PACKAGE LEAFLET

Package leaflet: Information for the user

<Invented name> 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 <Invented name> is and what it is used for

<Invented name> contains the active substance treosulfan. Treosulfan belongs to the group of anticancer medicines called alkylating agents. These agents inhibit tumour growth.

<Invented name> has been prescribed by your doctor for the treatment of advanced ovarian cancer after at least one prior standard therapy.

2. What you need to know before you are given <Invented name>

Do not use <Invented name>

• 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 <Invented name>.
• if you are breastfeeding

Warnings and precautions

Talk to your doctor or nurse before using <Invented name> if you:

• develop inflammation of the lungs which causes shortness of breath (allergic alveolitis or pulmonary fibrosis). If this happens to you, treatment with <Invented name> should be stopped.

You need to be aware of the following when using <Invented name>:

- 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;

If you are a woman of childbearing potential you must also use effective contraception e.g. birth control during therapy and for the first six months after therapy *(see section Pregnancy and breast-feeding).*

Other medicines and <Invented name>

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 <Invented name>.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant, or planning to have a baby, ask your doctor for advice before using this medicine. There are no or limited data for the use of Treosulfan 5 g powder for solution for infusion in pregnant and lactating women.

Pregnancy

Because foetal harm cannot be excluded , Treosulfan 5 g powder for solution for infusion should not be used during pregnancy unless your doctor considers it absolutely necessary . You must not become pregnant during treatment with Treosulfan 5 g powder for solution for infusion.

If you become pregnant during treatment with Treosulfan 5 g powder for solution for infusion, you must inform your doctor immediately.

Contraception in women

During treatment and for the first six month after treatment with Treosulfan 5 g powder for solution for infusion, you must use appropriate contraceptive measures if you are a woman of childbearing potential.

Breast-feeding

Since a possible transfer of the substance into the breast milk cannot be ruled out, you must not breast-feed during treatment with Treosulfan 5 g powder for solution for infusion.

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 <Invented name>

<Invented name> 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 dose that has been calculated specifically for you by the doctor.

Your doctor will calculate your required dose of <Invented name>, 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). During the course of <Invented name> 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 <Invented name>. 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 <Invented name> 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

Tell your doctor or nurse straight away if you notice any of the following:

• Allergic reactions **[Rare (may affect up to 1 in 1,000 people)]**: 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**[Very common (may affect more than 1 in 10 people)]**: 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 **[Very common (may affect more than 1 in 10 people)]** becoming short of breath or if your skin turns pale (since you might have fewer red blood cells than normal).

• Bleeding [**Very common (may affect more than 1 in 10 people)]** from gums, mouth or nose or if unexpected bruising appears (since you might have fewer platelets than normal).

- Difficulty in breathing [**Very rare (may affect up to 1 in 10,000 people)]** (since you might have an allergic reaction, inflammation or infection of the lung)

Very common (may affect more than 1 in 10 people):

• 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).

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).

• 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).

Tell your doctor or nurse straight away if you notice any of the symptoms above.

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 listed in Appendix V*. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store <Invented name>

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 <Invented name> contains

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

What <Invented name> looks like and contents of the pack

<Invented name> 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.

<Invented name> is available in packs of 1 vial or 5 vials per carton.

Vials may or may not be sleeved with plastic shrink sleeve/bottom (puck). This plastic sleeving is not in contact with the drug product and is there to provide additional protection during transportation. This improves the safe handling of the medicinal product by both healthcare professionals and pharmaceutical personnel.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

<To be completed nationally>

Manufacturer

MIAS Pharma Limited
Suite 2, Stafford House, Strand Road
Portmarnock, Co. Dublin
Ireland

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

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 perfusión EFG
Austria:	Treosulfan Tillomed 5g Pulver zur Herstellung einer Infusionslösung
Czech Republic:	Treosulfan Tillomed
Greece:	Treosulfan Tillomed 5g κόνις για διάλυμα προς έγχυση

Poland:	Treosulfan Zentiva
Romania:	Treosulfan Tillomed 5g Pulbere pentru soluţie perfuzabilă
Denmark:	Treosulfan Tillomed
Finland:	Treosulfan Tillomed infuusiokuiva-aine liuosta varten 5g
Norway:	Treosulfan Tillomed 5g Pulver til infusjonsvæske, oppløsning
Sweden:	Treosulfan Tillomed 5g Pulver till infusionsvätska, lösning
Belgium:	Treosulfan Tillomed 5g Poeder voor oplossing voor infusie Treosulfan Tillomed 5g poudre pour solution pour perfusion Treosulfan Tillomed 5g Pulver zur Herstellung einer Infusionslösung
Ireland:	Treosulfan Tillomed 5g powder for solution for infusion
Netherlands:	Treosulfan Tillomed 5g Poeder voor oplossing voor infusie
Portugal:	Treossulfano Tillomed 5g pó para solução *para perfusão*

This leaflet was last revised in <{MM/YYYY}>

Information for Healthcare Professionals

For single use only

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 <Invented name>

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 vial by shaking.

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 vial vigorously for a long period of time.

3. One side of the double sided cannula is placed into the rubber stopper of the water vial. The treosulfan vial 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 vial while the vial 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.