Endo Begins Shipment of Generic MIACALCIN® (calcitonin salmon) Injection

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DUBLIN, Nov. 18, 2021 /PRNewswire/ -- Endo International plc (NASDAQ: ENDP) announced today that its Par Sterile Products business has begun shipping calcitonin salmon injection, USP, multi-dose vials (2 mL) following final approval from the U.S. Food and Drug Administration for its Abbreviated New Drug Application. Par's calcitonin salmon injection is AP-rated to Viatris' MIACALCIN® and is indicated for the early treatment of hypercalcemic emergencies, along with other appropriate agents, when a rapid decrease in serum calcium is required. Calcitonin salmon injection is also used to treat postmenopausal osteoporosis in women greater than 5 years postmenopause and to treat symptomatic Paget's disease of bone when alternative treatments are not suitable for these conditions.

"We are very pleased to offer this generic, therapeutically equivalent calcitonin salmon injectable," said Scott Sims, Senior Vice President and General Manager, Sterile Injectables at Endo. "Our product is manufactured in our U.S. facility in Rochester, MI and it provides health care practitioners and their appropriate patients a cost-effective, high-quality treatment option."

According to IQVIA data, U.S. sales of calcitonin salmon injection were approximately $170M for the 12 months ended September 2021.

MIACALCIN® is a registered trademark of Novartis AG, licensed to the Viatris Companies.

IMPORTANT SAFETY INFORMATION

INDICATIONS
Calcitonin salmon injection is indicated for the treatment of symptomatic Paget's disease of bone in patients with moderate to severe disease characterized by polyostotic involvement with elevated serum alkaline phosphatase and urinary hydroxyproline excretion. There is no evidence that the prophylactic use of calcitonin salmon is beneficial in asymptomatic patients. Calcitonin salmon injection should be used only in patients who do not respond to alternative treatments or for whom such treatments are not suitable (e.g., patients for whom other therapies are contraindicated or for patients who are intolerant or unwilling to use other therapies).

Calcitonin salmon injection is indicated for the early treatment of hypercalcemic emergencies, along with other appropriate agents, when a rapid decrease in serum calcium is required, until more specific treatment of the underlying disease can be accomplished. It may also be added to existing therapeutic regimens for hypercalcemia such as intravenous fluids and furosemide, oral phosphate or corticosteroids, or other agents.

Calcitonin salmon injection is indicated for the treatment of postmenopausal osteoporosis in women greater than 5 years postmenopause. The evidence of efficacy for calcitonin salmon injection is based on increases in total body calcium observed in clinical trials. Fracture reduction efficacy has not been demonstrated. Calcitonin salmon injection should be reserved for patients for whom alternative treatments are not suitable (e.g., patients for whom other therapies are contraindicated or for patients who are intolerant or unwilling to use other therapies).

Important Limitations of Use
Due to the possible association between malignancy and calcitonin salmon use, the need for continued therapy should be re-evaluated on a periodic basis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
Hypersensitivity to calcitonin salmon or any of the excipients. Reactions have included anaphylaxis with death, bronchospasm, and swelling of the tongue or throat.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions
Serious hypersensitivity reactions have been reported in patients receiving calcitonin salmon injection, e.g., bronchospasm, swelling of the tongue or

throat, anaphylactic shock, and death due to anaphylaxis. Appropriate medical support and monitoring measures should be readily available when calcitonin salmon injection is administered. If anaphylaxis or other severe hypersensitivity/allergic reactions occur, initiate appropriate treatment.

For patients with suspected hypersensitivity to calcitonin salmon, skin testing should be considered prior to treatment utilizing a dilute, sterile solution of calcitonin salmon injection. Healthcare providers may wish to refer patients who require skin testing to an allergist.

Hypocalcemia
Hypocalcemia associated with tetany (i.e., muscle cramps, twitching) and seizure activity has been reported with calcitonin salmon injection therapy. Hypocalcemia must be corrected before initiating therapy. Other disorders affecting mineral metabolism (such as vitamin D deficiency) should also be effectively treated. In patients at risk for hypocalcemia, provisions for parenteral calcium administration should be available during the first several administrations of calcitonin salmon and serum calcium and symptoms of hypocalcemia should be monitored. Use of calcitonin salmon injection for the treatment of postmenopausal osteoporosis is recommended in conjunction with an adequate intake of calcium and vitamin D.

Malignancy
In a meta-analysis of 21 randomized, controlled clinical trials with calcitonin salmon (nasal spray or investigational oral formulations), the overall incidence of malignancies reported was higher among calcitonin salmon-treated patients (4.1%) compared with placebo-treated patients (2.9%). This suggests an increased risk of malignancies in calcitonin salmon-treated patients compared to placebo-treated patients. It is not possible to exclude an increased risk when calcitonin salmon is administered long-term subcutaneously, intramuscularly, or intravenously. The benefits for the individual patient should be carefully considered against possible risks.

