Trisenox® (arsenic trioxide) – New indication

- On January 15, 2018, Teva announced the FDA approval of Trisenox (arsenic trioxide) in combination with tretinoin for the 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 also approved for the 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.
- Approval of the new indication for Trisenox was based on data from a clinical study of 162 patients with newly-diagnosed low-risk APL. Patients were randomized to receive Trisenox plus tretinoin for induction and consolidation or chemotherapy plus tretinoin for induction, consolidation, and maintenance. Efficacy was based on the event-free survival (EFS) rate at 2 years.
    - With a median follow-up of 34.4 months, the 2 year EFS rate was 94% in the Trisenox plus tretinoin arm (n = 77) versus 82% in the chemotherapy plus tretinoin arm (n = 79), a treatment difference of 11% (95% CI: 1, 22; p = 0.048).
    - The overall survival (OS) was 99% (95% CI: 93, 100) in the Trisenox plus tretinoin arm vs. 91% (95% CI: 86, 97) in the chemotherapy plus tretinoin arm. The difference in 2-year OS rate between the arms was 8% (95% CI: 0, 16).
- Trisenox carries a boxed warning for differentiation syndrome and cardiac conduction abnormalities.
- A new update was also added to the *Warnings and Precautions* section of the Trisenox drug label regarding hepatotoxicity.
    - In clinical trials, 44% of patients with newly-diagnosed low-risk APL treated with Trisenox 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 > 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.
- For patients with newly diagnosed low-risk APL, a treatment course consists of 1 induction cycle and 4 consolidation cycles.
- Refer to the Trisenox drug label for specific dosing recommendations for all indications.