October 28, 2016

Eisai Co., Ltd.
EA Pharma Co., Ltd.

Application Submitted for Proton Pump Inhibitor Pariet® in Japan Seeking Approval for Additional Dosage and Administration for Maintenance Therapy of Proton Pump Inhibitor Resistant Reflux Esophagitis

Eisai Co., Ltd. (Headquarters, Tokyo; CEO, Haruo Naito; "Eisai") and Eisai's subsidiary for gastrointestinal disease area EA Pharma Co., Ltd. (Headquarters, Tokyo; President & CEO, Hajime Shimizu; "EA Pharma") announced today that Eisai has submitted an application in Japan seeking approval for additional dosage and administration of 10 mg twice-daily dosing of the proton pump inhibitor Pariet® (generic name: rabeprazole sodium) for use in the maintenance therapy of proton pump inhibitor-resistant reflux esophagitis (reflux esophagitis in which healing is not achieved with usual doses of proton pump inhibitors currently approved for the treatment of reflux esophagitis). In Japan, Eisai is the marketing and manufacturing authorization holder for Pariet, while EA Pharma is responsible for distribution.

Reflux esophagitis is a condition which causes erosion and ulceration of the mucosal lining of the esophagus due to the regurgitation of stomach acid and other content, as well as frequent and persistent symptoms such as heartburn, discomfort in the throat, belching, heaviness in the stomach and bloating. While symptoms may improve, they often reoccur and relapse, and it is often the case that patients need continued appropriate control including drug therapy. For the treatment of reflux esophagitis, use of proton pump inhibitors is recommended. Pariet 10 mg once-daily oral dosing is already approved for maintenance therapy during remission as well. For some patients, however, existing treatments are not always enough to achieve satisfactory therapeutic effects. In order to broaden the range of treatment options available to such patients with proton pump inhibitor-resistant reflux esophagitis, Eisai and EA Pharma have been jointly developing twice-daily dosing of Pariet, at a dose of 10 mg respectively, for maintenance therapy.

The application was made based on the results of double-blind controlled Phase III clinical study, which evaluated the efficacy and safety of twice-daily dosing of Pariet 10 mg Tablets against once-daily dosing of Pariet 10 mg Tablets in patients with reflux esophagitis who had inadequate response to the treatment with proton pump inhibitors according to the currently approved dosing regimen in Japan.

Currently approved in more than 100 countries worldwide, Pariet was first launched in Japan in 1997, where it is indicated for multiple uses, including for the treatment of gastric ulcer, duodenal ulcer, reflux esophagitis, non-erosive gastroesophageal reflux disease, the prevention of recurrent gastric or duodenal ulcer caused by low-dose aspirin therapy and as an adjunct therapy in *Helicobacter pylori (H. pylori)* eradication.

By expanding current indications for Pariet, Eisai and EA Pharma aim to increase the clinical value of the drug so as to further contribute to the range of treatment options available to patients with acid-related diseases.

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More Information

1. About Pariet

Pariet is a proton pump inhibitor that was discovered and developed by Eisai Co., Ltd. First launched in Japan in 1997, it is approved in more than 100 countries and territories worldwide. In Japan, Pariet is indicated for multiple uses, including for the treatment of gastric ulcer, duodenal ulcer, reflux esophagitis, non-erosive gastroesophageal reflux disease, the prevention of recurrent gastric or duodenal ulcer caused by low-dose aspirin therapy and as an adjunctive therapy in *Helicobacter pylori (H. pylori)* eradication, and is available in 5 mg, 10 mg and 20 mg tablet formulations based on evidence collected in Japanese patients. In addition, in December 2010, Eisai was granted domestic approval for additional twice-daily 10 mg and twice-daily 20 mg dosage and administration of Pariet for treatment of patients with reflux esophagitis who are unable to obtain satisfactory relief with conventional proton pump inhibitor treatment. Most recently, Eisai received marketing authorization in Japan in August 2013 for two types of triple formulation packs (combination packs) for *H. pylori* eradication, both of which contain Pariet. Among the most commonly reported adverse reactions are rash, urticaria, itching sensation, diarrhea, and loose stool.

2. Current dosage and administration of Pariet for reflux esophagitis

The usual adult dose for oral use is 10 mg of rabeprazole sodium administered once daily. However, the dosage may be increased up to 20 mg orally once daily depending on the severity of symptoms. The usual administration should be restricted to up to 8 weeks. For patients who do not achieve satisfactory therapeutic effects by proton pump inhibitors, Pariet can be given orally at a dose of 10 mg or 20 mg twice daily for additional 8 weeks. The dosing at 20 mg twice daily, however, should be limited to those patients who have severe mucosal injury.

For the maintenance therapy of reflux esophagitis showing repeated recurrence and recrudescence, the dose for oral use is 10 mg once daily.

3. About Eisai

Eisai Co., Ltd. is an R&D-focused global pharmaceutical company based in Japan. Eisai gives first thought to patients and their families, and to increasing the benefits health care provides, having the corporate mission "*human health care* (*hhc*)". With a global network of R&D, production and sales bases, about 10000 employees are engaged in development and provision of innovative new drugs over the world in the disease areas with high unmet medical needs, focusing on "neurology" and "oncology" as strategically important areas.

For more information on Eisai Co., Ltd., please see www.eisai.co.jp

4. About EA Pharma Co., Ltd.

EA Pharma Co., Ltd., a subsidiary of Eisai Co., Ltd. for gastrointestinal disease area, was established in April 2016 by integration of the gastrointestinal business unit with at least 60 years history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma is a gastrointestinal specialty pharma with a full value chain covering R&D, logistics and sales & marketing.

For more information on EA Pharma Co., Ltd., please see http://www.eapharma.co.jp/