FYCOMPA® (perampanel) is indicated in patients with epilepsy aged 4 years and older for partial-onset seizures (POS) with or without secondarily generalized seizures and adjunctive therapy for patients aged 12 years and older for primary generalized tonic-clonic (PGTC) seizures.

Fycompa™
(perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL CIII

FYCOMPA® POCKET

DOSING GUIDE

Please see additional Important Safety Information throughout and accompanying **Prescribing Information**, including Boxed WARNING.

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® (perampanel)
- 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 seizures clinical trials, hostility- and aggression-related adverse reactions occurred in 12% and 20% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg per 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.

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Start low, go slow

Fycompa™ (perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL C-III

May increase dose based on clinical response and tolerability by increments of 2 mg once daily no more frequently than at weekly intervals.[1]

HOW FYCOMPA® IS SUPPLIED

TABLETS

2mg 4mg 6mg

8mg 10mg 12mg

Tablets are not actual size.

&

ORAL SUSPENSION

0.5 mg/mL oral suspension
(2 mg=4 mL)

Please see additional Important Safety Information throughout and accompanying Prescribing Information, including Boxed WARNING.

IMPORTANT SAFETY INFORMATION (CONT'D)

SERIOUS PSYCHIATRIC AND BEHAVIORAL REACTIONS (CONT'D)

These effects in FYCOMPA® (perampanel)-treated patients led to dose reduction, interruption, and discontinuation more frequently than placebo-treated patients. Homicidal ideation and/or threat have also been reported postmarketing in patients treated with FYCOMPA. The combination of alcohol and FYCOMPA significantly worsened mood and increased anger. 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 (PGTC) 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 and behavior emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

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Once-daily Dosing at Bedtime

Fycompa™ (perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL

IN PARTIAL-ONSET SEIZURES (WITH OR WITHOUT SECONDARY GENERALIZATION)[1]

FYCOMPA tablets. Not actual sizes.

1. Increase dose gradually by 2 mg increments, using weekly intervals at a minimum. **Longer intervals may be more appropriate for your patient**, depending on individual clinical response and tolerability.[1]
2. **Assess at 4 mg**. Some patients with partial-onset seizures may respond at 4 mg.[1,2,†]

When dosing FYCOMPA Oral Suspension, simply **double the tablet dose in mg to get the dose in mL** (example: 6 mg = 12 mL).[1]

If your patient is taking moderate or strong CYP3A4 inducers: Starting dose is 4 mg.[1,†]

12 mg is the highest dose studied.[1,†]

For pediatric patients (aged 4 years and older), **dosing is not based on weight**.[3]

*In POS patients, a dose of 12 mg once daily resulted in somewhat greater reductions in seizure rates than the dose of 8 mg once daily, but with a substantial increase in adverse reactions.[1]

†Closely monitor patients when starting or withdrawing moderate or strong CYP3A4 inducers (including enzyme-inducing AEDs such as carbamazepine, phenytoin, and oxcarbazepine). Dose adjustment may be necessary.[1]

‡For patients taking enzyme-inducing agents, a maintenance dose has not been established. Individual dose should be titrated to clinical response and tolerability.[1]

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PARTIAL-ONSET SEIZURES (WITH OR WITHOUT SECONDARY GENERALIZATION)[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

DIZZINESS AND GAIT DISTURBANCE

FYCOMPA® (perampanel) 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 seizure trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per 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 seizure clinical trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 2% of placebo-treated patients. These adverse reactions occurred mostly during the titration phase. These adverse reactions were also observed in the PGTC seizure clinical trial.

SOMNOLENCE AND FATIGUE

FYCOMPA caused dose-dependent increases in somnolence and fatigue-related events. Somnolence was reported in 16% and 18% of patients in the partial-onset seizure trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 7% of placebo-treated patients. Fatigue-related events were reported in 12% and 15% of patients in the partial-onset seizure trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 5% of placebo-treated patients. These adverse reactions occurred mostly during the titration phase. These adverse reactions were also observed in the PGTC 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. Patients should be carefully observed for signs of central nervous system (CNS) depression when FYCOMPA is used with other drugs with sedative properties because of potential additive effects.

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Once-daily Dosing at Bedtime

Fycompa™ (perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL

PRIMARY GENERALIZED TONIC-CLONIC SEIZURES[1]

FYCOMPA tablets. Not actual sizes.

1. Increase dose gradually by 2 mg increments, using weekly intervals at a minimum. **Longer intervals may be more appropriate for your patient**, depending on individual clinical response and tolerability.[1]

When dosing FYCOMPA Oral Suspension, simply **double the tablet dose in mg to get the dose in mL** (example: 6 mg = 12 mL).[1]

If your patient is taking moderate or strong CYP3A4 inducers:
Starting dose is **4 mg.**[1,†]

12 mg is the highest dose studied.[1,†]

For pediatric patients (aged 4 years and older), **dosing is not based on weight**.[3]

*In primary generalized tonic-clonic seizure patients, 8 mg is the recommended maintenance dose. Patients who are tolerating FYCOMPA at 8 mg once daily and require further reduction of seizures may benefit from a dose increase up to 12 mg once daily if tolerated.[1]
†Closely monitor patients when starting or withdrawing moderate or strong CYP3A4 inducers (including enzyme-inducing AEDs such as carbamazepine, phenytoin, and oxcarbazepine). Dose adjustment may be necessary.[1]
‡For patients taking enzyme-inducing agents, a maintenance dose has not been established. Individual dose should be titrated to clinical response and tolerability.[1]

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PRIMARY GENERALIZED TONIC-CLONIC SEIZURES[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

FALLS

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

DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)

DRESS, also known as **multiorgan hypersensitivity**, has been reported in patients taking AEDs, including FYCOMPA. DRESS may be fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling, in association with other organ system involvement. If signs or symptoms are present, immediately evaluate the patient and discontinue FYCOMPA if an alternative etiology for signs or symptoms cannot be established.

