Package leaflet: Information for the patient

Trisenox 2 mg/ml concentrate for solution for infusion

arsenic trioxide

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

What is in this leaflet:

1. What TRISENOX is and what it is used for

TRISENOX is used in adult patients with newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL), and in adult patients, whose disease has not responded to other therapies. APL is a unique type of myeloid leukaemia, a disease in which abnormal white blood cells and abnormal bleeding and bruising occur.

2. What you need to know before you are given TRISENOX

TRISENOX must be given under the supervision of a physician experienced in the treatment of acute leukaemias.

You must not receive TRISENOX
If you are allergic to arsenic trioxide or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
You must talk to your doctor or nurse before you are given TRISENOX, if
- you have impaired kidney function
- you have any liver problems.

Your doctor will take the following precautions:
- Tests will be performed to check the amount of potassium, magnesium, calcium and creatinine in your blood before your first dose of TRISENOX
- You should have an electrical recording of the heart (electrocardiogram ECG) performed before your first dose
- Blood tests (potassium, calcium, magnesium and liver function) should be repeated during your treatment with TRISENOX
- In addition, you will receive electrocardiograms twice weekly
- If you are at risk for a certain type of abnormal heart rhythm (e.g. torsade de pointes or QTc prolongation), your heart will be monitored continuously
- Your doctor may monitor your health during and after treatment, since arsenic trioxide, the active substance in TRISENOX, may cause other cancers. You should report any new and exceptional symptoms and circumstances whenever you see your doctor
- Follow-up of your cognitive and mobility functions if you are at risk for vitamin B1 deficiency.

Children and adolescents
TRISENOX is not recommended in children and adolescents below 18 years of age.

Other medicines and TRISENOX
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

In particular tell your doctor
- if you are taking any of various types of medicines which could cause a change in the rhythm of your heartbeat. These include:
  - some types of antiarrhythmics (medicines used to correct irregular heart beats, e.g. quinidine, amiodarone, sotalol, dofetilide)
  - medicines to treat psychosis (loss of contact with reality, e.g. thioridazine)
  - medicines for depression (e.g. amitriptyline)
  - some types of medicines to treat bacterial infections (e.g. erythromycin and sparfloxacin)
  - some medicines to treat allergies such as hay fever, called antihistamines (e.g. terfenadine and astemizole)
  - any medicines that cause a decrease in magnesium or potassium in your blood (e.g. amphotericin B)
  - cisapride (a medicine used to relieve certain stomach problems).

  The effect of these medicines on your heartbeat can be made worse by TRISENOX. You must be sure to tell your doctor about all medicines you are taking.
- if you are taking or have recently taken any medicine which may affect your liver. If you are not sure, show the bottle or pack to your doctor.

TRISENOX with food and drink
There are no restrictions on your food or drink while you are receiving TRISENOX.

Pregnancy
Ask your doctor or pharmacist for advice before taking any medicine.

TRISENOX may cause harm to the foetus when used by pregnant women.

If you are able to become pregnant, you must use effective birth control during treatment with TRISENOX and for 6 months following completion of treatment.

If you are pregnant or you become pregnant during the treatment with TRISENOX, you must ask your doctor for advice.

Men should also use effective contraception and be advised to not father a child while receiving TRISENOX and for 3 months following completion of treatment.

Breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
The arsenic in TRISENOX passes into breast milk.
Because TRISENOX can harm nursing infants, do not breast-feed while on and until two weeks after the last dose of TRISENOX.

Driving and using machines
TRISENOX is expected to have no or negligible influence on your ability to drive and use machines.
If you experience discomfort or if you feel unwell after a TRISENOX injection, you should wait until the symptoms go away before driving or using machines.

TRISENOX contains sodium
TRISENOX contains less than 1 mmol sodium (23 mg) per dose. This means that the medicine is essentially 'sodium-free'.

3. How TRISENOX is given

Duration and frequency of treatment

Patients with newly diagnosed acute promyelocytic leukaemia
Your doctor will give you TRISENOX once every day as an infusion. In your first treatment cycle, you may be treated every day up to 60 days at most or until your doctor determines that your disease is better. If your disease responds to TRISENOX, you will be given 4 additional treatment cycles. Each cycle consists of 20 doses given 5 days per week (followed by 2 days interruption) for 4 weeks followed by 4 weeks interruption. Your doctor will decide exactly how long you must continue on therapy with TRISENOX.

Patients with acute promyelocytic leukaemia, whose disease has not responded to other therapies
Your doctor will give you TRISENOX once every day as an infusion. In your first treatment cycle, you may be treated every day up to 50 days at most or until your doctor determines that your disease is better. If your disease responds to TRISENOX, you will be given a second treatment cycle of 25 doses given 5 days per week (followed by 2 days interruption) for 5 weeks. Your doctor will decide exactly how long you must continue on therapy with TRISENOX.

Method and route of administration

TRISENOX must be diluted with a solution containing glucose or a solution containing sodium chloride.

TRISENOX is normally given by a doctor or a nurse. It is given as a drip (infusion) into a vein over 1-2 hours, but the infusion may last longer if side effects like flushing and dizziness occur.

