Endo Launches First Generic Version of Noxafil® (posaconazole) Injection

June 29, 2023

DUBLIN, June 29, 2023 /PRNewswire/ -- Endo International plc (OTC: ENDPQ) announced today that its Par Sterile Products business has begun shipping posaconazole injection (18 mg/mL), the first generic version of Merck's Noxafil® in the U.S., following final approval from the U.S. Food and Drug Administration of its Abbreviated New Drug Application.

"We're pleased to provide choices to healthcare providers," said Scott Sims, Senior Vice President and General Manager, Injectable Solutions & Generics at Endo. "The first generic version of Noxafil® injection does just that, while also strengthening our product portfolio and underscoring our reputation as a reliable, quality supplier."

Posaconazole injection is indicated for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia (low white blood cell counts) from chemotherapy.

According to IQVIA ™, Noxafil® vial sales were approximately $25 million for the 12 months ended May 31, 2023.

Noxafil® is a registered trademark of Merck Sharp & Dohme LLC.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
Hypersensitivity
Posaconazole is contraindicated in persons with known hypersensitivity to posaconazole or other azole antifungal agents.
Use with Sirolimus
Posaconazole is contraindicated with sirolimus. Concomitant administration of posaconazole with sirolimus increases the sirolimus blood concentrations by approximately 9-fold and can result in sirolimus toxicity.
QT Prolongation with Concomitant Use with CYP3A4 Substrates
Posaconazole is contraindicated with CYP3A4 substrates that prolong the QT interval. Concomitant administration of posaconazole with the CYP3A4 substrates, pimozide and quinidine may result in increased plasma concentrations of these drugs, leading to QTc prolongation and cases of torsades de pointes.
HMG-CoA Reductase Inhibitors Primarily Metabolized Through CYP3A4
Coadministration with the HMG-CoA reductase inhibitors that are primarily metabolized through CYP3A4 (e.g., atorvastatin, lovastatin, and simvastatin) is contraindicated since increased plasma concentration of these drugs can lead to rhabdomyolysis.
Use with Ergot Alkaloids
Posaconazole may increase the plasma concentrations of ergot alkaloids (ergotamine and dihydroergotamine) which may lead to ergotism.
Use with Venetoclax
Coadministration of posaconazole with venetoclax at initiation and during the ramp-up phase is contraindicated in patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) due to the potential for increased risk of tumor lysis syndrome.

WARNINGS AND PRECAUTIONS
Calcineurin-Inhibitor Toxicity: Concomitant administration of posaconazole with cyclosporine or tacrolimus increases the whole blood trough concentrations of these calcineurin-inhibitors. Frequent monitoring of tacrolimus or cyclosporine whole blood trough concentrations should be performed during and at discontinuation of posaconazole treatment and the tacrolimus or cyclosporine dose adjusted accordingly.
Arrhythmias and QT Prolongation: Some azoles, including posaconazole, have been associated with prolongation of the QT interval on the electrocardiogram. In addition, cases of torsades de pointes have been reported in patients taking Posaconazole. Posaconazole should be administered with caution to patients with potentially proarrhythmic conditions. Do not administer with drugs that are known to prolong the QTc interval and are metabolized through CYP3A4.

Electrolyte Disturbances: Electrolyte disturbances, especially those involving potassium, magnesium or calcium levels, should be monitored and corrected as necessary before and during posaconazole therapy.
Hepatic Toxicity: Hepatic reactions (e.g., mild to moderate elevations in alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, total bilirubin,and/or clinical hepatitis) have been reported in clinical trials. The elevations in liver tests were generally reversible on discontinuation of therapy, and in some instances these tests normalized without drug interruption. Liver tests should be evaluated at the start of and during the course of posaconazole therapy. Patients who develop abnormal liver tests during Posaconazole therapy should be monitored. Discontinuation must be considered if clinical signs and symptoms consistent with liver disease develop that may be attributable to posaconazole.
Renal Impairment: Posaconazole injection should be avoided in patients with moderate or severe renal impairment (eGFR <50 mL/min), unless an assessment of the benefit/risk to the patient justifies the use of posaconazole injection. In patients with moderate or severe renal impairment (eGFR <50 mL/min), receiving the Posaconazole injection, accumulation of the intravenous vehicle, SBECD, is expected to occur. Serum creatinine levels should be closely monitored in these patients, and, if increases occur, consideration should be given to changing to oral NOXAFIL therapy.
Midazolam Toxicity: Concomitant administration of posaconazole with midazolam increases the midazolam plasma concentrations by approximately 5-fold. Patients must be monitored closely for adverse effects associated with high plasma concentrations of midazolam and benzodiazepine receptor antagonists must be available to reverse these effects.
Vincristine Toxicity: Concomitant administration of azole antifungals, including posaconazole injection, with vincristine has been associated with neurotoxicity and other serious adverse reactions, including seizures, peripheral neuropathy, syndrome of inappropriate antidiuretic hormone secretion, and paralytic ileus. Reserve azole antifungals, including posaconazole injection, for patients receiving a vinca alkaloid, including vincristine, who have no alternative antifungal treatment options.
Venetoclax Toxicity: Concomitant administration of posaconazole, a strong CYP3A4 inhibitor, with venetoclax may increase venetoclax toxicities, including the risk of tumor lysis syndrome (TLS), neutropenia, and serious infections. In patients with CLL/SLL, administration of posaconazole during initiation and the ramp-up phase of venetoclax is contraindicated. Refer to the venetoclax labeling for safety monitoring and dose reduction in the steady daily dosing phase in CLL/SLL patients. For patients with acute myeloid leukemia (AML), dose reduction and safety monitoring are recommended across all dosing phases when coadministering posaconazole with venetoclax. Refer to the venetoclax prescribing information for dosing instructions.

