For the treatment of adults with newly-diagnosed low-risk APL

FIRST LINE FIRST STRIKE

With TRISENOX® (arsenic trioxide) injection + tretinoin[1]

Full Prescribing Information

Please see an important Dear HCP letter concerning TRISENOX lots 7B05125, 7B05126, 7B05127, 7G04417, 7G04418, 7K05225, 7H00931

Please see DHCP letter regarding vial concentration

INDICATION

- TRISENOX is indicated in combination with tretinoin for treatment of adults with newly-diagnosed low-risk acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t(15;17) translocation or PML/RAR-alpha gene expression.
- TRISENOX is indicated for induction of remission and consolidation in patients with APL who are refractory to, or have relapsed from, retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or PML/RAR-alpha gene expression.

IMPORTANT SAFETY INFORMATION

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WARNING: DIFFERENTIATION SYNDROME AND CARDIAC CONDUCTION ABNORMALITIES

Differentiation Syndrome: Patients with acute promyelocytic leukemia (APL) treated with TRISENOX® (arsenic trioxide) injection have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, weight gain or peripheral edema, hypotension, and renal, hepatic, or multi-organ dysfunction, in the presence or absence of leukocytosis. If differentiation syndrome is suspected, immediately initiate high-dose corticosteroid therapy and hemodynamic monitoring until resolution of signs and symptoms. Temporary discontinuation of TRISENOX may be required.

Cardiac Conduction Abnormalities: Arsenic trioxide can cause QTc interval prolongation, complete atrioventricular block, and a torsade de pointes-type ventricular arrhythmia, which can be fatal. Before initiating therapy, assess the QTc interval, correct pre-existing electrolyte abnormalities, and consider discontinuing drugs known to prolong QTc interval. Do not administer TRISENOX to patients with ventricular arrhythmia or prolonged QTcF.

Contraindications: TRISENOX is contraindicated in patients who are hypersensitive to arsenic.

Differentiation Syndrome: In clinical trials, 16-23% of patients treated with TRISENOX for APL developed differentiation syndrome. Differentiation syndrome has been observed with and without concomitant hyperleukocytosis, and it has occurred as early as day 1 of induction to as late as the second month induction therapy. When TRISENOX is used in combination with tretinoin, prednisone prophylaxis is advised.

Cardiac Conduction Abnormalities: In the clinical trials of patients with newly-diagnosed low-risk APL treated with TRISENOX in combination with tretinoin, 11% experienced QTc prolongation > 450 msec for men and > 460 msec for women throughout the treatment cycles. In the clinical trial of patients with relapsed or refractory APL treated with TRISENOX monotherapy, 40% had at least one ECG tracing with a QTc interval greater than 500 msec. A prolonged QTc was observed between 1 and 5 weeks after start of TRISENOX infusion, and it usually resolved by 8 weeks after TRISENOX infusion. There are no data on the effect of TRISENOX on the QTc interval during the infusion of the drug.

The risk of torsade de pointes is related to the extent of QT prolongation, concomitant administration of QT prolonging drugs, a history of torsade de pointes, pre-existing QT interval prolongation, congestive heart failure, administration of potassium-wasting diuretics, or other conditions that result in hypokalemia or hypomagnesemia. The risk may be increased when TRISENOX is co-administered with medications that can lead to electrolyte abnormalities (such as diuretics or amphotericin B).

Hepatotoxicity: In the clinical trials, 44% of patients with newly-diagnosed low-risk APL treated with TRISENOX® (arsenic trioxide) injection in combination with tretinoin experienced elevated aspartate aminotransferase (AST), alkaline phosphatase, and/or serum bilirubin. These abnormalities resolved with temporary discontinuation of TRISENOX and/or tretinoin. During treatment with TRISENOX, monitor liver chemistries at least 2-3 times per week through recovery from toxicities. Withhold treatment with TRISENOX and/or tretinoin if elevations in AST), alkaline phosphatase, and/or serum bilirubin occur to greater than 5 times the upper limit of normal.

Long-term liver abnormalities can occur in APL patients treated with TRISENOX in combination with tretinoin. In a published series, mild liver dysfunction and hepatic steatosis were seen in 15% and 43%, respectively, of patients at a median of 7 years (range 0-14 years) after treatment with arsenic trioxide in combination with tretinoin.

Carcinogenesis: The active ingredient of TRISENOX, arsenic trioxide, is a human carcinogen. Monitor patients for the development of second primary malignancies.

Embryo-Fetal Toxicity: TRISENOX can cause fetal harm when administered to a pregnant woman. One patient who became pregnant while receiving arsenic trioxide had a miscarriage. Conduct pregnancy testing prior to initiating treatment and advise pregnant women of the potential risk to a fetus. Advise patients of reproductive potential to use effective contraception during treatment with TRISENOX and after treatment for 6 months in females and 3 months in males. TRISENOX may also impair fertility in males.

Lactation: TRISENOX is excreted in human milk. Because of the potential for serious adverse reactions in the breastfed child, discontinue breastfeeding during treatment with TRISENOX and for two weeks after the final dose.

Patients with Renal Impairment: Exposure of arsenic trioxide may be higher in patients with severe renal impairment. Patients with severe renal impairment (creatinine clearance less than 30 mL/min) should be monitored for toxicity when these patients are treated with TRISENOX, and a dose reduction may be warranted. The use of TRISENOX in patients on dialysis has not been studied.

Patients with Hepatic Impairment: Since limited data are available across all hepatic impairment groups, caution is advised in the use of TRISENOX in patients with hepatic impairment. Monitor patients with severe hepatic impairment (Child-Pugh Class C) who are treated with TRISENOX for toxicity.

Most Common Adverse Reactions: The most common adverse reactions (greater than 30%) were leukocytosis, neutropenia, thrombocytopenia, nausea, vomiting, diarrhea, abdominal pain, hepatic toxicity, fever, rigors, fatigue, insomnia, tachycardia, QTc prolongation, edema, hyperglycemia, hypokalemia, hypomagnesemia, dyspnea, cough, rash or itching, sore throat, arthralgia, headaches, paresthesia, and dizziness.

Please see Full Prescribing Information, including Boxed Warnings.

TO REPORT SIDE EFFECTS

1-888-483-8279

USMedInfo@tevapharm.com

CONTACT US

For health care professionals or patients with specific medical questions about TRISENOX®, please contact:

Teva Medical Information
1-888-4TEVARX
(1-888-483-8279)
To request more information about TRISENOX, click here.

Reference: 1. TRISENOX® (arsenic trioxide) injection [Current Prescribing Information]. North Wales, PA; Teva Pharmaceuticals.