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Eisai Co., Ltd.

EISAI RECEIVES APPROVAL FOR INDICATION EXPANSION OF ANTI-EPILEPTIC AGENT FYCOMPA® FOR USE IN PEDIATRIC PATIENTS

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced that it has been received approval from the European Commission for the use of its in-house discovered and developed anti-epileptic agent (AED) Fycompa® (generic name: perampanel) in the treatment of pediatric patients. This approval extends the use of Fycompa as an adjunctive therapy for partial-onset seizures (POS) (with or without secondary generalization) by expanding the approved age range from 12 years and above to 4 years and above, and for primary generalized tonic-clonic seizures (PGTCS) from 12 years and above to 7 years and above.

The approval was based on the results of Phase III (Study 311) and Phase II (Study 232) clinical studies conducted globally to evaluate Fycompa as an adjunctive therapy in pediatric patients with POS or PGTCS. Study 311 evaluated the safety, tolerability, and exposure-efficacy relationship of Fycompa when administered as an adjunctive therapy in pediatric patients aged 4 to less than 12 years with inadequately controlled POS or PGTCS. This study showed that the safety and efficacy of the Fycompa combination therapy in pediatric epilepsy patients with poorly controlled partial seizures (ages 4 to less than 12 years) were similar to those in patients aged 12 years and older. The most common adverse events (incidence of 10% or higher) observed in this study were somnolence, nasopharyngitis, pyrexia, vomiting, dizziness, influenza, and irritability. Study 232 evaluated the pharmacokinetics, efficacy, and long-term safety of Fycompa as an adjunctive therapy in pediatric patients with epilepsy (from 2 to less than 12 years of age). The adverse events (≥10% in the Fycompa arms) observed in Study 232 were pyrexia, fatigue, vomiting, irritability, somnolence, dizziness, and upper respiratory tract infection.

Fycompa is a first-in-class AED discovered at Eisai's Tsukuba Research Laboratories. The agent is a highly selective, noncompetitive AMPA receptor antagonist that is postulated to reduce neuronal hyper-excitation associated with seizures by targeting glutamate activity at AMPA receptors on postsynaptic membranes. In Japan and the United States, Fycompa is currently approved for monotherapy and adjunctive use in the treatment of POS (with or without secondarily generalized seizures) in patients with epilepsy 4 years of age and older, as well as adjunctive treatment for PGTCS in patients with epilepsy 12 years of age and older.

Eisai considers neurology, including epilepsy, a therapeutic area of focus. As we offer several treatment options in Europe, including Fycompa, Eisai pursues its mission to provide "seizure freedom" to a greater number of patients with epilepsy. Eisai seeks to address the diverse needs of, as well as increasing the benefits provided to, patients with epilepsy and their families.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

[Notes to editors]

1. About Fycompa (generic name: perampanel)

Fycompa is a first-in-class anti-epileptic agent (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. Fycompa is available in drug form to be taken once daily orally at bedtime. A tablet and fine granule formulation have been approved in Japan. An oral suspension formulation and tablet have been approved in the United States and Europe.

Fycompa is currently approved in more than 70 countries and territories, including Japan, the United States, China, and other countries in Europe and in Asia 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 Europe the approved age range will be expanded to 4 years and above based on this approval. In addition, Fycompa has been approved in more than 65 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 Europe the approved age range will be expanded to 7 years and above based on this approval.
In Japan and the United States, Fycompa is approved 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. To date, Fycompa has been used to treat more than 300,000 patients worldwide across all indications.
Eisai is conducting a global Phase III clinical study (Study 338) for the agent in patients with seizures associated with Lennox-Gastaut syndrome. In addition, Eisai is conducting development of an injection formulation.

2. About Study 311 [1]

Study 311 is a global (United States, Europe, Japan, South Korea), open-label Phase III clinical study evaluating the safety, tolerability, and exposure efficacy relationship of the Fycompa oral suspension when administered as an adjunctive therapy in 180 pediatric epilepsy patients aged 4 to less than 12 with inadequately controlled partial-onset seizures or primary generalized tonic-clonic seizures. This study comprised a treatment phase, including a titration period of up to 11 weeks and a maintenance period of up to 12 weeks and an extension phase. In this study, 2 to 16 mg of Fycompa was taken orally once daily before bedtime. Primary endpoints were safety and tolerability. Efficacy was similar to that observed in patients 12 years of age and older. The most common adverse events (incidence of 10% or higher) observed in this study were somnolence, nasopharyngitis, pyrexia, vomiting, dizziness, influenza, and irritability, which is consistent with the safety profile of Fycompa to date.

3. About Study 232 [2]

Study 232 was a global (United States, Europe), multicenter, open-label clinical study with an extension phase to evaluate 63 pediatric patients with epilepsy (ages 2 to less than 12). The study evaluated the pharmacokinetics, safety, tolerability and efficacy of Fycompa oral suspension taken at the same time as other AEDs. Administration of once-daily Fycompa was titrated from 0.015 mg/kg to 0.18 mg/kg, and long-term safety was confirmed after 11 weeks of treatment and an extension phase (41 weeks). The adverse events (≥10% in the Fycompa arms) observed in Study 232 were pyrexia, fatigue, vomiting, irritability, somnolence, dizziness, upper respiratory tract infection.

4. About Epilepsy

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.

Epilepsy affects approximately 1 million people in Japan, 3.4 million people in the United States, 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,[3] this is a disease with significant unmet medical needs. Although onset occurs at any age, onset is most common in people aged 18 and younger and the elderly. As causes and clinical symptoms of pediatric epilepsy are not uniform, and prognoses can range from very positive cases to obstinate cases, special consideration for each patient is required of treatments.

[1] A. Fogarasi et al. Open-label study to investigate the safety and efficacy of adjunctive perampanel in pediatric patients (4 to <12 years) with inadequately controlled focal seizures or generalized tonic-clonic seizures *Epilepsia.* 2020 Jan;61(1):125-137.

[2] J. Ben Renfroe et al. Adjunctive Perampanel Oral Suspension in Pediatric Patients From ≥2 to <12 Years of Age With Epilepsy: Pharmacokinetics, Safety, Tolerability, and Efficacy *J Child Neurol.* 2019 Apr;34(5):284-294

[3] "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