Teva Announces U.S. FDA Approval of TRISENOX® (arsenic trioxide) Injection for First Line Treatment of Acute Promyelocytic Leukemia

JERUSALEM--(BUSINESS WIRE)--Jan. 15, 2018-- Teva Pharmaceutical Industries Ltd. (NYSE and TASE: TEVA) announced that the U.S. Food and Drug Administration (FDA) has approved the use of TRISENOX® (arsenic trioxide) injection 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. The approval was based on a Priority Review by the FDA on data from published scientific literature and a review of Teva's global safety database for arsenic trioxide.

"Today's approval to expand the indication of TRISENOX is a testament to Teva's commitment to providing solutions to advance cancer care," said Paul Rittman, Senior Vice President and General Manager, Teva Oncology. "This label expansion represents an important benefit as TRISENOX is now an FDA-approved first line treatment option for patients with acute promyelocytic leukemia."

The new indication reinforces the current practice guidelines by the National Comprehensive Cancer Network® (NCCN).

Please see the Full Prescribing Information for TRISENOX® and the Important Safety Information below including Boxed Warning regarding: DIFFERENTIATION SYNDROME AND CARDIAC CONDUCTION ABNORMALITIES.

TRISENOX® (arsenic trioxide) Injection IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME AND CARDIAC CONDUCTION ABNORMALITIES

Differentiation Syndrome: Patients with acute promyelocytic leukemia (APL) treated with TRISENOX 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 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 tests prior to starting 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.

TO REPORT SIDE EFFECTS: Contact us at 1-888-483-8279 or USMedinfo@tevapharma.com

Indications

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.
- 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.

About Teva

Teva Pharmaceutical Industries Ltd. (NYSE and TASE: TEVA) is a leading global pharmaceutical company that delivers high-quality, patient-centric healthcare solutions used by approximately 200 million patients in 100 markets every day. Headquartered in Israel, Teva is the world's largest generic medicines producer, leveraging its portfolio of more than 1,800 molecules to produce a wide range of generic products in nearly every therapeutic area. In specialty medicines, Teva has the world-leading innovative treatment for multiple sclerosis as well as late-stage development programs for other disorders of the central nervous system, including movement disorders, migraine, pain and neurodegenerative conditions, as well as a broad portfolio of respiratory products. Teva is leveraging its generics and specialty capabilities in order to seek new ways of addressing unmet patient needs by combining drug development with devices, services and technologies. Teva's net revenues in 2016 were $21.9 billion. For more information, visit www.tevapharm.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 regarding the expanded indication for TRISENOX®, which are based on management's current beliefs and expectations and are subject to substantial risks and uncertainties, both known and unknown, that could cause our future results, performance or achievements to differ significantly from that expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to:

- the uncertainty of commercial success of TRISENOX®;
- our specialty medicines business, including: competition for our specialty products, especially Copaxone®, our leading medicine, which faces competition from existing and potential additional generic versions and orally-administered alternatives; our ability to achieve expected results from investments in our product pipeline; competition from companies with greater resources and capabilities; and the effectiveness of our patents and other measures to protect our intellectual property rights;
- our business and operations in general, including: uncertainties relating to the potential success and our ability to effectively execute a restructuring plan; uncertainties relating to the potential benefits and success of our new organizational structure and recent senior management changes; our ability to develop and commercialize additional pharmaceutical products; manufacturing or quality control problems, which may damage our reputation for quality production and require costly remediation; interruptions in our supply chain; disruptions of our or third party information technology systems or breaches of our data security; the restructuring of our manufacturing network, including potential related labor unrest; the impact of continuing consolidation of our distributors and customers; and variations in patent laws that may adversely affect our ability to manufacture our products; our ability to consummate dispositions on terms acceptable to us; adverse effects of political or economic instability, major hostilities or terrorism on our significant worldwide operations; and our ability to successfully bid for suitable acquisition targets or licensing opportunities, or to consummate and integrate acquisitions;
- compliance, regulatory and litigation matters, including: costs and delays resulting from the extensive governmental regulation to which we are subject; the effects of reforms in healthcare regulation and reductions in pharmaceutical pricing, reimbursement and coverage; potential additional adverse consequences following our resolution with the U.S. government of our FCPA investigation; governmental investigations into sales and marketing practices; potential liability for sales of generic products prior to a final resolution of outstanding patent litigation; product liability claims; increased government scrutiny of our patent settlement agreements; failure to comply with complex Medicare and Medicaid reporting and payment obligations; and environmental risks; and other factors discussed in our Annual Report on Form 20-F for the year ended December 31, 2016 ("Annual Report"), including in the section captioned "Risk Factors," and in our other filings with the U.S. Securities and Exchange Commission, which are available at www.sec.gov and www.tevapharm.com. Forward-looking statements speak only as of the date on which they are made, and we assume no obligation to update or revise any forward-looking statements or other information contained herein, whether as a result of new information, future events or otherwise. You are cautioned not to put undue reliance on these forward-looking statements.

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