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Eisai Co., Ltd.

NEW DRUG APPLICATION FOR PERAMPANEL FOR ADJUNCTIVE TREATMENT OF PARTIAL ONSET SEIZURES ACCEPTED IN CHINA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) has announced that the National Medical Products Administration of China has accepted for review a New Drug Application for Eisai's antiepileptic drug (AED) perampanel (generic name, product name: Fycompa®) as an adjunctive treatment for partial onset seizures in epilepsy patients 12 years of age and older. This NDA is the first to be submitted for perampanel in China.

This application for perampanel in partial onset seizures in China was based on the results of three Phase III clinical studies conducted mainly in Europe and the United States, as well as the results of a Phase III clinical study (Study 335) conducted mainly in Asia including China and Japan.
In China it is estimated that there are approximately 9 million patients with epilepsy, with approximately 60% being affected by partial-onset seizures, and 40% of these patients with partial-onset seizures require adjunctive treatment.[1] As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[2] this is a disease with significant unmet medical need.

Perampanel is a first-in-class AED discovered at Eisai's Tsukuba Research Laboratories. Administered orally once-daily, it is a highly selective, noncompetitive AMPA receptor antagonist that reduces neuronal hyperexcitation associated with seizures by targeting glutamate activity at AMPA receptors on postsynaptic membranes.
Perampanel has been approved in over 55 countries around the world as an adjunctive treatment for partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 12 years of age and older. In addition, perampanel has been approved in over 50 countries around the world as an adjunctive treatment for primary generalized tonic clonic seizures in patients with epilepsy 12 years of age and older. In the United States, perampanel is also indicated for monotherapy and adjunctive use in the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older.

Eisai considers neurology including epilepsy, a therapeutic area of focus, and is striving to deliver perampanel to patients in China as soon as possible. In pursuit of our mission to provide “seizure freedom” to a greater number of patients living with epilepsy, Eisai seeks to address the diverse needs of, as well as increasing the benefits provided to, patients with epilepsy and their families.

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[Notes to editors]

1. About perampanel (generic name, product name: Fycompa)

Perampanel is a first-in-class AED discovered and developed by Eisai. With epileptic seizures being mediated by the neurotransmitter glutamate, the agent is a highly selective, noncompetitive AMPA receptor antagonist that reduces neuronal hyperexcitation associated with seizures by targeting glutamate activity at AMPA receptors on postsynaptic membranes. Perampanel is available in tablet form to be taken once daily orally at bedtime. In addition, an oral suspension formulation has been approved in the United States.

Perampanel is currently approved in more than 55 countries and territories, including the United States, Japan, in Europe and in Asia as adjunctive treatment for partial-onset seizures (with or without secondarily generalized seizures) in patients with epilepsy 12 years of age and older. An application seeking approval for use in the treatment of partial-onset seizures has now been filed in China. In addition, perampanel has been approved in more than 50 countries, including the United States, Japan, in Europe and in Asia for treatment as an adjunctive therapy for primary generalized tonic clonic seizures in patients with epilepsy 12 years of age and older. In the United States, perampanel is also indicated for monotherapy and adjunctive use in the treatment of partial-onset seizures (with or without secondarily generalized seizures) in patients with epilepsy 4 years of age and older.

Furthermore, Eisai is conducting a global Phase III clinical study (Study 338) for the agent in patients with seizures associated with Lennox-Gastaut syndrome. In Japan and Europe, Eisai is conducting a Phase III study in pediatric patients with epilepsy (Study 311). Additionally, a Phase III study of perampanel as monotherapy in untreated patients with partial-onset seizures 12 years of age and older is being conducted in Japan (Study 342).

2. About Study 335 upon which the NDA in China was based[3]

Study title:	A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Perampanel Administered as an Adjunctive Therapy in Subjects with Refractory Partial-onset Seizures
Study population:	710 patients aged 12 years and older who have a diagnosis of epilepsy with partial-onset seizures with or without secondarily generalized seizures receiving one to a maximum of three anti-epileptic drugs
Treatment administered:	Perampanel oral tablets, 4 mg/day, 8 mg/day and 12 mg/day, once daily before bedtime Perampanel-matched placebo oral tablets, once daily before bedtime
Duration of treatment:	Prerandomization Phase: 6 weeks Randomization Phase (treatment): 19 weeks (Titration Period, 6 weeks; Maintenance Period, 13 weeks) Extension Phase: over 10 weeks
Study locations:	Japan, China, South Korea, Australia, Thailand, Malaysia, Taiwan
Primary endpoint:	Percent change in seizure frequency per 28 days during treatment relative to baseline
Results:	The percent change in seizure frequency in the placebo group was -10.8% while in the perampanel (4 mg, 8 mg, 12 mg) groups it was -17.3%, -29.0% and -38.0%, respectively. The difference between perampanel and placebo was statistically significant for the perampanel 8 and 12 mg groups ($p=0.0003$ for 8 mg, $p<0.0001$ for 12 mg).
Adverse events:	The most common adverse events (≥10% in the perampanel arms and greater than placebo) were dizziness (22.7%, 28.6%, 42.2% in the perampanel 4 mg, 8 mg, 12 mg groups respectively and 5.7% for placebo) and somnolence (15.9%, 17.7%, 17.8% in the perampanel 4 mg, 8 mg, 12 mg groups respectively and 13.1% for placebo).

3. About Epilepsy

Epilepsy affects approximately 3.4 million people in the United States, 1 million people in Japan, 6 million people in Europe, 9 million people in China, and approximately 60 million people worldwide. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[2] this is a disease with significant unmet medical need.

Epilepsy is broadly categorized by seizure type, with partial-onset seizures accounting for approximately 60% of epilepsy cases and generalized seizures accounting for approximately 40%. In a partial-onset seizure, an abnormal electrical disturbance occurs in a limited area of the brain, and may subsequently spread throughout the brain, becoming a generalized seizure (known as a secondarily generalized seizure). In a generalized seizure, abnormal electrical disturbances occur throughout the brain, and can be followed by a loss of consciousness or physical symptoms manifested throughout the whole body.

[1] Clinical Guideline 2015 in China

[2] "The Epilepsies and Seizures: Hope Through Research. What are the epilepsies?" National Institute of Neurological Disorders and Stroke, accessed May 24, 2016, http://www.ninds.nih.gov/disorders/epilepsy/detail_epilepsy.htm#230253109

[3] Nishida T., et al. Adjunctive perampanel in partial-onset seizures: Asia-Pacific, randomized phase III study. *Acta Neurol Scand.* 2018; 137:392-399