No.19-10

February 13, 2019
Eisai Co., Ltd.

EISAI SUBMITS APPLICATION IN EUROPE SEEKING APPROVAL FOR FYCOMPA® AS TREATMENT FOR PEDIATRIC PATIENTS WITH EPILEPSY

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has submitted an application to the European Medicines Agency (EMA) for its in-house discovered antiepileptic drug (AED) Fycompa® (perampanel) seeking approval for use in pediatric patients with epilepsy.
This application aims to expand the indication for Fycompa, which is already approved for adjunctive use in patients aged 12 years and older with partial-onset seizures (with or without secondarily generalized seizures) or primarily generalized tonic-clonic seizures, to cover pediatric patients as well.

This application was based on the results of Phase III (Study 311) and Phase II (Study 232) clinical studies conducted globally to evaluate Fycompa as adjunctive therapy in pediatric patients. Study 311 evaluated the safety, tolerability, as well as relationship between efficacy and blood concentration of Fycompa when administered as an adjunctive therapy in pediatric patients (age 4 to less than 12 years) with inadequately controlled partial-onset seizures or tonic-clonic seizures. Study 232 evaluated the pharmacokinetics, efficacy, and long-term safety of adjunctive perampanel in pediatric patients (from 2 to less than 12 years of age). Detailed results of both studies will be presented at upcoming academic conferences, respectively.

Discovered at Eisai's Tsukuba Research Laboratories, Fycompa is a first-in-class AED that is a highly selective, noncompetitive AMPA receptor antagonist which reduces neuronal hyperexcitation by targeting glutamate activity at AMPA receptors on postsynaptic membranes. Available in tablet form to be taken orally once daily, Fycompa has been approved in over 55 countries in the world and has been used to treat more than 200,000 patients worldwide to date. Regarding the indication covering pediatric patients, Fycompa was approved in the United States in September 2018, and an application was submitted in Japan in January 2019.

It is estimated that there are approximately 6 million patients with epilepsy in Europe, and although onset occurs at any age, onset is most common in people aged 18 and younger and the elderly.

Eisai considers neurology including epilepsy, a therapeutic area of focus, and in continued 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 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 AMPA receptors on postsynaptic membranes. Fycompa 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.

Fycompa 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 adjunctive treatment of partial-onset seizures is under review in China, which has been designated for Priority Review. In addition, Fycompa 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 tonic-clonic seizures in patients with generalized epilepsy 12 years of age and older. In 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. In Japan, a supplementary new drug application has been filed seeking approval of Fycompa for use as monotherapy for partial-onset seizures, treatment for partial-onset seizures in pediatric patients aged 4 years and older, as well as a fine granule formulation.

Furthermore, Eisai is conducting a global Phase III clinical study (Study 338) for the agent in patients with epileptic seizures associated with Lennox-Gastaut syndrome.

2. About Study 311

Study title:	An Open-Label Study to Evaluate the Safety, Tolerability, and Exposure-Efficacy Relationship of Fycompa Oral Suspension When Administered as an Adjunctive Therapy in Pediatric Subjects (Age 4 to Less Than 12 Years) With Inadequately Controlled Partial-Onset Seizures or Primary Generalized Tonic Clonic Seizures
Study population:	180 patients aged 4 to 12 with inadequately controlled partial-onset seizures or primarily generalized tonic-clonic seizures
Treatment administered:	2 - 16 mg of Fycompa administered orally once daily before bedtime
Duration of treatment:	Treatment Phase (Titration Period: up to 11 weeks, Maintenance Period: up to 12 weeks) Extension Phase
Study locations:	Global (United States, Europe, Japan, Asia)
Primary endpoint:	Safety and tolerability
Results:	In the 180 patients who were administered Fycompa, 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

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

It has been reported that 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,[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 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] "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