ADVERSE REACTIONS
Adult Patients: Common adverse reactions in studies with posaconazole in adults are diarrhea, nausea, fever, vomiting, headache, coughing, and hypokalemia.
Pediatric Patients: Common adverse reactions (incidence >20% receiving 6 mg/kg posaconazole injection) in a study in pediatric patients are pyrexia, febrile neutropenia, vomiting, mucosal inflammation, pruritus, hypertension, hypokalemia, and stomatitis.

INDICATIONS
Treatment of Invasive Aspergillosis
Posaconazole injection is indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older.
Prophylaxis of Invasive Aspergillus and Candida Infections
Posaconazole is indicated for the prophylaxis of invasive Aspergillus and Candida infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.
Posaconazole injection: adults and pediatric patients 2 years of age and older

Click for full Prescribing Information.

About Endo
Endo (OTC: ENDPQ) is a specialty pharmaceutical company committed to helping everyone we serve live their best life through the delivery of quality, life-enhancing therapies. Our decades of proven success come from passionate team members around the globe collaborating to bring treatments forward. Together, we boldly transform insights into treatments benefiting those who need them, when they need them. Learn more at www.endo.com or connect with us on LinkedIn.

Cautionary Note Regarding Forward-Looking Statements
Certain information in this press release may be considered "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 and any applicable Canadian securities legislation, including, but not limited to, the statements by Mr. Sims, any statements relating to product launch, shipments, sales potential, quality, safety or cost. and any statements that refer to expected, estimated or anticipated future results or that do not relate solely to historical facts. Statements including words or phrases such as "believe," "expect," "anticipate," "intend," "estimate," "plan," "will," "may," "look forward," "intend," "guidance," "future," "potential" or similar expressions are forward-looking statements. All forward-looking statements in this communication reflect the Company's current views as of the date of this communication about its plans, intentions, expectations, strategies and prospects, which are based on the information currently available to it and on assumptions it has made. Actual results may differ materially and adversely from current expectations based on a number of factors, including, among other things, the outcome of the Company's contingency planning and restructuring activities; the timing, impact or results of any pending or future litigation, investigations, proceedings or claims, including opioid, tax and antitrust related matters; any actual or contingent liabilities; settlement discussions or negotiations; the Company's liquidity, financial performance, cash position and operations; the risks and uncertainties associated with chapter 11 proceedings; the time, terms and ability to confirm a sale of the Company's businesses under Section 363 of the U.S. Bankruptcy Code; the risk that the Company's chapter 11 cases may be converted to cases under chapter 7 of the Bankruptcy Code; the adequacy of the capital resources of the Company's businesses and the difficulty in forecasting the liquidity requirements of the operations of the Company's businesses; the unpredictability of the Company's financial results; the Company's ability to discharge claims in chapter 11 proceedings; negotiations with the holders of the Company's indebtedness and its trade creditors and other significant creditors; the risks and uncertainties with performing under the terms of the restructuring support agreement and any other arrangement with lenders or creditors while in chapter 11 proceedings; the performance, including the approval, introduction, and consumer and physician acceptance of new products and the continuing acceptance of currently marketed products; and the Company's ability to obtain and successfully manufacture, maintain and distribute a sufficient supply of products to meet market demand in a timely manner. The Company expressly disclaims any intent or obligation to update these forward-looking statements, except as required to do so by law.

Additional information concerning risk factors, including those referenced above, can be found in press releases issued by the Company, as well as the Company's public periodic filings with the U.S. Securities and Exchange Commission and with securities regulators in Canada, including the discussion under the heading "Risk Factors" in the Company's most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on

Form 10-Q or other filings with the U.S. Securities and Exchange Commission. Copies of the Company's press releases and additional information about the Company are available at www.endo.com or you can contact the Company's Investor Relations Department at relations.investor@endo.com.

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