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IMPORTANT PRESCRIBING INFORMATION UPDATE

Subject: Availability of TRISENOX® (arsenic trioxide) Injection
Updated to include Lot 7H00931

Dear Healthcare Professional:

We are providing an update regarding the supply of TRISENOX® (arsenic trioxide) Injection. Working with the U.S. Food and Drug Administration to avoid a critical shortage and to assure uninterrupted supply of this life-saving medicine, Teva has decided to release the following TRISENOX Lots manufactured in a site not identified in the FDA-approved application:

- **7G04417**
- **7G04418**
- **7H00931**

TRISENOX Lots **7G04417, 7G04418 and 7H00931** contain trace amounts of Cremophor® EL, a pharmaceutical grade excipient used in the solubilization of poorly water soluble drugs, such as the antineoplastic agent paclitaxel. Cremophor® EL is used in some FDA approved pharmaceutical products and has been found to have an association with acute hypersensitivity reactions. Acute and fatal hypersensitivity reactions have been reported to occur following administration of some antineoplastic agents in spite of premedication to prevent such reactions.

These TRISENOX lots have undergone a complete analytical and toxicological evaluation by Teva. The amount of Cremophor® EL in the TRISENOX ampules was found to be at levels less than 2 ppm. At these levels, the amount of Cremophor® EL at the recommended daily dose of 0.15 mg/kg (about 10 mg for a 70 kg patient or about 10 mL) of TRISENOX would be lower than 0.02 µL in total volume, and below the threshold reported in the scientific literature (2 µL/mL of serum) to elicit an anaphylactic or hypersensitivity reaction among patients receiving this medication.

Teva's goal is to supply TRISENOX without interruption to the healthcare providers and patients who need this medication. Teva will continue to seek FDA approval of its new manufacturing site to ensure sufficient supply of TRISENOX for prescribers and their patients as this remains a priority for Teva.

TRISENOX is indicated for the induction of remission and consolidation in patients with acute promyelocytic leukemia (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.

Action for the Healthcare Provider

TRISENOX Lots **7G04417, 7G04418 and 7H00931** contain trace amounts of Cremophor® EL at a level assessed to have a low probability of eliciting anaphylactic or hypersensitivity reactions among patients receiving this medication at recommended therapeutic doses.

Treating oncologists should assess the benefit versus risk for each individual patient, and monitor patients closely for signs and symptoms of an acute hypersensitivity reaction, such as dyspnea, flushing, rash, chest pain, tachycardia, hypotension, angioedema, and generalized urticaria during and for at least one hour after the administration of TRISENOX from these affected lots.

Please advise patients to immediately seek immediate medical attention should they develop new or recurring symptoms within 24 hours of drug administration.

Please ensure your staff and any provider in your institution who may be involved in the administration of TRISENOX receives a copy of this letter.

For Further Information

Please see the accompanying Full Prescribing Information for complete safety information before prescribing TRISENOX.

If you have any additional questions about product availability or ordering of TRISENOX Injection, please contact Teva Customer Service at 800-545-8800 (Select Option #3, then # 2).

Reporting Adverse Events

Health care providers and patients should report quality problems and all adverse events in patients taking TRISENOX Injection to Teva Pharmaceuticals at 1-888-483-8279, Option #2.

Adverse events or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting Program either online, or regular mail, or by fax:

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm
- **Regular mail or Fax**: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

You also may contact our medical information department at 1-888-483-8279, Option #2 or at USMedInfo@tevapharm.com if you have any questions about the information contained in this letter or the safe and effective use of TRISENOX Injection.

Please see the enclosed full prescribing information, including boxed warning, for TRISENOX.

Sincerely,

Denisa Hurtukova, MD
Vice President, Head of North America Medical Affairs
Teva Pharmaceuticals

Enclosures: Full prescribing information for TRISENOX® (arsenic trioxide) Injection