Oscar Clinical Guideline: Fycompa (perampanel) (PG176, Ver. 3)

Fycompa (perampanel)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Partial-onset seizures, also known as partial seizures, focal seizures or focal-onset seizures, start in a specific area or "focus" in the brain. There are several subtypes of focal seizures including: focal aware seizures, focal impaired awareness seizures, focal motor seizures, focal nonmotor seizures and focal bilateral tonic-clonic seizures. The specific symptoms of a partial-onset seizure can vary widely depending on the area of the brain where the seizure originates. Focal epilepsy may be due to a focal brain pathology (due to a known syndrome or genetic cause), or be due to an unknown cause. Focal seizures can be managed with both narrow spectrum (e.g., carbamazepine, gabapentin, oxcarbazepine, phenytoin, phenobarbital, primidone, tiagabine) and broad spectrum anti-seizure medications (e.g., brivaracetam, clobazam, felbamate, lacosamide, lamotrigine, levetiracetam, valproate, zonisamide) including Fycompa (perampanel).

Primary Generalized Tonic-Clonic Seizures (PGTCS), previously known as grand mal seizures , involve the entire brain from the onset of the seizure. These seizures typically have two phases. The tonic phase involves a sudden loss of consciousness and muscle stiffening, while the subsequent clonic phase involves rapid muscle contractions or convulsions.

Lennox-Gastaut syndrome (LGS) is a lifelong epileptic encephalopathy, causing chronic seizures and intellectual disability which presents in childhood. First-line management of LGS is typically valproate, however many require additional anti-seizure medications including lamotrigine, rufinamide, topiramate, clobazam, felbamate, fenfluramine, and Fymcompa (perampanel).

Fycompa (perampanel) is a non-competitive AMPA glutamate receptor antagonist indicated for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older and as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in those 12 years of age and older. While Fycompa has received orphan drug designation for the treatment of seizures associated with Lennox-Gastaut Syndrome (LGS), it is not FDA-approved for this indication. Use for LGS is considered off-label and requires careful assessment of risks and benefits.

Members receiving Fycompa (perampanel) should be closely monitored for psychiatric and behavioral side effects, particularly during the titration phase and at higher doses. These effects may include irritability, anger, aggression, hostility, homicidal ideation, and suicidal thoughts or behaviors. Monitoring is especially critical during the first 6 weeks of therapy and after dose increases. If severe psychiatric symptoms occur, the dose should be reduced or the medication discontinued, and the member should be referred for psychiatric evaluation.

Definitions

"Antiepileptic Drugs" Medications used to prevent or reduce the severity and frequency of seizures in various types of epilepsy.

"Partial seizures" are an older term that has been used to describe seizures that start in a specific part of the brain. The term "partial" reflects the fact that these seizures are localized to a specific area at the onset.

"Focal seizures" is a term that has been more recently adopted by the International League Against Epilepsy, replacing "partial seizures." This term is more descriptive of the fact that the seizure originates from a specific 'focus' in the brain.

"Lennox-Gastaut Syndrome (LGS)" is a rare and severe form of childhood-onset epilepsy characterized by multiple types of seizures and cognitive dysfunction. It typically begins between the ages of 2 and 6 and can be caused by various brain abnormalities or injuries, though in many cases its cause remains unknown.

"Orphan Drug" refers to a medicinal product designed for the prevention, diagnosis, or treatment of rare diseases or disorders. These are conditions that affect a small percentage of the population. In the United States, the Food and Drug Administration (FDA) defines an orphan drug as one "intended for the

treatment, prevention, or diagnosis of a rare disease or condition, which is one that affects less than 200,000 persons in the US" or meets cost recovery provisions of the act.

"Partial-onset Seizures (Focal Seizures)" are seizures that begin in a specific region or 'focus' of the brain. They can be further categorized into:

- Focal Onset Aware Seizures: Seizures where the individual remains conscious and aware throughout the event.
- Focal Onset Impaired Awareness Seizures: Seizures that impact an individual's consciousness or awareness during the event.

Medical Necessity Criteria for Initial Authorization

The Plan considers Fycompa (perampanel) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with a neurologist or epilepsy specialist; *AND*
2. IF the request is for Fycompa 0.5mg/mL Suspension, documentation indicating the member's inability or unwillingness to take the tablet form; *AND*
3. Fycompa (perampanel) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature*; AND*
4.
5. The member has a diagnosis of epilepsy AND meets the medical necessity criteria for the applicable indication listed below:

Partial-onset Seizures (Focal Seizures)

4. The member is 4 years of age or older; *AND*
5. The member has a diagnosis of focal seizures (i.e., partial-onset seizures, partial seizures); *AND*
6. The member has documented evidence of inadequate seizure control with at least TWO (2) alternate antiepileptic drugs at maximally tolerated doses. These may include, but are not limited to, the following:
    a. Carbamazepine; *and/or*
    b. Divalproex (use in those 9 years of age and younger is off-label); *and/or*
    c. Fosphenytoin; *and/or*
    d. Lacosamide; *and/or*
    e. Lamotrigine; *and/or*
    f. Levetiracetam; *and/or*
    g. Methsuximide; *and/or*
    h. Oxcarbazepine; *and/or*
    i. Phenobarbital; *and/or*
    j. Phenytoin; *and/or*
    k. Pregabalin; *and/or*
    l. Primidone; *and/or*

m. Tiagabine (use in those 11 years of age and younger is off-label)*; and/or*
n. Topiramate; *and/or*
o. Valproate (use in those 9 years of age and younger is off-label); *and/or*
p. Valproic acid (use in those 9 years of age and younger is off-label); *and/or*
q. Zonisamide (use in those 15 years of age and younger is off-label).

