dalfampridine ER (Ampyra®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO103

Description

Dalfampridine ER (Ampyra) is an orally administered broad-spectrum potassium channel blocker with an unknown mechanism of action for its therapeutic effect.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
dalfampridine ER (Ampyra)	Improve walking in patients with multiple sclerosis	10 mg tablets	60 tablets/30 days

Initial Evaluation

I. **Dalfampridine ER (Ampyra)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Must be prescribed by, or in consultation with, a neurologist; **AND**
   C. A diagnosis of **multiple sclerosis** when the following are met:
      1. Member does not have a history of seizures; **AND**
      2. Member has a creatinine clearance (CrCl) >50 mL/min; **AND**
      3. Member has difficulty walking or leg weakness; **AND**
         i. Member must be able to ambulate (i.e., not wheelchair bound); **AND**
      4. Member is taking concurrent disease modifying therapy for multiple sclerosis (i.e., glatiramer acetate, dimethyl fumarate, interferon beta-1a, etc.) unless contraindicated.; **AND**
      5. If request is for brand Ampyra, documentation of treatment with generic dalfampridine ER has been ineffective, contraindicated, or not tolerated

II. Dalfampridine ER (Ampyra) is considered investigational when used for all other conditions, including but not limited to:
   A. Acute spinal cord injury
   B. Disorder of neuromuscular transmission
   C. Alzheimer's disease, dementia

D. Botulism
E. Reversal of neuromuscular blockade
F. Toxicity of calcium channel blockers
G. Non-ambulating members with multiple sclerosis

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member is taking concurrent disease modifying therapy for multiple sclerosis (i.e., glatiramer acetate, dimethyl fumarate, interferon beta-1a, etc.) unless contraindicated.; **AND**
IV. Member has demonstrated disease stability or improvement (e.g improvement in walking distance or speed); **AND**
V. If request is for brand Ampyra, documentation of treatment with generic dalfampridine ER has been ineffective, contraindicated, or not tolerated

Supporting Evidence

I. Multiple sclerosis (MS) is a common immune-mediated inflammatory disease of the central nervous system, and is characterized by multifocal areas of demyelination with loss of oligodendrocytes and astroglial scarring. However, because symptoms are non-specific and there are no clinical findings that are unique to MS, evaluation and care of patients with MS should be conducted by a specialist.
II. Dalfampridine ER (Ampyra) was studied in two randomized controlled trials that evaluated improvement in the timed 25-foot walk using percentage of timed walk responders as the primary outcome. Patients included in the clinical trials were required to be able to ambulate. Dalfampridine ER (Ampyra) had a significantly greater number of responders compared to placebo in both trials. Trial one had 42.9% vs 9.3% responders ($p<0.0001$) for dalfampridine ER (Ampyra) and placebo respectively. Trial two had 35% vs 8% responders ($p<0.0001$) for dalfampridine ER (Ampyra) and placebo respectively.
III. Dalfampridine ER (Ampyra) has only been studied in patients aged 18 years and older; therefore, safety and efficacy of dalfampridine ER (Ampyra) in the pediatric population remains undefined.
IV. Use of dalfampridine ER (Ampyra) is contraindicated in patients with a prior history of seizure and in those with a CrCl less than 50 mL/min. Seizures have been reported in patients with no

history of seizure, and minor renal impairment (CrCl 51 to 80 mL/min) may increase risk of seizures. Permanent discontinuation is advised if seizures occur.

V. Dalfampridine ER (Ampyra) is typically seen as a complementary therapy to disease modifying therapy (DMT), which remains the standard of care for MS patients to prevent progression of disease. This position is supported by the Guidelines and Best Practices for Appropriate Use of Dalfampridine in Managed Care Populations published in the American Journal of Managed Care. However, multiple clinical trials and meta analyses have identified that the efficacy of dalfampridine is not dependent on DMT or any other medication. The FDA label notes that in the pivotal trials, the majority of patients (63%) were using DMT (interferons, glatiramer acetate, or natalizumab), but the magnitude of improvement in walking speed was independent of concomitant treatment with these agents. Notably, dalfampridine has the highest utility when initiated in the early stages of MS, and thus initiation soon after diagnosis is imperative to preserve motor function and ambulation. Although there may be instances where monotherapy with dalfampridine ER (Ampyra) may be appropriate based on patient specific characteristics, the use of dalfampridine ER (Ampyra) as complementary therapy to DMT remains appropriate to ensure all facets of MS are addressed.

Investigational or Not Medically Necessary Uses

I. Dalfampridine ER (Ampyra) has not been adequately studied for the following conditions and does not have established safety and efficacy in these populations:
   A. Acute spinal cord injury
   B. Disorder of neuromuscular transmission
   C. Alzheimer's disease, dementia
   D. Botulism
   E. Reversal of neuromuscular blockade
   F. Toxicity of calcium channel blockers

II. Dalfampridine ER (Ampyra) was only studied in patients able to ambulate and is not indicated for non-ambulating members with multiple sclerosis

References

1. Dalfampridine ER [Prescribing Information]. Basking Ridge, NJ: Micro Labs USA, Inc. March 2019.
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3. Goodman AD, Brown TR, Krupp LB, et al. Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial. Lancet. 2009;373(9665):732-8.
4. Goodman AD, Brown TR, Edwards KR, et al. A phase 3 trial of extended release oral dalfampridine in multiple sclerosis. Ann Neurol. 2010;68(4):494-502.

5. Goodman AD, Betoux F, Brown TR, et al. Long-term safety and efficacy of dalfampridine for walking impairment in patients with multiple sclerosis: Results of open-label extensions of two Phase 3 clinical trials. 2015, Vol. 21(10): 1322-1331.
6. Zhang E, Tian X, Li R, et al. Dalfampridine in the treatment of multiple sclerosis: a meta-analysis of randomized controlled trials. *Orphanet J Rare Dis*. (2021) 16:87.
7. Miravelle AA. Guidelines and Best Practices for Appropriate Use of Dalfampridine in Managed Care Populations. *Am J Manag Care*. 2011;17:S154-S160.
8. Baird JF, Sandroff BM, Motl RW. Therapies for mobility disability in persons with multiple sclerosis. *Expert Rev Neurother.* 2018 June; 18(6): 493-502.

Policy Implementation/Update:

Action and Summary of Changes	Date
Annual review completed. Adjusted length of initial duration to six months. Added requirement that member has difficulty walking to initial criteria and member is using in combination with DMT to renewal criteria. Updated supporting evidence.	03/2023
Added requirement to trial generic dalfampridine ER prior to branded Ampyra on continuation	05/2022
Transitioned criteria to policy	10/2019
Previous reviews	10/2011; 05/2013; 01/2016; 11/2018;