

September 22, 2017

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

**Additional Dosage and Administration of Proton Pump Inhibitor Pariet®
5 mg Tablets, 10 mg Tablets Approved in Japan 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, Yuji Matsue; “EA Pharma”) announced today that Eisai has obtained the approval of additional dosage and administration in Japan of the proton pump inhibitor Pariet® 5 mg Tablets and 10 mg Tablets (generic name: rabeprazole sodium) to administer 10 mg of rabeprazole sodium per dose twice-daily for the maintenance therapy of proton pump inhibitor-resistant reflux esophagitis (reflux esophagitis in which it is difficult to achieve satisfactory therapeutic effects by existing treatment with once-daily dosing of proton pump inhibitors). 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 of the mucosal lining of the esophagus due to the regurgitation of stomach acid and other causes, as well as frequent and persistent symptoms such as heartburn, discomfort in the throat and belching, with repeated recurrence and recrudescence. The prevalence of this condition in Japan is estimated to be 10%.¹ In many cases, 8 weeks of initial treatment followed by maintenance therapy with a once-daily proton pump inhibitor is sufficient to cure reflux esophagitis and prevent remission. However, in approximately 15% of reflux esophagitis cases, these treatments are not enough to achieve satisfactory therapeutic effects.² For patients with proton pump inhibitor-resistant reflux esophagitis, Pariet is the only proton pump inhibitor available for treatment by twice-daily dosing at 10 mg or 20 mg each. However, there is an 8 week dosing period limit, and after that, maintenance therapy by once-daily dosing at 10 mg occurs. With the above approval, Pariet becomes the only proton pump inhibitor available for maintenance therapy by twice-daily dosing at 10 mg and is anticipated to further fulfil unmet medical needs.

The above approval was made based on the results of a double-blind controlled Phase III clinical study conducted in Japan, in which the efficacy and safety of twice-daily dosing of Pariet 10 mg Tablets were evaluated against once-daily dosing of Pariet 10 mg Tablets in patients with reflux esophagitis who had inadequate response to existing treatment with proton pump inhibitors. In the primary endpoint of non-recurrence rates as confirmed by endoscopy at 52 weeks of maintenance therapy, the twice-daily dosing group demonstrated a statistically significant improvement over the once-daily group, with non-recurrence rate in the twice-daily dosing group at 73.9% compared to 44.8% in

the once-daily group ($P < 0.001$). Adverse drug reactions (at least 2 incidences) observed in the above study were diarrhea, increased blood pressure and increased blood thyroid stimulating hormone, which is consistent with the known safety profile of Pariet.

Eisai and EA Pharma consider it their mission as R&D-based pharmaceutical companies in possession of originator drugs to seek new value for long-listed drugs to increase patient benefits. The above approval will add a treatment option for patients with reflux esophagitis who had inadequate response to the existing treatment by proton pump inhibitors, and through this, the two companies aim to further contribute to the treatment of 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. ("Eisai") 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, anastomotic ulcer, reflux esophagitis, Zollinger-Ellison syndrome, 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 in Japan. 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.

2. Details of the above approval (The underlined parts are added.)

1) Product

Pariet[®] 5 mg Tablets, Pariet[®] 10 mg Tablets

2) Dosage and administration (Extract of the section of reflux esophagitis only)

* The section of reflux esophagitis is divided into the parts of <Curative Therapy> and <Maintenance Therapy>