Antibody Formation
Circulating antibodies to calcitonin salmon have been reported with calcitonin salmon injection. The possibility of antibody formation should be considered in any patient with an initial response to calcitonin salmon injection who later stops responding to treatment.

Urine Sediment Abnormalities
Coarse granular casts and casts containing renal tubular epithelial cells were reported in young adult volunteers at bed rest who were given injectable calcitonin salmon to study the effect of immobilization on osteoporosis. There was no other evidence of renal abnormality and the urine sediment normalized after calcitonin salmon was stopped. Periodic examinations of urine sediment should be considered.

ADVERSE REACTIONS
The safety of calcitonin salmon injection was assessed in open-label trials several months to two years in duration. The most common adverse reactions are discussed below.
Nausea: Nausea with or without vomiting has been noted in about 10% of patients treated with calcitonin salmon. It is most evident when treatment is first initiated and tends to decrease or disappear with continued administration.
Dermatologic Reactions: Local inflammatory reactions at the site of subcutaneous or intramuscular injection have been reported in about 10% of patients. Flushing of face or hands occurred in about 2% to 5% of patients. Skin rashes and pruritus of the ear lobes have also been reported.
Other Adverse Reactions: Nocturia, feverish sensation, pain in the eyes, poor appetite, abdominal pain, pedal edema, and salty taste have been reported in patients treated with calcitonin salmon injection.

DRUG INTERACTIONS
No formal drug interaction studies have been performed with calcitonin salmon injection.
Concomitant use of calcitonin salmon and lithium may lead to a reduction in plasma lithium concentrations due to increased urinary clearance of lithium. The dose of lithium may require adjustment.

OVERDOSAGE
The pharmacologic actions of calcitonin salmon injection suggest that hypocalcemic tetany could occur in overdose. Therefore, provisions for parenteral administration of calcium should be available for the treatment of overdose.

A dose of calcitonin salmon 1000 International Units (IU) subcutaneously may produce nausea and vomiting. Doses of 32 IU per kg per day for 1 to 2 days demonstrate no other adverse effects. Data on chronic high-dose administration are insufficient to assess toxicity.

Click for Full Prescribing Information for calcitonin salmon injection.

About Endo
Endo (NASDAQ: ENDP) 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 the best 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.

About Par Pharmaceutical
Par Pharmaceutical develops, manufactures and markets safe, innovative and cost-effective generic pharmaceutical and branded injectable products that help improve patient quality of life. Par, among the top leaders in the U.S. generics industry, possesses an expanding portfolio that includes sterile injectables, alternative dosage forms and other differentiated products. Par Pharmaceutical is an Endo company. Learn more at www.parpharm.com.

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 and any statements relating to market potential or product efficacy, sales, shipments, production, supply, demand or availability. Statements including words or phrases such as "believe," "expect," "anticipate," "intend," "estimate," "plan," "will," "may," "look forward," "intend," "future," "potential" or similar expressions are forward-looking statements. All forward-looking statements in this press release reflect Endo's current expectations of future events based on existing trends and information and represent Endo's judgment only as of the date of this press release. Actual results may differ materially and adversely from current expectations based on a number of factors affecting Endo's businesses, including, among other things, the following: the outcome of our strategic review, contingency planning and any potential restructuring; the timing, impact or results of any pending or future litigation, investigations or claims or actual or contingent liabilities, settlement discussions, negotiations or other adverse proceedings; our ability to satisfy judgments or settlements or pursue appeals including bonding requirements; our ability to adjust to changing market conditions; our ability to attract

and retain key personnel; our inability to maintain compliance with financial covenants and operating obligations which would expose us to potential events of default under our outstanding indebtedness; our ability to incur additional debt or equity financing for working capital, capital expenditures, business development, debt service requirements, acquisitions or general corporate or other purposes; our ability to refinance our indebtedness; a significant reduction in our short-term or long-term revenues which could cause us to be unable to fund our operations and liquidity needs or repay indebtedness. The occurrence or possibility of any such result has caused us to engage, and may result in further engagement in strategic reviews that ultimately may result in our pursuing one or more significant corporate transactions or other remedial measures, including on a preventative or proactive basis. Those remedial measures could include a potential corporate reorganization, restructuring or bankruptcy filing involving all or a portion of our business, asset sales or other divestitures, cost-saving initiatives, corporate realignments or strategic partnerships. Some of these measures could take significant time to implement and others may require judicial or other third-party approval. Any such actions may be complex, could entail significant costs and charges or could otherwise negatively impact shareholder value, and there can be no assurance that we will be able to accomplish any of these alternatives on terms acceptable to us, or at all, or that they will result in their intended benefits. Therefore, the reader is cautioned not to rely on these forward-looking statements. Endo 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 Endo, as well as Endo'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 Endo'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.

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