Endo Launches Ibuprofen-Famotidine Tablets, Generic Version of DUEXIS®

March 26, 2024

DUBLIN, March 26, 2024 /PRNewswire/ -- Endo International plc (OTC: ENDPQ) announced today that one of its operating companies, Par Pharmaceutical, Inc., launched ibuprofen-famotidine 800 mg/26.6 mg tablets, a generic version of Amgen's (formerly Horizon Therapeutics) DUEXIS®.

"We're proud to provide affordable choices to healthcare providers and their appropriate patients while strengthening our reputation as a reliable, quality supplier," said Scott Sims, Senior Vice President and General Manager, Injectable Solutions & Generics at Endo.

The combination medication is used to relieve the signs and symptoms of rheumatoid arthritis and osteoarthritis while decreasing the risk of developing ulcers of the stomach and upper intestines people may experience from ibuprofen alone.

According to IQVIA ™, ibuprofen-famotidine tablet sales were approximately $49 million for the 12 months ended December 31, 2023.

DUEXIS® is a registered trademark of Horizon Therapeutics USA, Inc.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Thrombotic Events

- **Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.**
- **Ibuprofen and famotidine is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.**

Gastrointestinal Bleeding, Ulceration, and Perforation

- **NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at a greater risk for serious GI events.**

CONTRAINDICATIONS:
Ibuprofen and famotidine tablets are contraindicated in the following patients:

- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to ibuprofen or famotidine or any components of the drug product.
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients.
- In the setting of coronary artery bypass graft (CABG) surgery.
- Ibuprofen and famotidine tablets should not be administered to patients with a history of hypersensitivity to other H_2-receptor antagonists. Cross sensitivity with other H_2-receptor antagonists has been observed.

WARNINGS AND PRECAUTIONS
Cardiovascular Thrombotic Events
Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI), and stroke, which can be fatal.

To minimize the potential risk for an adverse CV event in NSAID-treated patients, use the lowest effective dose for the shortest duration possible. Physicians and patients should remain alert for the development of such events, throughout the entire treatment course, even in the absence of

previous CV symptoms. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur.

Status Post Coronary Artery Bypass Graft (CABG) Surgery
Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke. NSAIDs are contraindicated in the setting of CABG.

Post-MI Patients
Avoid the use of ibuprofen and famotidine in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If ibuprofen and famotidine is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

Gastrointestinal Bleeding, Ulceration, and Perforation
NSAIDs, including ibuprofen, cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDS.

Strategies to Minimize the GI Risks in NSAID-treated patients:

- Use the lowest effective dosage for the shortest possible duration.
- Avoid administration of more than one NSAID at a time.
- Avoid use in patients at higher risk unless benefits are expected to outweigh the increased risk of bleeding. For such patients, as well as those with active GI bleeding, consider alternate therapies other than NSAIDs.
- Remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy.
- If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue ibuprofen and famotidine until a serious GI adverse event is ruled out.
- In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding.

Active Bleeding
When active and clinically significant bleeding from any source occurs in patients receiving ibuprofen and famotidine, the treatment should be withdrawn. Patients with initial hemoglobin values of 10 g or less who are to receive long-term therapy should have hemoglobin values determined periodically.

Hepatotoxicity
Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue ibuprofen and famotidine immediately, and perform a clinical evaluation of the patient.

Hypertension
NSAIDs, including ibuprofen and famotidine, can lead to new onset of hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazide diuretics, or loop diuretics may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

Heart Failure and Edema
Fluid retention and edema have been observed in some patients treated with NSAIDs. Use of ibuprofen may blunt the CV effects of several therapeutic agents used to treat these medical conditions (e.g., diuretics, ACE inhibitors, or angiotensin receptor blockers [ARBs]).

Avoid the use of ibuprofen and famotidine in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If ibuprofen and famotidine is used in patients with severe heart failure, monitor patients for signs and symptoms of worsening heart failure.

Renal Toxicity and Hyperkalemia
Renal Toxicity
Avoid the use of ibuprofen and famotidine in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal failure. If ibuprofen and famotidine is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Hyperkalemia
Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state.

Anaphylactic Reactions
Ibuprofen has been associated with anaphylactic reactions in patients with and without known hypersensitivity to ibuprofen and in patients with aspirin-sensitive asthma. Seek emergency help if an anaphylactic reaction occurs.

Seizures
Central nervous system (CNS) adverse effects including seizures, delirium, and coma have been reported with famotidine in patients with moderate (creatinine clearance <50 mL/min) and severe renal insufficiency (creatinine clearance <10 mL/min), and the dosage of the famotidine component in ibuprofen and famotidine is fixed. Therefore, ibuprofen and famotidine is not recommended in patients with creatinine clearance < 50 mL/min.

Exacerbation of Asthma Related to Aspirin Sensitivity
Because cross-reactivity between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, ibuprofen and famotidine is contraindicated in patients with this form of aspirin sensitivity. When ibuprofen and famotidine is used in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

Serious Skin Reactions
NSAIDs, including ibuprofen, which is a component of ibuprofen and famotidine tablets, can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Inform patients about the signs and symptoms of serious skin reactions and to discontinue the use of ibuprofen and famotidine at the first appearance of skin rash or any other sign of hypersensitivity. Ibuprofen and famotidine is contraindicated in patients with previous serious skin reactions to NSAIDs.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as ibuprofen and famotidine. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. If such signs or symptoms are present, discontinue ibuprofen and famotidine and evaluate the patient immediately.

Fetal Toxicity
Limit use of NSAIDs, including ibuprofen and famotidine, between about 20 to 30 weeks in pregnancy due to the risk of oligohydramnios/fetal renal dysfunction. Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/fetal renal dysfunction and premature closure of the fetal ductus arteriosus.

Masking of Inflammation and Fever
The pharmacological activity of ibuprofen and famotidine in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

Laboratory Monitoring
Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs, consider monitoring patients on long-term NSAID treatment with a CBC and chemistry profile periodically.

Concomitant NSAID Use
Ibuprofen and famotidine tablets contain ibuprofen as one of its active ingredients. It should not be used with other ibuprofen-containing products. The concomitant use of NSAIDs, including aspirin, with ibuprofen and famotidine may increase the risk of adverse reactions.

Aseptic Meningitis
If signs or symptoms of meningitis develop in a patient on ibuprofen and famotidine, the possibility of its being related to ibuprofen should be considered.

Ophthalmological Effects
Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If a patient develops such complaints while receiving ibuprofen and famotidine, the drug should be discontinued, and the patient should have an ophthalmologic examination which includes central visual fields and color vision testing.

ADVERSE EVENTS
Most common adverse reactions (>1% and greater than ibuprofen alone) are nausea, diarrhea, constipation, upper abdominal pain, and headache.

INDICATION AND USAGE
Ibuprofen and famotidine tablets, a combination of the NSAID ibuprofen and the histamine H_2-receptor antagonist famotidine, is indicated for the relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastrointestinal ulcers, which in the clinical trials was defined as a gastric and/or duodenal ulcer, in patients who are taking ibuprofen for those indications. The clinical trials primarily enrolled patients less than 65 years of age without a prior history of gastrointestinal ulcer. Controlled trials do not extend beyond 6 months.

Click for Full Prescribing Information, including BOXED WARNING and Medication Guide.

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, quality, affordability, efficacy, reliability or sales, 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 complete a chapter 11 plan of reorganization or to pursuen an alternative emergence transaction; 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.

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