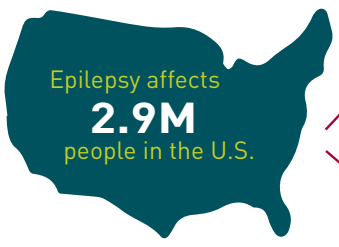
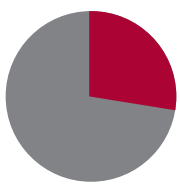
Fycompa™ (perampanel) tablets C-III

NOW FDA APPROVED

for adjunctive therapy in the treatment of
Primary Generalized Tonic-Clonic (PGTC) Seizures
in patients with epilepsy age 12 and older

EPILEPSY AND PGTC SEIZURES





ABOUT 30%
of patients' seizures may not be adequately controlled with current treatment

PGTC SEIZURES
are one of the most common and severe forms of generalized seizures, with a high incidence of morbidity and mortality

SAFETY AND EFFICACY OF FYCOMPA FOR TREATMENT OF PGTC SEIZURES

A Phase 3, randomized, double-blind, placebo-controlled clinical trial (Study 332) among...

- 162 patients, age 12 and older
- Taking 1-3 antiepileptic drugs (AEDs)
- Experiencing at least 3 PGTC seizures in the 8-week baseline period

RESULTED IN

76%
MEDIAN REDUCTION IN PGTC SEIZURE FREQUENCY*
for patients taking FYCOMPA (n=81) which was compared to 38% for placebo patients (n=81)**

64% of patients (n=81) experiencing at least a **50%** or greater **REDUCTION IN PGTC SEIZURE FREQUENCY†**
versus 40% for the placebo patients (n=81)*

* Primary endpoint
** These results were statistically significant compared to placebo patients
† Secondary endpoint

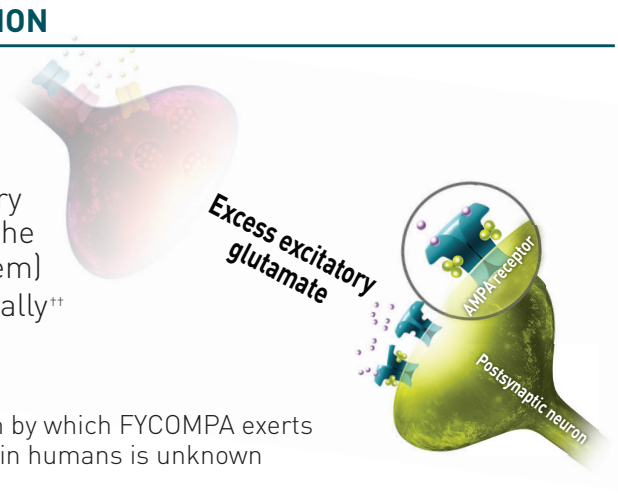
The most frequently reported adverse events
(greater than or equal to 10% and greater than placebo)
in patients treated with FYCOMPA:

dizziness | fatigue | headache | somnolence | irritability

The adverse event profile was similar to that seen for the controlled Phase 3 partial-onset seizure trials.

NOVEL MODE OF ACTION

FYCOMPA blocks **GLUTAMATE** (the primary excitatory neurotransmitter in the central nervous system) activity post-synaptically††



††The precise mechanism by which FYCOMPA exerts its antiepileptic effects in humans is unknown

FDA APPROVED FOR TWO INDICATIONS

Now FDA approved for PGTC seizures, FYCOMPA was previously approved as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures, in patients with epilepsy age 12 and older

To assist patients with access to their medication, Eisai offers a FYCOMPA Savings Card, which can be activated or downloaded by registering at **FYCOMPA.com.** Please see Full Prescribing Information.

Eisai is committed to **ADVANCING EPILEPSY CARE** and making contributions to help address the diversified needs of epilepsy patients and their families as part of its corporate *human health care (hhc)* mission.

Indications:
FYCOMPA (perampanel) is indicated as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures and primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older.