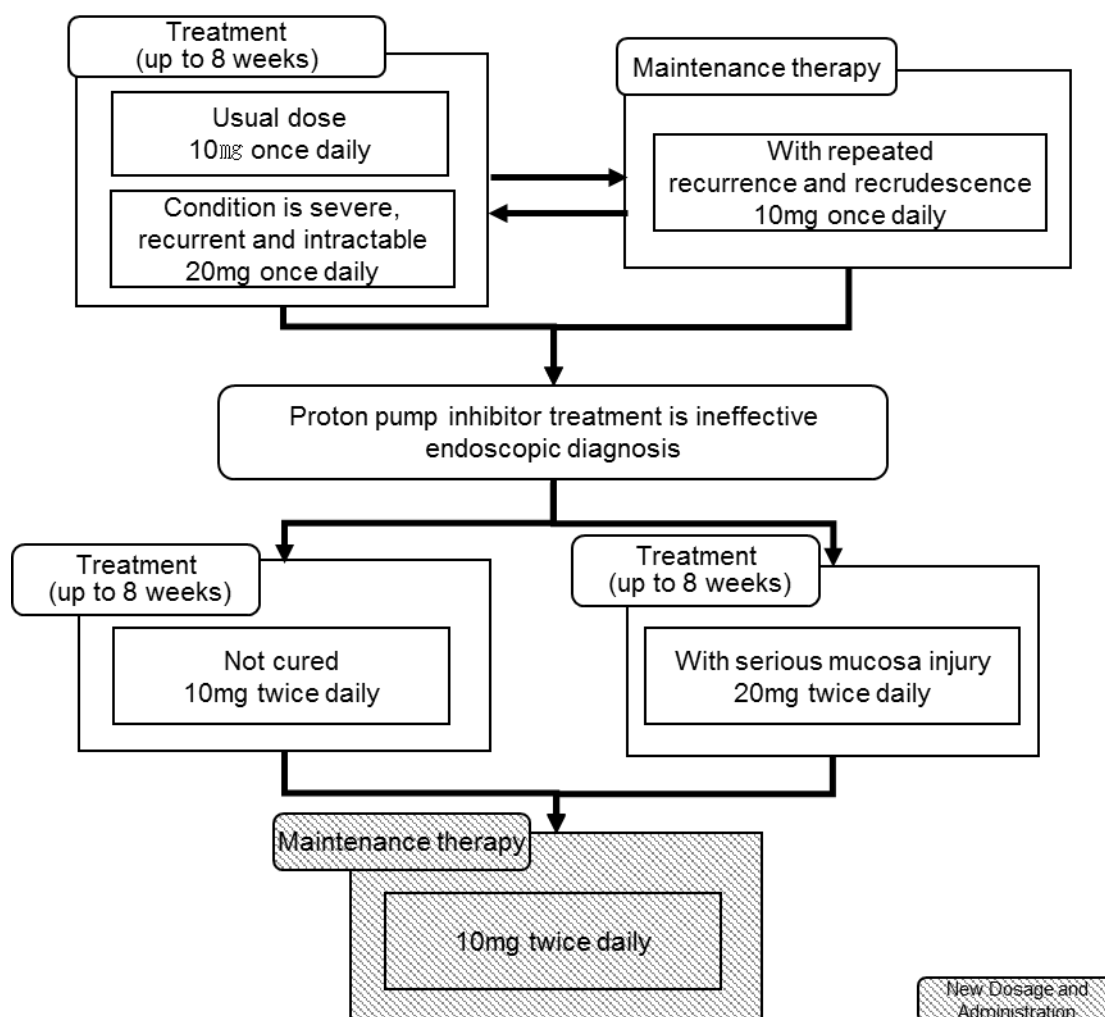
<Curative Therapy>

For treatment of 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.

<Maintenance Therapy>

For the maintenance therapy of reflux esophagitis showing repeated recurrence and recrudescence, the usual adult dose for oral use is 10 mg of rabeprazole sodium once-daily. For the maintenance therapy of reflux esophagitis in patients who do not achieve satisfactory therapeutic effects by proton pump inhibitors, Pariet can be given orally at a dose of 10 mg twice-daily.

3. About usage of Pariet for reflux esophagitis



4. 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.com

5. About EA Pharma

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

<https://www.eapharma.co.jp/en/>

¹ Japanese Society of Gastroenterology, GERD Diagnosis Guidelines, 2015 (2nd Revised Edition)

² Chiba N., et al, Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a meta-analysis, *Gastroenterology*. 1997;112(6):1798-810.