No. 20-31

June 25, 2020
Eisai Co., Ltd.

EISAI RECEIVES APPROVAL FOR PARKINSON'S DISEASE TREATMENT EQUFINA® IN SOUTH KOREA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that Eisai Korea Inc., Eisai's subsidiary in South Korea, has received marketing approval of Parkinson's disease treatment Equfina® (safinamide mesilate, "safinamide") for the indication of treatment of idiopathic Parkinson's disease as adjunctive therapy with levodopa-containing products in patients with end of dose motor fluctuations from the regulatory authority in South Korea (Ministry of Food and Drug Safety). The marketing authorization application for safinamide in South Korea was submitted in July 2019, and through the approval of this application, South Korea became the first country in Asia outside of Japan to grant marketing approval for safinamide.

This approval is primarily based on a double-blind, placebo-controlled, phase III study (SETTLE study) in overseas countries, including South Korea, to evaluate the efficacy and safety of 24-week oral administration of the once-daily safinamide as an add-on to levodopa in patients with Parkinson's disease with motor fluctuations.[1]
In the SETTLE study, the primary endpoint was the change in mean daily "on" time (period of time in which Parkinson's disease symptoms are suppressed) from baseline to 24 weeks of the treatment phase. Regarding the primary endpoint, safinamide increased the "on" time by 0.96 hours (95% CI: 0.56, 1.37, $p<0.001$) more than placebo, showing a statistically significant extension in "on" time. The most common three adverse drug reactions observed with patients with safinamide were dyskinesia, nausea and somnolence.

Under the license agreement signed between Eisai and Meiji Seika Pharma Co., Ltd. (Headquarters: Tokyo, "Meiji") in March 2017, Eisai obtained exclusive marketing rights for safinamide in Japan, as well as development and marketing rights in Asia. Meiji obtained manufacturing and marketing approval for safinamide in Japan in September 2019, and Eisai launched safinamide in Japan in November 2019.

The estimated number of patients with Parkinson's disease is approximately 150,000 in South Korea. Parkinson's disease has high unmet medical needs because of inadequate symptom control using current medications, necessitating new treatment options. This disease is designated as a rare intractable disease in South Korea.
Together with providing Equfina as a new treatment option for Parkinson's disease to patients in South Korea, Eisai will make further contributions to address the diversified needs of and increase the benefits provided to Parkinson's disease patients and their families in Japan and Asia.

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[Notes to editors]

1. About Equfina (safinamide mesylate "safinamide")

Safinamide is a selective monoamine oxidase B (MAO-B) inhibitor, which reduces the degradation of excreted dopamine, helping to maintain the density of dopamine in the brain. Additionally, safinamide blocks sodium ion channels and inhibits glutamate release, and as such has potential as a new Parkinson's disease treatment which possesses both dopaminergic and non-dopaminergic mechanisms.

Safinamide was discovered and developed by Newron Pharmaceuticals S.p.A. (Headquarters: Milan, Italy, "Newron"). In 2011, Newron entered into a licensing agreement with Meiji, granting Meiji exclusive rights to develop, manufacture and commercialize the drug in Japan and Asia. Eisai has exclusive rights for marketing in Japan, as well as for development and marketing in Asia* based on a licensing agreement signed between Eisai and Meiji. Safinamide mesilate is marketed under the name "Xadago" in 15 countries in Europe, the United States and Australia, and under the name "Onstryv" in Canada.

* South Korea, Taiwan, Brunei, Cambodia, Laos, Malaysia, the Philippines, Indonesia, Thailand, Vietnam, Myanmar, Singapore, Hong Kong, and Macau

2. About the clinical phase III study (SETTLE study)[1]

The SETTLE study was a placebo-controlled, double blinded, and parallel group clinical phase III study conducted in overseas countries. The efficacy and safety of 24-week oral administration of once-daily safinamide as add-on to levodopa in patients with Parkinson's disease with wearing-off phenomena of motor fluctuations were compared to placebo. Administration started with 50mg in safinamide group, and increased to 100mg as tolerated. The primary endpoint was the change in mean daily "on" time (period of time in which Parkinson's disease symptoms are suppressed) from baseline to 24 weeks of the treatment phase, and verified the superiority of safinamide over placebo. Regarding the primary endpoint, safinamide increased the "on" time by 0.96 hours (95% CI: 0.56, 1.37, $p<0.001$) more than placebo, showing a statistically significant extension in "on" time. The adverse drug reactions (ADR) incidence rates in this study were 27.6% for placebo and 28.5% for safinamide. The most common three ADRs observed with patients with safinamide were dyskinesia, nausea and somnolence.

3. About Parkinson's disease

Parkinson's disease is a neurodegenerative disease which causes motor impairment, with symptoms including tremors in the limbs, muscular rigidity and shuffling gait. It is caused by degeneration of the dopamine nervous system, which leads to a shortage of dopamine, a neurotransmitter in the brain. The estimated number of patients with Parkinson's disease is approximately 150,000 in South Korea (Eisai's internal estimates). The number of patients suffering from Parkinson's disease is approximately 3 million patients in Asia,[2] and 200,000 patients in Japan.[3] The number of patients is increasing due to aging of the population.[4] Levodopa is widely used to treat Parkinson's disease by replenishing the brain's supply of dopamine. However, as the disease progresses, levodopa's duration of effect decreases, and there are cases of Parkinson's disease symptoms returning before the next dose ("wearing-off" phenomenon). To prevent the "wearing-off" phenomenon, a combination therapy with a drug that has a different mechanism of action than that of levodopa is used.

[1] Schapira AH et al. Assessment of Safety and Efficacy of Safinamide as a Levodopa Adjunct in Patients With Parkinson Disease and Motor Fluctuations: A Randomized Clinical Trial. *JAMA Neurol.* 2017;74(2):216-224

[2] E Ray Dorsey et al. Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016 *Lancet Neurol.* 2018;17:939–53

[3] Japanese Society of Neurology. Treatment and Management Guideline 2018 for Parkinson's Disease

[4] Japan Intractable Diseases Information Center: http://www.nanbyou.or.jp/