Primary Generalized Tonic-Clonic Seizures

4. The member is 12 years of age or older; *AND*
5. The member has a diagnosis of primary generalized tonic-clonic seizures; *AND*
6. The member has documented evidence of inadequate seizure control with at least TWO (2) alternate antiepileptic drugs at maximally tolerated doses. These may include, but are not limited to, the following:
    a. Carbamazepine; *and/or*
    b. Divalproex (use in those 9 years of age and younger is off-label); *and/or*
    c. Fosphenytoin; *and/or*
    d. Lamotrigine; *and/or*
    e. Levetiracetam; *and/or*
    f. Phenobarbital; *and/or*
    g. Phenytoin; *and/or*
    h. Topiramate; *and/or*
    i. Valproic acid (use in those 9 years of age and younger is off-label).

Seizures Associated with Lennox-Gastaut Syndrome

4. The member has a diagnosis of Lennox-Gastaut Syndrome; *AND*
5. The member has documented evidence of inadequate seizure control with at least TWO (2) alternate antiepileptic drugs at maximally tolerated doses. These may include, but are not limited to, the following:
    a. Cannabidiol; *and/or*
    b. Clobazam; *and/or*
    c. Clonazepam; *and/or*
    d. Felbamate; *and/or*
    e. Fenfluramine; *and/or*
    f. Lamotrigine; *and/or*
    g. Rufinamide; *and/or*
    h. Topiramate.

If the above prior authorization criteria are met, the requested product will be authorized for up to a lifetime.

Experimental or Investigational / Not Medically Necessary

Fycompa (perampanel) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Alcohol use disorder (AUD). There is not enough evidence to support the use for AUD. One study (NCT04502589) did not study Fycompa (perampanel) versus a control (e.g., placebo or standard of care) and was very small (n=4). Another small (n=22) study (NCT02120365) assessed Fycompa (perampanel) versus placebo, however, the primary and secondary outcomes for the measure of the effects of alcohol (both stimulant and sedative effects) on the participants was not significant. Thus there is a lack of safety and efficacy for AUD at this time.
- Amyotrophic Lateral Sclerosis (ALS). A systematic review of Fycompa (perampanel) found limited efficacy against placebo for ALS functioning rating scale scores, and high rates of adverse effects (including aggression, somnolence, anger and dysarthria). At this time there is not sufficient evidence to support the safety and efficacy of Fycompa (perampanel) for the management of ALS.Bipolar Disorder (BD). There is no high quality data to support the efficacy and safety of Fycompa (perampanel) for this indication.
- Diabetic Neuropathies. In an randomized controlled unpublished study (NCT00592904) of 262 participants treated with placebo or Fycompa (perampanel), there was not a reported significant difference in mean change from baseline of reported pain using the short form-McGill Pain Questionnaire and the visual analog scale by week 48. An additional randomized controlled unpublished study (NCT00505284) of 352 participants, there was not a reported significant change in average pain from baseline by week 15; it appeared that there was a lower rate of responders amongst Fycompa (perampanel) treated participants compared to placebo (36.6%, 32.4%, 39.4%, 31.9%, and 56.3% for Fycompa [perampanel] 2 mg, 4 mg, 6mg, 8 mg, and placebo, respectively). Electroencephalography (where Fycompa [perampanel] is not treating the underlying epilepsy diagnosis).
- Essential Tremor. Only one open-label study has been conducted for managing essential tremors with Fycompa (perampanel). There is no high quality data to support the efficacy and safety of Fycompa (perampanel) for this indication.
- Major Depressive Disorder (MDD). There is no high quality data to support the efficacy and safety of Fycompa (perampanel) for this indication.
- Neuropathic Pain. In a randomized controlled study of 146 participants being managed for post-herpetic neuralgia, there was not a significant difference between Fycompa (perampanel) and placebo over the course of 15 weeks (NCT00592774). There are no other studies for Fycompa (perampanel) in the management of neuropathic pain in humans, thus we lack safety and efficacy to support use for this indication at this time.Other forms of Epilepsies not included in this policy; *or*
- Parkinson's Disease (PD). In three randomized controlled trials, Fycompa (perampanel) failed to show benefit in those with Parkinson’s disease for managing “off” time during the day, when combined with usual care.

- Post Traumatic Stress Disorder (PTSD). There is no high quality data to support the efficacy and safety of Fycompa (perampanel) for this indication.
- Prophylaxis of migraine headaches. One randomized controlled trial (n=206, NCT00154063) did not find a significant difference in change from baseline of the frequency of migraines over a 28 day period between Fycompa (perampanel) and placebo after 19 weeks. A smaller study (n=31) showed some benefit of migraine prophylaxis in those with comorbid epilepsy; however this was hypothesis generating, and further studies looking at comorbid migraine and epilepsy may be warranted to consider Fycompa (perampanel) safe and effective for migraine prophylaxis.

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