FDA Approves Pediatric Indication for EMEND® (aprepitant) Capsules in Combination with Other Antiemetic Agents

Release Date:
Wednesday, September 2, 2015 8:00 am EDT

Terms:
Prescription Medicine News  Corporate News  Latest News

Dateline City:
KENILWORTH, N.J.

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved a supplemental New Drug Application (sNDA) for EMEND® (aprepitant) capsules, a substance P/neurokinin 1 (NK1) receptor antagonist. With this expanded indication, EMEND capsules are now approved for use in combination with other antiemetic agents in patients 12 years of age and older and patients less than 12 years who weigh at least 30 kg (approximately 66 pounds) for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). EMEND has not been studied for treatment of established nausea and vomiting. Chronic continuous administration of EMEND is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.

With this approval, EMEND is the first and only NK1 receptor antagonist to be approved for the prevention of acute and delayed phases of chemotherapy-induced nausea and vomiting (CINV) in patients 12 to 17 years of age and patients less than 12 years who weigh at least 30 kg receiving HEC or MEC. The approval was supported by data from a pivotal Phase 3 study that showed adding EMEND to a standard regimen for prevention of CINV in HEC or MEC regimens resulted in a reduction of emetic events.

EMEND is contraindicated in patients with any known sensitivity to any component of this drug. EMEND is also contraindicated for patients taking pimozide.

There is no commercially available dosage formulation of EMEND appropriate for patients less than 12 years of age and weighing less than 30 kg. Therefore, EMEND is indicated for the prevention of nausea and vomiting associated with HEC or MEC in patients 12 years of age and older and patients less than 12 years of age who weigh at least 30 kg.

Data Supporting the Expanded FDA Approval

The FDA approval of this expanded indication for EMEND (aprepitant) was based in part on findings from a randomized, double-blind, active-comparator-controlled clinical study that assessed EMEND in combination with ondansetron (OND) regimen compared to ondansetron alone (control regimen) for the prevention of CINV in patients 12 to 17 years of age and patients less than 12 years of age who weighed at least 30 kg (n=63 and 69, respectively) receiving HEC or MEC. Intravenous dexamethasone was permitted at the discretion of the physician. The primary endpoint was complete response (no vomiting, retching and no use of rescue medication) in the delayed phase (25 to 120 hours following initiation of chemotherapy). Other pre-specified endpoints included: complete response in the acute phase (0 to 24 hours following initiation of chemotherapy), complete response in the overall phase (up to 120 hours following initiation of chemotherapy), and safety and tolerability. For the population aged 12 to 17 years and patients less than 12 years who weighed at least 30 kg (n=132), data included in the label show that in the delayed phase, a 49.2 percent (n=31/63) complete response rate was observed in the EMEND regimen compared to 18.8 percent (n=13/69) in the control regimen; in the acute phase, a 55.6 percent (n=35/63) complete response was observed in the EMEND regimen compared to 37.7 percent (n=26/69) in the control regimen; and, in the overall phase, a 34.9 percent (n=22/63) complete response was observed in the EMEND regimen compared to 13.0 percent (n=9/69) in the control regimen.

The most common adverse reactions reported in pooled studies of 352 pediatric patients receiving HEC or MEC treated with the EMEND regimen (versus the control regimen) were neutropenia (13% vs 11%), headache (9% vs 5%), diarrhea (6% vs 5%), decreased appetite (5% vs 4%), cough (5% vs 3%), fatigue (5% vs 2%), hemoglobin decreased (5% vs 4%), dizziness (5% vs 1%), and hiccups (4% vs 1%).

“The FDA approval of this expanded indication for EMEND is the result of our commitment to fully realizing the potential of our therapies to help as many patients as possible,” said Stuart Green, vice president, clinical research, Merck Research Laboratories. “Historically, significant improvements in pediatric medicine have been slow due to many challenges such as clinical trial size. However, at Merck, these obstacles have invigorated our efforts to bring forward a new option for these patients.”

About EMEND
EMEND® (aprepitant) is a selective high-affinity antagonist of human substance P/neurokinin 1 (NK\textsubscript{1}) receptors. Aprepitant has little or no affinity for serotonin (5-HT\textsubscript{3}), dopamine, and corticosteroid receptors, the targets of existing therapies for chemotherapy-induced nausea and vomiting (CINV).

EMEND (aprepitant) is indicated in combination with other antiemetic agents in patients 12 years of age and older and patients less than 12 years of age who weigh at least 30 kg for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of HEC including high-dose cisplatin as well as nausea and vomiting associated with initial and repeat courses of MEC. EMEND has not been studied for the treatment of established nausea and vomiting. Chronic continuous administration of EMEND is not recommended because it has not been studied, and because the drug interaction profile may change during chronic continuous use.

Selected Safety Information

EMEND is contraindicated in patients who are hypersensitive to any component of the product. Hypersensitivity reactions including anaphylactic reactions have been reported.

