

U.S. FDA APPROVES EISAI'S ANTIEPILEPTIC AGENT FYCOMPA® AS ADJUNCTIVE TREATMENT FOR PRIMARY GENERALIZED TONIC-CLONIC SEIZURES

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that its U.S. subsidiary Eisai Inc. has received approval from the U.S. Food and Drug Administration (FDA) for an indication expansion regarding the use of its in-house developed antiepileptic agent Fycompa® (perampanel hydrate) as an adjunctive treatment of primary generalized tonic-clonic (PGTC) seizures in patients with epilepsy 12 years of age and older.

The FDA's decision to approve the indication expansion was based on a placebo-controlled clinical phase III study (Study 332) of Fycompa in 164 patients aged 12 years and older with PGTC seizures. In the study, a statistically significant reduction in PGTC seizure frequency was observed in the Fycompa group compared with placebo (Fycompa: -76.5%, placebo: -38.4%, $p < 0.0001$). Additionally, the responder rate for Fycompa was 64.2%, which was a statistically significant improvement over the responder rate for placebo of 39.5% ($p = 0.0019$). 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 dizziness, fatigue, headache, somnolence and irritability.

Fycompa is a first-in-class AED discovered and developed by Eisai. 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 was approved 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 the United States in October 2012 and was launched in January 2014.

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)¹, making them one of the most severe forms of epileptic seizures. Through this indication expansion, Fycompa can now be used as an adjunctive treatment for primary, in addition to, secondarily generalized tonic-clonic seizures.

Epilepsy affects approximately 2.9 million people in the United States. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs², 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.

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

[Notes to editors]

1. About Fycompa (perampanel)

Fycompa is a first-in-class AED discovered and developed by Eisai. With epileptic seizures being primarily 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 as an adjunctive treatment (once-daily oral dose) of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 12 years of age and older, and has been launched in over 25 countries.

Applications seeking an additional indication for the adjunctive treatment of PGTC seizures in patients with epilepsy 12 years of age and older were filed with regulatory authorities in Europe and the United States in August 2014. In addition to receiving approval in the United States, the European Medicines Agency's Committee for Medicine Products for Human Use issued a positive opinion regarding this indication in Europe in May 2015. Applications are also under review in Switzerland and Russia.

Furthermore, a Phase III study of Fycompa in partial-onset seizures (Study 335) conducted in Asia, including Japan, met its primary endpoint. 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. Meanwhile, Eisai is conducting Phase II studies in Europe and the United States for partial-onset epilepsy in pediatric patients.

2. About Study 332³

Study Title:	A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Adjunctive Perampanel in Primary Generalized Tonic Clonic (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:	-Percent change in PGTC seizure frequency (U.S.): Percent change from baseline in PGTC seizure frequency per 28 days during treatment -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
Results:	-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 ($p < 0.0001$). -The responder rate for Fycompa was 64.2%, which was a statistically significant improvement over the responder rate for placebo of 39.5% ($p = 0.0019$). -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

Epilepsy affects approximately 2.9 million people in the United States, 2.4 million people in Europe (G5: United Kingdom, France, Germany, Italy and Spain), 1 million people in Japan, and more than 50 million people worldwide. 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)¹, 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.

¹ Shorvon S, Tomson T. "Sudden unexpected death in epilepsy." *Lancet*, 2011; 378:2028-2038

² "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

³ 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