness). Regular blood tests will be performed by your doctor or nurse in order to monitor these side effects.
- Stomach upsets, including nausea (feeling sick) with or without vomiting (being sick).
- Mild hair loss. 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 or a drop in blood pressure).
- 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).

Very rare (may affect up to 1 in 10,000 people):

- Severe general infection (sepsis).
- 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 a drop in glucose levels within 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, scarring or infection of the lungs).
- Hives or an itchy rash; inflammation of the skin with or without scales forming (scleroderma and psoriasis), reddening of the skin (erythema).
- Inflammation of the bladder, causing pain or more frequent and urgent urination, with or without bloody urine (haemorrhagic cystitis).
- Feeling of becoming unwell (flu-like symptoms).
- Painful redness or swelling at the injection site (in the case of treosulfan solution leakage into the surrounding tissue).

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in the Yellow Card Scheme 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 Treosulfan

Keep this medicine out of the sight and reach of children.

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

Do not store the reconstituted product in a refrigerator (2-8 °C), as this might cause precipitation. Solutions showing any sign of precipitation should not be used.

Do not refrigerate.

Chemical and physical in-use stability has been demonstrated for 12 hours at 30°C. From a microbiological point of view, unless the method of reconstitution precludes the risk of microbiological contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6 Contents of the pack and other information

What Treosulfan contains

- The active ingredient is treosulfan. Each vial contains 5g of treosulfan.
- After reconstitution, 1 ml of solution contains 50mg of treosulfan.

What Treosulfan looks like and contents of the pack

Treosulfan is a white, crystalline cake or powder and is supplied in colourless glass vials, each vial containing 5g of treosulfan.

The dry-powder is mixed with water for injections in the vial to form a solution before it is given to you.

Treosulfan is available in packs of 1 vial or 5 vials per carton.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Tillomed Laboratories Ltd
220 Butterfield
Great Marlings
Luton, LU2 8DL
United Kingdom

Manufacturer

Emcure Pharma UK Ltd
Basepoint Business Centre,
110 Butterfield, Great Marlings,
Luton, LU2 8DL
United Kingdom

This medicinal product is authorised in the Member States of the EEA under the following names:

United Kingdom:	Treosulfan 5g powder for solution for infusion
Germany:	Treosulfan Tillomed 5g Pulver zur Herstellung einer Infusionslösung.
France:	Treosulfan Tillomed 5g poudre pour solution pour perfusion
Italy:	Treosulfan Tillomed
Spain:	Treosulfano Tillomed 5g polvo para solución para infusión EFG

This leaflet was last revised in 12/2017.

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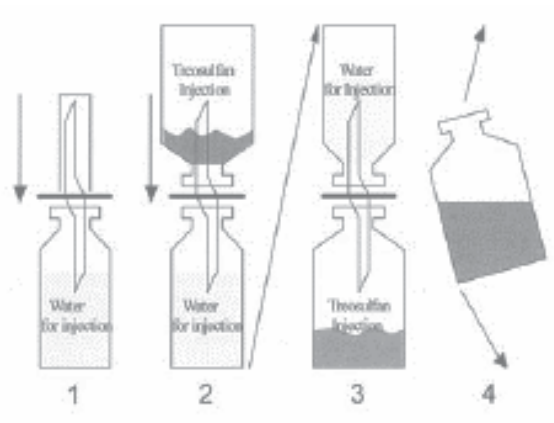
This procedure is very important, because moistening the powder causes the powder to stick to the surface, resulting in caking. In the case of caking occurring, shake the bottle vigorously for a long period of time.

3. One side of the double sided cannula is placed into the rubber stopper of the water bottle. The treosulfan bottle is then placed on the other end of the cannula with the bottom on top.

The whole construction is converted and the water is left to 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. See below diagram for aiding the reconstitution process.



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