PART III: CONSUMER INFORMATION

PrTRISENOX®
Arsenic trioxide for injection
Ampoule 10 mg/10 mL (1 mg/mL)
Vial 12 mg/6 mL (2 mg/mL)

This leaflet is part III of a three-part "Product Monograph" published when TRISENOX was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about TRISENOX. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
TRISENOX is used to treat patients with acute promyelocytic leukemia (APL) who are refractory to, or have relapsed from retinoid and anthracycline chemotherapy. APL is a unique type of myeloid leukemia, a disease in which abnormal white blood cells and abnormal bleeding and bruising occur.

What it does:
The active substance in TRISENOX, arsenic trioxide, is a chemical that has been used in medicines for many years, including for the treatment of leukemia. The way it works in this disease is not completely understood. It is thought to prevent the production of deoxyribonucleic acid (DNA), which is necessary for leukemia cells to grow. Arsenic trioxide may induce death of the cancer cells by degrading a fusion protein found in the cancer cells.

When it should not be used:
Do not take TRISENOX if:

- you are allergic or hypersensitive to arsenic or any of the nonmedicinal ingredients in TRISENOX.
- you are pregnant or breastfeeding.

What the medicinal ingredient is:
Arsenic trioxide.

What the non-medicinal ingredients are:
Hydrochloric acid, sodium hydroxide and water for injection.

What dosage forms it comes in:
Ampoule:
TRISENOX is available as a sterile and clear concentrated solution that contains 10 mg of arsenic trioxide. TRISENOX is supplied in 10 mL ampoules. Each carton contains 10 single-use glass ampoules.

Vial:
TRISENOX is available as a sterile and clear concentrated solution that contains 12 mg of arsenic trioxide. TRISENOX is supplied in 6 mL vials. Each carton contains 10 single-use glass vials.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Treatment with TRISENOX may lead to a condition called "APL Differentiation Syndrome" which includes difficulty in breathing, weight gain, coughing, chest pain, fever and may cause death.
- TRISENOX has an effect on the electrical activity of the heart known as prolongation of the QT interval. The prolongation of the QT interval can lead to arrhythmias such as torsade pointes, which may be experienced as dizziness, palpitations and fainting and can result in death.
- Before your first dose of TRISENOX, your doctor will perform a 12-lead electrocardiogram (ECG) and will perform tests to check the amount of potassium, magnesium, calcium and creatinine in your blood.
- While taking TRISENOX, avoid taking drugs that cause a change in the rhythm of your heartbeat or drugs that cause a change in electrolyte levels (potassium, calcium and magnesium).
- TRISENOX should be administered under the supervision of a physician who is experienced in the management of patients with acute leukemia.
- Treatment with Trisenox may cause a condition called Encephalopathy (brain disease) which sometimes may lead to death.

BEFORE you use TRISENOX® talk to your doctor or pharmacist if:

- you have kidney or liver problems;
- you have any problems with your heart, including irregular heartbeat;
- you plan to become pregnant. TRISENOX may cause harm to the fetus when used by pregnant women. If you are able to become pregnant, you must use effective birth control during treatment with TRISENOX and 3 months after the TRISENOX therapy has stopped.
- you are pregnant or you become pregnant during the treatment with TRISENOX, you must ask your doctor for advice;
- you are breast-feeding. Arsenic will be present in the milk of TRISENOX patients who are breast-feeding. Because of the potential for serious side-effects in nursing infants from TRISENOX, do not breast-feed while on TRISENOX and 3 months after the TRISENOX therapy has stopped.

Men should also use effective contraception during treatment with TRISENOX and for 3 months after TRISENOX therapy has stopped.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with TRISENOX include:
Various types of medicines which may have unwanted effect on the function of the heart (QT prolongation) such as:

- antiarrhythmics (e.g., quinidine, procainamide, disopyramide, amiodarone, sotalol, ibutilide, dronedarone, flecainide, propafenone) - used to treat irregular heart beat
- antipsychotics (e.g., chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone) - used to treat schizophrenia or other psychiatric diseases
- antidepressants (e.g., fluoxetine, citalopram, venlafaxine, amitriptyline, imipramine, maprotiline) - used to treat depression
- opioids (e.g., methadone)
- antibiotics (e.g., erythromycin, clarithromycin, telithromycin, moxifloxacin, levofloxacin, ciprofloxacin) - used to treat infections
- tacrolimus - used to prevent organ rejection

- antimalarials (e.g., quinine, chloroquine) - used to treat malaria
- antifungals (e.g., ketoconazole, fluconazole, voriconazole) - used to treat infections
- domperidone - used to treat gastrointestinal disorders
- dolasetron, ondansetron - used to treat nausea
- vorinostat , vandetanib, sunitinib, nilotinib, lapatinib -used to treat cancer
- salmeterol, formoterol - used to treat asthma

Any medicines that cause imbalance in the electrolytes in your body:

- diuretics (water pills)
- laxatives and enemas
- amphotericin B
- high dose corticosteroids

Anthracyclines – cancer chemotherapy drugs

The above lists of potentially interacting drugs are not comprehensive.

