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Eisai Co., Ltd.
Meiji Seika Pharma Co., Ltd.

MEIJI AND EISAI ANNOUNCE PARKINSON'S DISEASE TREATMENT EQUFINA® TABLETS (SAFINAMIDE MESILATE) APPROVED IN JAPAN

Meiji Seika Pharma Co., Ltd. (Headqurters: Tokyo, CEO: Daikichiro Kobayashi, "Meiji") and Eisai Co., Ltd. (Headqurters: Tokyo, CEO: Haruo Naito, "Eisai") today announced the manufacturing and marketing approval in Japan for the indication of improvement of wearing-off phenomenon in patients with Parkinson's disease under treatment with a drug containing levodopa for Equfina® TABLETS (safinamide mesilate, "safinamide"), which was developed for use in the treatment of patients with Parkinson's disease was obtained. In Japan, Meiji holds the manufacturing and marketing approval for safinamide, and Eisai exclusively sells the safinamide.

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. There are approximately 200,000 patients suffering from Parkinson's disease in Japan[1], and the number of patients is increasing due to the aging of the population.[1, 2] Drugs containing levodopa are 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 ("on" time) decreases, and there are cases where patients may experience wearing-off phenomena, a return of Parkinson's disease symptoms before the next dose. Safinamide through its main mechanism of action as a selective monoamine oxidase B (MAO-B) inhibitor, increases the density of endogenous dopamine in the brain and exogenous dopamine from levodopa-containing drugs.

This manufacturing and marketing approval is based on a double-blind, placebo-controlled Phase II/III study (study ME2125-3) to evaluate the efficacy and safety of safinamide as add-on therapy and an open label Phase III study (study ME2125-4) to evaluate the safety and efficacy of long-term administration of safinamide in Japanese patients with Parkinson's disease with wearing-off phenomena who are currently receiving levodopa, as well as global clinical trials.
In study ME2125-3, the change in mean daily "on" time from baseline to 24 weeks of the treatment phase, which is the primary endpoint, of treatment with safinamide 50 mg and 100 mg were statistically significant compared to placebo-controlled treatment. The most common adverse drug reactions (ADRs) (incidence 3% and higher) observed with patients with safinamide 50 mg and 100 mg were dyskinesia and visual hallucination. Also in study ME2125-4, with regard to the change in mean daily "on" time from baseline to 52 weeks of the treatment phase, the "on" time with long-term administration of safinamide was extended, and showed the continued effectiveness.The most common ADRs

(incidence 3% and higher) observed with patients were dyskinesia, falls, and constipation.

By providing Equifina TABLETS as a new option for Parkinson's disease treatment, Meiji and Eisai will make further contributions to address the diverse needs of, and increase the benefits provided to, Parkinson's disease patients and their families.

<Notes to editors>

1. About Equfina® TABLETS (generic name: 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 possesses both dopaminergic and non-dopaminergic mechanisms.
Global and domestic clinical trials of safinamide in combination with levodopa for the treatment of mid- to late-stage Parkinson's disease showed extended "on" time and an improvement in motor function.[3,4]

2. About Licensing Agreement between Eisai and Meiji for Safinamide

Safinamide was discovered and developed by Newron Pharmaceuticals S.p.A. (Headquarters: Italy, Milan, "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. Under the license agreement signed between Eisai and Meiji in March 2017, Eisai has the exclusive rights to market safinamide in Japan, as well as to develop and market safinamide in Asia*. Safinamide is marketed under the name "Xadago" in 17 countries in Europe and the United States.

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

3. About study ME2125-3 (Phase II/III Clinical Study)

Study ME2125-3 was a multicenter, double-blind, placebo-controlled, randomized, parallel group study to evaluate the efficacy and safety of two doses of safinamide (50 and 100 mg, once a day for 24 weeks) administered orally as add-on therapy in Japanese patients with Parkinson's disease with wearing-off phenomenon who are currently receiving a drug containing levodopa. In this study, the primary endpoint was the change in mean daily "on" time from baseline to 24 weeks of the treatment phase, and verified the superiority of each dose of safinamide over placebo. Regarding the changes from baseline of mean daily "on" time of 24 weeks of treatment, the increases of 1.39 hours (95%CI: 0.67,2.11) with safinamide 50 mg and 1.66 hours (95%CI: 0.93,2.39) with safinamide 100 mg were shown compared to placebo, and statistically significant "on" time extension were indicated in patients with both safinamide 50 mg and 100 mg. The most common ADRs (incidence 3% and higher) observed in patients taking safinamide 50 mg and 100 mg were dyskinesia and visual hallucination.

4. About study ME2125-4 (Phase III Clinical Study)

Study ME2125-4 was an open-label, multicenter study to evaluate the long-term efficacy and safety of two doses of safinamide (50 and 100 mg, once a day for 52 weeks) administered orally as add-on therapy in Japanese patients with Parkinson's disease with wearing-off phenomenon who are currently receiving a drug containing levodopa. In this study, in addition to evaluating the safety of long-term administration of safinamide, the study evaluated the change in mean daily "on" time from baseline to 52 weeks of the treatment phase as the primary efficacy endpoint. Regarding the changes (Least Square Mean (LSM) ± Standard Deviation of Lateral Position (SDLP)) from baseline of mean daily "on" time of 52 weeks of treatment, it was 1.42±2.72 hours, and the continuous efficacy of long term administration was shown. The most common ADRs (incidence 3% and higher) observed were dyskinesia, falls, and constipation.

5. About Parkinson’s Disease

Parkinson's disease is a neurodegenerative disease which causes motor impairment, including shaking 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. According to the estimation of Japanese Society of Neurology, there are approximately 200,000 patients suffering from Parkinson’s disease in Japan.[1] Also, the approximate 3 million patients suffer from Parkinson’s disease in Asia.[5] The number of patients increasing due to the aging of the population.[2] Levodopa is widely used to treat Parkinson's disease by replenishing the brain's supply of dopamine. However, as the disease progresses, the duration of a drug containing levodopa of effect (“on” time) decreases, and there are cases of Parkinson's disease symptoms returning before the next dose (“wearing-off” phenomenon). To prevent the “wearing-off” phenomenon, combination therapy with a drug that has a different mechanism of action to a drug containing levodopa is administered.

6. About Eisai Co., Ltd.

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our hhc philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Oncology and Neurology.

As a global pharmaceutical company, our mission extends to patients around the world through our investment and participation in partnership-based initiatives to improve access to medicines in developing and emerging countries.

For more information about Eisai Co., Ltd., please visit https://www.eisai.com/.

7. About Meiji Seika Pharma Co., Ltd.

In order to protect and improve people's health and lives, Meiji Seika Pharma, as a “Speciality and Generic Pharmaceuticals Company,” runs its pharmaceutical business in the two main fields, infectious disease and central nervous system disorders, as well as generic drugs. Meiji Seika Pharma strives to respond to diversified medical needs and contributes to the well-being of people worldwide.

For details, please visit its corporate website:
https://www.meiji.com/global/about-us/corporate-profile/meiji-seika-pharma/

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

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

[3] Borgohain R et al. Randomized Trial of Safinamide Add-On to Levodopa in Parkinson's Disease With Motor Fluctuations. *Mov Disord.* 2014 Feb;29(2):229-37

[4] 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 Feb 1;74(2):216-224

[5] 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