TRISENOX must not be mixed with, or infused through the same tube with other medicines.

If your doctor or nurse gives you more TRISENOX than he/she should
You may experience convulsions, muscle weakness and confusion. If this happens, treatment with TRISENOX must be stopped immediately and your doctor will treat the arsenic overdose.

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

The following information is intended for medical or healthcare professionals only:

ASEPTIC TECHNIQUE MUST BE STRICTLY OBSERVED THROUGHOUT HANDLING OF TRISENOX SINCE NO PRESERVATIVE IS PRESENT.

Dilution of TRISENOX
TRISENOX must be diluted before administration.
Personnel should be trained to handle and dilute arsenic trioxide and should wear appropriate protective clothing.

CAUTION, NOTICE NEW CONCENTRATION (2 mg/ml)

Dilution: Carefully insert the needle of a syringe into the vial and withdraw the required volume. TRISENOX must then be diluted immediately with 100 to 250 ml of glucose 50 mg/ml (5 %) solution for injection or sodium chloride 9 mg/ml (0.9 %) solution for injection.

Unused portions of each vial must be discarded properly. Do not save any unused portions for later administration.

Use of TRISENOX
TRISENOX is for single use only. It must not be mixed with or concomitantly administered in the same intravenous line with other medicinal products.

TRISENOX must be administered intravenously over 1-2 hours. The infusion duration may be extended up to 4 hours if vasomotor reactions are observed. A central venous catheter is not required.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor or nurse straight away if you notice the following side effects, as these may be signs of a severe condition called "differentiation syndrome", which might be fatal:
- difficulty in breathing
- coughing
- chest pain
- fever.

Tell your doctor or nurse straight away if you notice one or more of the following side effects, as these may be signs of allergic reaction:
- difficulty in breathing
- fever
- sudden weight gain
- water retention
- fainting
- palpitations (strong heartbeat you can feel in your chest).

While on treatment with TRISENOX, you may experience some of the following reactions:

Very common (may affect more than 1 in 10 people):
- fatigue (weariness), pain, fever, headache
- nausea, vomiting, diarrhoea
- dizziness, muscle pain, numbness or tingling
- rash or itching, increased blood sugar, oedema (swelling due to excess fluid)
- shortness of breath, fast heart beat, abnormal ECG heart tracing
- reduced potassium or magnesium in the blood, liver function tests abnormal including presence of excess bilirubin or gamma-glutamyltransferase in the blood.

Common (may affect up to 1 in 10 people):
- reduction in blood cell counts (platelets, red and/or white blood cells), increased white blood cells
- chills, increased weight
- a fever due to an infection and low levels of white blood cells, herpes zoster infection
- chest pain, bleeding in the lung, hypoxia (low oxygen level), collection of fluid around the heart or the lung, low blood pressure, abnormal heart rhythm
- fit, joint or bone pain, inflammation of the blood vessels
- increased sodium or magnesium, ketones in the blood and urine (ketoacidosis), renal function tests abnormal, kidney failure
- stomach (abdominal) ache
- redness of the skin, swollen face, blurred vision.

Not known (frequency cannot be estimated from the available data):
- lung infection, infection in the blood
- inflammation of the lungs which causes chest pain and breathlessness, cardiac failure
- dehydration, confusion
- Cerebral disease (Encephalopathy, Wernicke encephalopathy) with various manifestations including difficulties to use arms and legs, speech disorders and confusion.

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 the Yellow Card Scheme at: http://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 TRISENOX

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.

This medicine does not require any special storage conditions.

After dilution, if not used immediately, storage times and conditions before use are the responsibility of your doctor, pharmacist or nurse and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in a sterile environment.

This medicine must not be used if you notice foreign particulate matter or if the solution is discoloured.

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 to protect the environment.

6. Contents of the pack and other information

What TRISENOX contains
- The active substance is arsenic trioxide. Each ml of concentrate contains 2 mg of arsenic trioxide. Each vial of 6 ml contains 12 mg of arsenic trioxide.
- The other ingredients are sodium hydroxide, hydrochloric acid and water for injections. See section 2 "TRISENOX contains sodium".

What TRISENOX looks like and contents of the pack
- TRISENOX is a concentrate for solution for infusion (sterile concentrate). TRISENOX is supplied in glass vials as a concentrated, clear, colourless, aqueous solution. Each carton contains 10 single-use glass vials.

Marketing Authorisation Holder
Teva UK Limited, Ridings Point, Whistler Drive, Castleford, WF10 5HX
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Manufacturer
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The diluted solution must be clear and colourless. All parenteral solutions must be inspected visually for particulate matter and discoloration prior to administration. Do not use the preparation if foreign particulate matter is present.

After dilution in intravenous solutions, TRISENOX is chemically and physically stable for 24 hours at 15-30 °C and 72 hours at refrigerated (2-8 °C) temperatures. From a microbiological point of view, the product must be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Procedure for proper disposal
Any unused product, any items that come into contact with the product and waste material must be disposed of in accordance with local requirements.

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