EMEND is contraindicated in patients taking pimozide. Inhibition of CYP3A4 by aprepitant could result in elevated plasma concentrations of this drug which is a CYP3A4 substrate, potentially causing serious or life-threatening reactions, such as QT prolongation. Aprepitant is a substrate, a weak-to-moderate (dose-dependent) inhibitor, and an inducer of CYP3A4. Use of EMEND with other drugs that are CYP3A4 substrates, may result in increased plasma concentrations of the concomitant drug. Use of EMEND with strong or moderate CYP3A4 inhibitors (e.g., ketoconazole, diltiazem) may increase plasma concentrations of aprepitant and result in an increased risk of adverse reactions related to EMEND. Use of EMEND with strong CYP3A4 inducers (e.g.,rifampin) may result in a reduction in aprepitant plasma concentrations and decreased efficacy of EMEND.

Co-administration with oral dexamethasone: reduce the dose of oral dexamethasone by approximately 50%. Co-administration with intravenous methylprednisolone: reduce the dose of intravenous methylprednisolone by approximately 25%. Co-administration with oral methylprednisolone: reduce the dose of oral methylprednisolone by approximately 50%.

Monitor patients taking vinblastine, vincristine, or ifosfamide or other chemotherapeutic agents that are metabolized by CYP3A4 for chemotherapeutic-related adverse reactions. No dosage adjustments are needed when etoposide, vinorelbine, paclitaxel, or docetaxel are administered.

Coadministration of EMEND (aprepitant) with warfarin, a CYP2C9 substrate, may result in a clinically significant decrease in International Normalized Ratio (INR) of prothrombin time. In patients on chronic warfarin therapy, monitor the INR in the 2-week period, particularly at 7 to 10 days, following initiation of the 3-day regimen of EMEND (aprepitant) with each chemotherapy cycle.

Upon coadministration with EMEND, the efficacy of hormonal contraceptives (including birth control pills, skin patches, implants, and certain IUDs) may be reduced during administration of and for 28 days following the last dose of EMEND. Advise patients to use alternative or back-up methods of contraception during treatment with EMEND and for 1 month following the last dose of EMEND.

In HEC and MEC clinical studies with adults, EMEND in combination with ondansetron and dexamethasone (EMEND regimen) was compared with ondansetron and dexamethasone alone (standard therapy). The most common adverse reactions reported in at least 3% of patients treated with the EMEND regimen and at a greater incidence than standard therapy, were: fatigue (13% EMEND regimen vs 12% standard therapy), diarrhea (9% vs 8%), asthenia (7% vs 6%), dyspepsia (7% vs 5%), abdominal pain (6% vs 5%), hiccups (5% vs 3%), decreased white blood cell count (4% vs 3%), dehydration (3% vs 2%), and increased alanine aminotransferase (3% vs 2%).

In HEC and MEC clinical studies in pediatric patients, EMEND in combination with ondansetron with or without dexamethasone (EMEND regimen) was compared to ondansetron with or without dexamethasone (control regimen). The most common adverse reactions reported in at least 3% of patients treated with the EMEND regimen and at a greater incidence than the control regimen, were: neutropenia (13% EMEND regimen vs 11% control regimen), headache (9% vs 5%), diarrhea (6% vs 5%), decreased appetite (5% vs 4%), cough (5% vs 3%), fatigue (5% vs 2%), decreased hemoglobin (5% vs 4%), dizziness (5% vs 1%), and hiccups (4% vs 1%).

Dosing of EMEND Capsules

EMEND is administered as part of a 3-day regimen for the prevention of nausea and vomiting associated with HEC or MEC in adults and pediatric patients 12 years of age and older and patients less than 12 years of age who weigh at least 30 kg, who can swallow oral capsules. The recommended dosage of EMEND is a 125-mg capsule given on Day 1 of chemotherapy, followed by 80-mg capsules given on each of Days 2-3. In adults, the regimen includes coadministration with dexamethasone and a 5-HT\textsubscript{3} antagonist. In pediatric patients receiving HEC or MEC who are 12 years and older or weighing at least 30 kg, and who can swallow oral capsules, the regimen includes coadministration of a 5-HT\textsubscript{3} antagonist and may include coadministration of a corticosteroid such as dexamethasone. Please refer to the package insert for EMEND (aprepitant) for detailed dosing instructions regarding the coadministration of a corticosteroid. Please also refer to the package insert of the selected 5-HT\textsubscript{3} antagonist for the recommended dosage of the 5-HT\textsubscript{3} antagonist.

Our Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck Oncology, helping people fight cancer is our passion and supporting accessibility to our cancer medicines is our commitment. Our focus is on pursuing research in immuno-oncology, and we are accelerating every step in the journey – from lab to clinic – to potentially bring new hope to people with cancer. For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.
About Merck

Today’s Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on Twitter, Facebook and YouTube.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company’s 2014 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).


Language:
English

Contact:
Merck
Media:
Doris Li, 908-740-1903
An Phan, 908-255-6325
or
Investors:
Justin Holko, 908-740-1879

Ticker Slug:
Ticker: MRK
Exchange: NYSE