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Eisai Co., Ltd.

EUROPEAN COMMISSION APPROVES INDICATION EXPANSION OF EISAI'S ANTIEPILEPTIC AGENT FYCOMPA® FOR ADJUNCTIVE TREATMENT OF PRIMARY GENERALIZED TONIC-CLONIC SEIZURES

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that its U.K. subsidiary Eisai Europe Ltd. has received approval from the European Commission (EC) for an indication expansion regarding the use of its in-house developed antiepileptic agent Fycompa® (perampanel hydrate) for the adjunctive treatment of primary generalized tonic-clonic (PGTC) seizures in adult and adolescent patients from 12 years of age with idiopathic generalized epilepsy.

PGTC seizures are one of the most severe forms of generalized seizures, accounting for approximately 60% of generalized epilepsy and approximately 20% of all epilepsy cases.[1] The approval was based on a placebo-controlled study (Study 332)[2] to evaluate the efficacy and safety of adjunctive Fycompa therapy in 164 patients aged 12 years and older with PGTC seizures. In the study, the responder rate for Fycompa was 64.2%, which was a statistically significant improvement over the responder rate for placebo of 39.5% ($p=0.0019$). Additionally, a reduction in PGTC seizure frequency of 76.5% was observed in the Fycompa group, which was statistically significant when compared to a reduction of 38.4% for placebo ($p<0.0001$). Furthermore, 30.9% of patients treated with Fycompa were free of PGTC seizures (12.3% for placebo) during the 13 week maintenance period. The most common adverse events for Fycompa were, respectively, dizziness, fatigue, headache, somnolence and irritability.

Fycompa was launched in Europe as an adjunctive treatment for partial-onset seizures (with or without secondarily generalized seizures) in adult and adolescent patients from 12 years of age with epilepsy in September 2012. Through this indication expansion, Fycompa can now be used as an adjunctive treatment for primary, in addition to, secondarily generalized tonic-clonic seizures. Generalized tonic-clonic seizures can cause significant injury to patients from falling down suddenly and are the most important risk factor associated with sudden unexpected death in epilepsy (SUDEP),[3] making them one the most severe forms of epileptic seizures.

Epilepsy affects nearly 6 million people in Europe. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[4] this is a disease with significant unmet medical needs. Eisai considers epilepsy a therapeutic area of focus and by providing multiple treatment options in addition to Fycompa as part of an extensive epilepsy product portfolio, Eisai seeks to make continued contributions 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 hydrate)

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.

The agent is currently approved in more than 45 countries and territories, including Europe and the United States, as an adjunctive treatment (once-daily oral dose) of partial-onset seizures (with or without secondarily generalized seizures) in adult and adolescent patients from 12 years of age with epilepsy, and has been launched in over 25 countries.

Applications seeking an additional indication for the adjunctive treatment of primary generalized tonic-clonic (PGTC) seizures in adult and adolescent patients from 12 years of age with generalized epilepsy were filed with regulatory authorities in Europe and the United States in August 2014. Approval for the United States was received on June 19, 2015, and now approval for Europe has been received as well. Applications are also under review in Switzerland, Russia, Canada and Australia.

In addition, a Phase III study of Fycompa in partial-onset seizures (Study 335) conducted in Asia, including Japan, met its primary endpoint and the company plans to submit a regulatory application covering both PGTC seizures and partial-onset seizures based on Study 332 and Study 335 in Japan during the first half of fiscal 2015. Furthermore, Eisai is conducting Phase II studies in Europe and the United States for partial-onset epilepsy in pediatric patients.

2. About Study 332[2]

Study title:	A Multicenter, Double-blind, Randomized, Placebo-controlled Study to Evaluate the Efficacy and Safety of Adjunctive Perampanel in PGTC Seizures
Study population:	164 patients aged 12 years and older with PGTC seizures receiving one to a maximum of three anti-epileptic drugs
Primary objective:	To demonstrate the efficacy of adjunctive perampanel therapy, compared to placebo, on PGTC seizures
Treatment administered:	(Placebo-controlled) Perampanel oral tablets, once daily, up to 8 mg/day (Titration Period), randomized dose 8 mg/day (Maintenance Period)
Duration of treatment:	Prerandomization Phase (Screening and Baseline Periods): up to 12 weeks; Randomization Phase (treatment): 17 weeks (Titration Period, 4 weeks; Maintenance Period, 13 weeks); Extension Phase: over 38 weeks
Study locations:	U.S., Europe, Japan, Asia
Primary endpoints:	-Responder rate (EU): Percentage of patients who experience a 50% or greater reduction in PGTC seizure frequency per 28 days in the Maintenance period relative to baseline -Percent change in PGTC seizure frequency (U.S.): Percent change from baseline in PGTC seizure frequency per 28 days during treatment
Results:	-The responder rate for Fycompa was 64.2%, which was a statistically significant improvement over the responder rate for placebo of 39.5% (p=0.0019). -A reduction in PGTC seizure frequency of 76.5% was observed in the Fycompa group, which was statistically significant when compared to a reduction of 38.4% for placebo (p<0.0001). -For patients who had been unable to adequately control PGTC seizures with existing AEDs, 30.9% of patients treated with Fycompa were free of PGTC seizures (12.3% for placebo) during the 13 week Maintenance period.

Adverse events:	The most common adverse events (>10% in the Fycompa arm and greater than placebo) for Fycompa and placebo were, respectively, dizziness (32.1% vs 6.1%), fatigue (14.8% vs 6.1%), headache (12.3% vs 9.8%), somnolence (11.1% vs 3.7%) and irritability (11.1% vs 2.4%).

3. About Generalized Tonic-Clonic Seizures

Generalized tonic-clonic seizures can cause significant injury to patients from falling down suddenly and is the most important risk factor associated with sudden unexpected death in epilepsy (SUDEP),[3] making them one of the most severe forms of epileptic seizures.

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.

4. About Primary Generalized Tonic-Clonic Seizures in Patients with Generalized Epilepsy

Epilepsy affects nearly 6 million people in Europe, 2.9 million people in the United States, 1 million people in Japan, and more than 50 million people worldwide.

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%. Primary generalized tonic-clonic seizures are one of the most common and most severe forms of generalized seizures, accounting for approximately 60% of generalized epilepsy and approximately 20% of all epilepsy cases.[1]

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

[2] French JA, et al. “Adjunctive Perampanel for Treatment of Drug-Resistant Primary Generalized Tonic-Clonic Seizures in Patients with Idiopathic Generalized Epilepsy: A Double-Blind, Randomized, Placebo-Controlled Phase III Trial.” Abstract. *68th American Epilepsy Society (AES) Annual Meeting*, 2014; 2.389

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

[4] “The Epilepsies and Seizures: Hope Through Research. What are the epilepsies?” National Institute of Neurological Disorders and Stroke, accessed June 19, 2015, http://www.ninds.nih.gov/disorders/epilepsy/detail_epilepsy.htm#230253109