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Eisai Co., Ltd.

EISAI SUBMITS SUPPLEMENTAL NEW DRUG APPLICATION TO U.S. FDA FOR FYCOMPA® AS TREATMENT FOR PEDIATRIC PATIENTS WITH EPILEPSY

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") has announced that it has submitted to the U.S. Food and Drug Administration (FDA) a supplemental New Drug Application (sNDA) for Eisai's antiepileptic drug (AED) Fycompa® (perampanel) seeking approval for an indication expansion to cover pediatric patients with epilepsy.
This sNDA aims to expand the indication for Fycompa in the United States, which currently covers monotherapy and adjunctive use in the treatment of partial-onset seizures (with or without secondarily generalized seizures) in patients with epilepsy 12 years of age and older, to also include children with epilepsy 2 years of age and older. Based on data accumulated to date, the sNDA also seeks to potentially expand the pediatric indication to include children 2 years of age and older for the treatment of primary generalized tonic-clonic seizures.

Fycompa has been approved in over 55 countries in the world as an adjunctive treatment for partial-onset seizures (with or without secondarily generalized seizures) as well as primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older. In the United States, Fycompa has also been approved as monotherapy use for the treatment of partial-onset seizures (with or without secondarily generalized seizures).

This application was based on the interim results of a Phase III clinical study (Study 311) as well as the results from a Phase II clinical study (Study 232). Both studies suggested the safety and efficacy of adjunctive treatment with Fycompa was similar between adult and pediatric patients.
Study 311 evaluated the safety, tolerability and exposure-efficacy relationship of Fycompa when administered as an adjunctive therapy in children (ages 4 to less than 12 years) with inadequately controlled partial onset seizures or primary generalized tonic clonic seizures. Study 232 is evaluated the pharmacokinetics, efficacy and long-term safety of Fycompa when given as an adjunctive therapy in pediatric subjects from 2 to less than 12 years of age with epilepsy.

Furthermore, regarding the pediatric indication for Fycompa, Eisai has received from the FDA a Written Request for pediatric studies, which means that Priority Review designation is possible.

Fycompa is a first-in-class AED discovered at Eisai's Tsukuba Research Laboratories. It is a highly selective, noncompetitive AMPA receptor antagonist that reduces neuronal hyperexcitation associated with seizures by targeting glutamate activity at postsynaptic AMPA receptors.

Epilepsy affects approximately 2.9 million people in the United States, 1 million people in Japan, 6 million people in Europe, and approximately 60 million people worldwide. While epilepsy affects people of all ages, incidence is particularly high among children and the elderly. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[1] this is a disease with significant unmet medical need.

Eisai considers neurology a therapeutic area of focus, and together with the worldwide provision of Fycompa, seeks to further contribute to addressing 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 Fycompa (perampanel)

Fycompa 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 postsynaptic AMPA receptors. Fycompa is available in tablet form to be taken once daily orally at bedtime. In addition, a new oral suspension formulation has been approved and is being marketed in the United States.

Fycompa is currently approved in more than 55 countries and territories, including Japan, the United States, and in Europe 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, Fycompa has been approved in more than 45 countries, including Japan, the United States, and in Europe as an adjunctive therapy for primary generalized tonic-clonic (PGTC) seizures in patients with epilepsy 12 years of age and older.

Fycompa is also indicated in the United States for the treatment of partial-onset seizures (with or without secondarily generalized seizures) and the adjunctive treatment of PGTC in patients with epilepsy aged 12 and older.

Furthermore, Eisai is conducting respective global Phase III studies for the agent in pediatric patients with partial-onset seizures or PGTC seizures and in patients with seizures associated with Lennox-Gastaut syndrome. Additionally, a Phase III study as monotherapy for partial-onset seizures is being conducted in Japan.

For further information on Fycompa in the United States, including Important Safety Information, please visit the Fycompa product website (https://fycompa.com).

2. About Study 311

Study 311 is a global (United States, Europe, Japan, Asia) multicenter, open-label, single-arm trial with an extension phase to evaluate the safety, tolerability and exposure-efficacy relationship of Fycompa oral suspension when administered as an adjunctive therapy in approximately 160 pediatric patients (ages 4 to less than 12 years) with inadequately controlled partial-onset seizures or primary generalized tonic-clonic seizures.

Following the 23 week treatment phase in which patients are titrated to receive 2 to 16 mg of Fycompa orally once-daily, long term safety will be assessed during an extension phase. In Japan, pediatric patients with partial-onset seizures will be titrated to receive 2 to 12 mg of Fycompa orally once-daily. The adverse events (≥10% in the perampanel arms) observed in Study 311 were somnolence, nasopharyngitis, dizziness, irritability.

3. About Study 232

Study 232 was a global (United States, Europe), multicenter, open-label, long-term administration clinical study in approximately 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 perampanel arms) observed in Study 232 were pyrexia, fatigue, vomiting, irritability, somnolence, dizziness, upper respiratory tract infection.

4. About Epilepsy

Epilepsy affects approximately 2.9 million people in the United States, 1 million people in Japan, 6 million people in Europe, and approximately 60 million people worldwide. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[1] 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 sometimes 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.

Accounting for approximately 60% of generalized epilepsy and approximately 20% of all epilepsy cases,[2] generalized tonic-clonic seizures are one of the most common and most severe forms of epileptic seizures as they can cause significant injury to patients from falling down suddenly, and the frequency of these seizures is the most important risk factor associated with sudden unexpected death in epilepsy (SUDEP).[3]

For the majority of patients, a generalized tonic-clonic seizure begins with a loss of consciousness without any prior warning symptoms and a sudden contraction of the tonic muscles, causing the patient to fall down (tonic phase). This is followed by violent convulsions (clonic phase) until the muscles finally relax, and the patient is left with a disturbance of consciousness. As this is a serious event, it is seen as a major hindrance on daily life. While the seizure generally only lasts a few minutes, the patient will often feel confused, groggy or drowsy for a short period of time before returning to normal.

[1] “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

[2] Hauser WA, et al. *Epilepsia*, 34(3):453-468,1993

[3] Shorvon S, Tomson T.“Sudden unexpected death in epilepsy.” *Lancet*, 2011; 378:2028-2038