Important Safety Information

WARNING: SERIOUS PSYCHIATRIC AND BEHAVIORAL REACTIONS

- **Serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported in patients taking FYCOMPA**
- **These reactions occurred in patients with and without prior psychiatric history, prior aggressive behavior, or concomitant use of medications associated with hostility and aggression**
- **Advise patients and caregivers to contact a healthcare provider immediately if any of these reactions or changes in mood, behavior, or personality that are not typical for the patient are observed while taking FYCOMPA or after discontinuing FYCOMPA**
- **Closely monitor patients particularly during the titration period and at higher doses**
- **FYCOMPA should be reduced if these symptoms occur and should be discontinued immediately if symptoms are severe or are worsening**

Serious Psychiatric and Behavioral Reactions
In the partial- onset clinical trials, hostility- and aggression-related adverse reactions occurred in 12% and 20% of clinical trial patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 6% of patients in the placebo group. These effects were dose-related and generally appeared within the first 6 weeks of treatment, although new events continued to be observed through more than 37 weeks. These effects in FYCOMPA-treated patients led to dose reduction, interruption, and discontinuation more frequently than placebo-treated patients. The combination of alcohol and FYCOMPA significantly worsened mood and increased anger. Homicidal ideation and/or threat have also been reported postmarketing in patients treated with FYCOMPA. Patients taking FYCOMPA should avoid the use of alcohol. Patients, their caregivers, and families should be informed that FYCOMPA may increase the risk of psychiatric events. Patients should be monitored during treatment and for at least one month after the last dose of FYCOMPA, and especially when taking higher doses and during the initial few weeks of drug therapy (titration period) or at other times of dose increases. Similar serious psychiatric and behavioral events were observed in the primary generalized tonic-clonic seizure clinical trial.

Suicidal Behavior and Ideation
Antiepileptic drugs (AEDs), including FYCOMPA, increase the risk of suicidal thoughts or behavior in patients. Anyone considering prescribing FYCOMPA or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Patients, their caregivers, and families should be informed of the risk and advised to monitor and immediately report the emergence or worsening of depression, suicidal thoughts or behavior, thoughts about self-harm, and/or any unusual changes in mood or behavior. Should suicidal thoughts or behavior emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Dizziness and Gait Disturbance
FYCOMPA caused dose-related increases in events related to dizziness and disturbance in gait or coordination. Dizziness and vertigo were reported in 35% and 47% of patients in the partial-onset seizures clinical trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 10% of placebo- treated patients. Gait disturbance related events were reported in 12% and 16% of patients in the partial-onset seizures clinical trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 2% of placebo-treatedpatients. These adverse reactions occurred mostly during the titration phase. These adverse reactions were also observed in the primary generalized tonic-clonic seizure clinical trial.

Somnolence and Fatigue
FYCOMPA caused dose-dependent increases in somnolence and fatigue-related events. Somnolencewas reported in 16% and 18% of patients in the partial-onset seizures trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 7% of placebo patients. Fatigue-related events were reported in 12% and 15% of patients in the partial-onset seizures trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 5% of placebo patients. These adverse reactions occurred mostly during the titration phase. These adverse reactions were also observed in the primary generalized tonic-clonic seizure clinical trial . Patients should be advised against engaging in hazardous activities requiring mental alertness, such as operating motor vehicles or dangerous machinery, until the effect of FYCOMPA is known.

Falls
Falls were reported in 5% and 10% of patients in the partial-onset seizures clinical trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 3% of placebo-treated patients.

Withdrawal of AEDs
A gradual withdrawal is generally recommended with antiepileptic drugs to minimize the potential of increased seizure frequency, but if withdrawal is a response to adverse events, prompt withdrawal can be considered.

Most Common Adverse Reactions
The most common adverse reactions (≥5% and ≥1% higher than placebo) include dizziness, somnolence, fatigue, irritability, falls, nausea, weight gain, vertigo, ataxia, headache, vomiting, contusion, abdominal pain, and anxiety.

Drug Interactions
FYCOMPA may decrease the efficacy of contraceptives containing levonorgestrel. Plasma levels of FYCOMPA were decreased when administered with carbamazepine, phenytoin, or oxcarbazepine. Concomitant use with strong CYP3A inducers such as St. John's wort or rifampin should be avoided. Multiple dosing of FYCOMPA 12 mg/day enhanced the effects of alcohol on vigilance and alertness, and increased levels of anger, confusion, and depression. These effects may also be seen when FYCOMPA is used in combination with other CNS depressants.

Pregnancy Category C and Lactation
FYCOMPA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Physicians are advised to recommend that pregnant patients taking FYCOMPA enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. Caution should be exercised when FYCOMPA is administered to a nursing woman.

Hepatic and Renal Impairment
Use in patients with severe hepatic or severe renal impairment is not recommended. Dosage adjustments are recommended in patients with mild or moderate hepatic impairment. Use with caution in patients with moderate renal impairment.

Drug Abuse and Dependence
FYCOMPA is a Schedule III controlled drug substance and has the potential to be abused or lead to drug dependence.