WITHDRAWAL OF AEDs

A gradual withdrawal is generally recommended with AEDs 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 in patients aged 12 years and older receiving FYCOMPA (≥5% and ≥1% higher than placebo) include dizziness, somnolence, fatigue, irritability, falls, nausea, weight gain, vertigo, ataxia, headache, vomiting, contusion, abdominal pain, and anxiety. Adverse reactions in patients aged 4 to <12 years were generally similar to patients aged 12 years and older.

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Dosing in specific populations

Fycompa™ (perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL

PATIENTS WITH HEPATIC IMPAIRMENT

Starting Dose: In patients with mild and moderate hepatic impairment, the starting dose is 2 mg or 4 mL once daily.

Titration: Increase dosage by increments of 2 mg or 4 mL no more frequently than every 2 weeks.

The maximum recommended daily dose is 6 mg or 12 mL for patients with mild hepatic impairment and 4 mg or 8 mL for patients with moderate hepatic impairment.

Special considerations: Use in patients with severe hepatic impairment is not recommended.

PATIENTS WITH RENAL IMPAIRMENT

Titration: Dose adjustment is not required in patients with mild renal impairment. A slower titration may be considered based on clinical response and tolerability.

Special considerations: Use with caution in patients with moderate renal impairment with close monitoring.

Use in patients with severe renal impairment or patients undergoing hemodialysis is not recommended.

ELDERLY PATIENTS

Titration: Dosage increases no more frequently than every 2 weeks.

Special considerations: Because of increased likelihood for adverse reactions in elderly patients, dosing titration should proceed slowly in patients aged 65 years and older.

PEDIATRIC POS PATIENTS (AGED ≥4 Y)

Titration: Pediatric patients ≥4 years of age can be dosed similarly to adults.

Special considerations: No dosage adjustment is required. Has not been studied in patients aged <4 years.

PEDIATRIC PGTC SEIZURE PATIENTS (AGED ≥12 Y)

Titration: Pediatric patients ≥12 years of age can be dosed similarly to adults.

Special considerations: No dosage adjustment is required. Has not been studied in patients aged <12 years.

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IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS

FYCOMPA® (perampanel) may decrease the efficacy of contraceptives containing levonorgestrel. Plasma levels of perampanel were decreased when administered with known moderate and strong CYP3A4 inducers, including, carbamazepine, phenytoin, or oxcarbazepine. Multiple dosing of FYCOMPA 12 mg per 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 AND LACTATION

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 pregnant or nursing women as there are no adequate data on the developmental risk associated with use in pregnant women, and no data on the presence of perampanel in human milk, the effects on the breastfed child, or the effects of the drug on milk production.

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 substance and has the potential to be abused and lead to drug dependence and withdrawal symptoms including anxiety, nervousness, irritability, fatigue, asthenia, mood swings, and insomnia.

REFERENCES: 1. FYCOMPA US Prescribing Information. Coral Gables, FL: Catalyst Pharmaceuticals, Inc. **2.** Krauss GL, Serratosa JM, Villanueva V, Endziniene M, Hong Z, French J, Yang H, Squillacote D, Edwards HB, Zhu J, Laurenza A. Randomized phase III study 306: adjunctive perampanel for refractory partial-onset seizures. *Neurology*. 2012 May 1;78(18):1408-15. **3.** Data on file. Catalyst Pharmaceuticals, Inc., Coral Gables, FL.

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Drug interactions

Fycompa™ (perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL

WITH MODERATE OR STRONG CYP3A4 INDUCERS

- Concomitant use of known moderate or strong CYP3A4 inducers, including carbamazepine, phenytoin, and oxcarbazepine, with FYCOMPA decreased plasma levels of perampanel by approximately 50% to 67%.
- The starting doses for FYCOMPA should be increased in the presence of moderate or strong CYP3A4 inducers.
- When these moderate or strong CYP3A4 inducers are introduced or withdrawn from a patient's treatment regimen, the patient should be closely monitored for clinical response and tolerability.

WITH CONTRACEPTIVES

- FYCOMPA at a dose of 12 mg or 24 mL per day may reduce levonorgestrel exposure by 40%.
- Use of FYCOMPA with contraceptives containing levonorgestrel may render them less effective.
- Additional nonhormonal forms of contraception are recommended.

WITH ALCOHOL AND OTHER CNS DEPRESSANTS

- May increase CNS depression; effects of FYCOMPA on complex tasks such as driving ability are additive or supra-additive to the impairment effects of alcohol.
- Multiple dosing of FYCOMPA 12 mg per day also enhanced the effects of alcohol to interfere with 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.
- Patients should limit activity until they have experience with concomitant use of CNS depressants.
- Advise patients not to drive or operate machinery until they have gained sufficient experience on FYCOMPA to gauge whether it adversely affects these activities.

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Catalyst pharmaceuticals