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines even those not prescribed (including any over-the-counter drugs, vitamins, or herbal medicines).

PROPER USE OF THIS MEDICATION

Usual dose:
TRISENOX must be injected under the supervision of a physician experienced in the treatment of acute leukemias.

Your doctor will dilute TRISENOX with 100 to 250 mL of glucose 50 mg/mL (5%) injection, or sodium chloride 9 mg/mL (0.9%) injection.

Your doctor will infuse TRISENOX through a tube into a blood vessel over 1-2 hours, but the infusion may last longer if side-effects like flushing and dizziness occur.

Your doctor will give you TRISENOX once every day as a single infusion each day. 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 a second treatment cycle of 25 doses, given 5 days per week followed by a 2 day break for 5 weeks. Your doctor will decide exactly how long you must continue on therapy with TRISENOX.

Overdose:
If you experience symptoms suggestive of acute arsenic toxicity such as convulsions, muscle weakness and confusion, TRISENOX must be stopped immediately and your doctor will treat the arsenic overdose.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

TRISENOX can have side effects, like all medicines, but not everybody gets them. For further information about any of these side effects, ask a doctor or pharmacist.

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 can lead to death:

- difficulty in breathing

- coughing
- chest pain
- fever
- weight gain

You might experience encephalopathy (a general term for brain disease) with various symptoms including difficulties to use arms and legs, speech disorders and confusion. The frequency of this side effect is not known.

If you experience any symptom that bothers you or does not go away contact your doctor or seek medical attention as soon as possible.

The following very common side effects (> 10%) have been observed during clinical trials involving patients taking TRISENOX.

- increased heart rate, feeling of your heart pounding
- eye irritation, blurred vision
- nausea, diarrhea, vomiting, stomach pain, constipation, upper stomach pain, indigestion, bleeding in the mouth
- feeling weak or tired
- fever, chills
- swelling, swelling of the limbs
- chest pain
- pain or redness or swelling at the injection site
- inflammation of the sinuses, cold sores, cold-like symptoms, pneumonia
- weight gain
- abnormal breath sounds
- decreased appetite
- pain (joint pain, muscle pain, bone pain, back pain, neck pain, pain in limbs)
- headache
- dizziness
- pins and needles feeling, reduced sense of touch, trembling
- sleeplessness, feeling anxious, depression
- blood in urine
- bleeding from vagina
- cough, shortness of breath, throat pain, nose bleeds, wheezing, crackling sounds in your lungs
- inflammation of the skin, itchiness, bruises, dry skin, redness
- increased sweating
- low blood pressure, flushing, high blood pressure, paleness

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and call your doctor or pharmacist**
		Only if severe	**In all cases**	
Very Common	Difficulty in breathing			√
	Coughing			√
	Chest pain			√
	Fever			√
	Weight gain			√
	Irregular heartbeat, fainting, loss of consciousness (QT prolongation)		√	
	Diarrhoea	√		
	Nausea, Vomiting	√		
	Fast heartbeat, pounding sensation		√	
	Fatigue (weariness) Weakness	√		
	Numbness or tingling in your feet or hands	√		
	Unusual bruising or bleeding		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		**Talk with your doctor or pharmacist**		**Stop taking drug and call your doctor or pharmacist**
		Only if severe	**In all cases**	
	Any sign of high blood sugar : extreme thirst, frequent urination, extreme hunger, weakness or blurred vision	√		
	Pain		√	
Uncommon	Brain disease called Encephalopathy			√

This is not a complete list of side effects. For any unexpected effects while taking* TRISENOX®*, contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of reach and sight of children.
Do not use after expiry date which is stated on the ampoule or vial label.
Store at controlled room temperature (15 to 30ºC). Do not freeze.

Do not use TRISENOX if you notice foreign particulate matter or if the solution is discoloured.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For questions or concerns and to find the full product monograph prepared for healthcare professionals, go to http://www.tevacanadainnovation.ca or contact the sponsor, Teva Canada Innovation at 1-833-662-5644.

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