



BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Dalfampridine (Ampyra®)

Policy # 00275

Original Effective Date: 10/20/2010

Current Effective Date: 11/20/2013

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member's contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider the use of dalfampridine (Ampyra®)[†] as a treatment to improve walking in patients with multiple sclerosis to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for the use of dalfampridine (Ampyra) as a treatment to improve walking in patients with multiple sclerosis will be considered when all of the following criteria are met:

- Patient is at least 18 years of age; and
- Patient has a documented diagnosis of multiple sclerosis; and
- Patient is able to walk 25 feet without resting; and
(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient does not have a history of seizures; and
- Patient has normal renal function (creatinine clearance [CrCl] greater than 50ml/min); and
 - o Patient is being started on initial therapy with Ampyra; or
 - o Patient has been receiving Ampyra and has demonstrated an improvement in walking (for extension requests).
(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of dalfampridine (Ampyra) when patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary****).

Based on review of available data, the Company considers the use of dalfampridine (Ampyra) for any other indication not listed in the above criteria or for any off-label use to be **investigational.***

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of dalfampridine (Ampyra) when any of the following criteria are NOT met to be **not medically necessary****:

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- Patient is able to walk 25 feet without resting
- Patient has been receiving Ampyra and has demonstrated an improvement in walking (for extension requests).

Note: The use of dalfampridine (Ampyra) is not recommended for patients unable to walk 25 feet without resting or for patients with severe impairment of ambulation that are essentially restricted to a wheelchair. These patients have an Expanded Disability Status Score (EDSS) of 7 or higher. See Appendix for EDSS.

Background/Overview

Dalfampridine (Ampyra) is a potassium channel blocker indicated to improve walking in patients with multiple sclerosis (MS). This was demonstrated by an increase in walking speed.

Multiple sclerosis is a chronic inflammatory disease that affects the central nervous system, resulting in damage to nerves in the brain and spinal cord. Collective damage ultimately leads to progressive physical and cognitive disabilities.

Multiple sclerosis affects approximately 400,000 people in the United States and 2.5 million people worldwide. The progress, severity, and specific symptoms of MS are unpredictable and vary from 1 person to another, although up to 50% cite difficulties with walking. Symptoms can be mild, such as numbness in the limbs, or severe, such as paralysis or loss of vision. About half of all people with MS experience cognitive impairments such as difficulties in concentration, attention, memory, and judgment, although these symptoms are usually mild and are frequently overlooked.

The approved dose of dalfampridine (Ampyra) is 10mg twice daily. The prescribed dose of dalfampridine (Ampyra) should not exceed 10mg twice daily. At doses of dalfampridine (Ampyra) higher than 10mg twice daily, patients with MS are at an increased risk of seizures.

Seizures are associated with higher doses in patients with MS and spinal cord injuries, and history of a seizure disorder is a contraindication to taking this medication. Moderate or severe renal impairment (CrCl \leq 50mL/min) is also a contraindication to treatment with dalfampridine (Ampyra). If a patient has mild renal impairment (CrCl 51–80mL/min), the estimated CrCl should be known before initiating treatment with dalfampridine (Ampyra). In this population, plasma levels may approach those seen at doses greater than 10mg twice daily, increasing the risk of seizures. Common adverse events reported during the randomized, controlled trials described above included impaired balance among 5% of dalfampridine (Ampyra)-treated patients compared to 1% of patients taking placebo. Impaired balance is of particular concern for multiple sclerosis patients who already may be at increased risk of falls.

Patients taking dalfampridine (Ampyra) should be re-evaluated periodically to assess the clinical benefit and potential adverse effects of treatment. Three months after initiating dalfampridine (Ampyra), the Timed 25-Foot Walk Test may be re-administered. A 20% or greater improvement in walking speed is a desired response. Stability of or improvement in EDSS scores may also be considered a successful response. Thereafter, re-assessments may be undertaken at 3-month to 1-year intervals.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In January, 2010, the FDA approved Ampyra (dalfampridine) extended-release tablets to improve walking ability in patients with MS. In clinical trials, patients treated with dalfampridine had faster walking speeds than those treated with placebo. It is the first drug to be approved for this indication.

Dalfampridine is intended as an adjunct to other MS drugs, does not change the course of the disease, and does not keep MS from getting worse. Multiple sclerosis is a chronic, often disabling, disease that affects the central nervous system—the brain, spinal cord, and optic nerves.

Dalfampridine is contraindicated in patients with moderate to severe kidney disease and in those with a history of seizures. In clinical trials, the most common adverse events included urinary tract infection, insomnia, dizziness, headache, nausea, weakness, back pain, balance disorder, swelling in the nose or throat, constipation, diarrhea, indigestion, throat pain, and burning, tingling or itching of skin.

Ampyra will be manufactured under licenses from Elan of Dublin, Ireland, and distributed by Acorda Therapeutics Inc. of Hawthorne, NY.

Rationale/Source

Two randomized, placebo-controlled clinical trials, 4 administered the Timed 25-Foot Walk test (T25FW) to a total of 540 patients with multiple sclerosis who were able to perform this test in 8 to 60 seconds at baseline (normal ≤ 6.25 seconds). Patients exhibiting a sustained improvement in walking speed in 3 of 4 measurements were identified as “responders.” In the first study, 78 of 224 patients (35%) in the treatment group and 6 of 72 patients (8%) in the placebo group met responder criteria, a statistically significant difference. In the second study, 51 of 119 patients (43%) in the treatment group and 11 of 118 patients (9%) in the placebo group met responder criteria, a statistically significant difference. In both studies, patients in the treatment group were able to complete the T25FW approximately 1 second faster than patients in the placebo group on average. How improvement of this magnitude in walking speed relates to a patient’s ability to complete both activities of daily living (ADLs) and instrumental activities of daily living (IADLs) or how it might improve quality of life is not known. No correlation was found between any baseline characteristic, including baseline performance on the T25FW, and response to dalfampridine (Ampyra).

These studies also assessed the effect of dalfampridine (Ampyra) on lower extremity muscle strength. One study demonstrated a statistically significant improvement in strength while the other did not. The FDA indication for dalfampridine (Ampyra) does not include improved leg strength.

Summary

There is evidence of a small increase in walking speed (i.e., 1 second on the Timed 25-Foot Walk test) with dalfampridine (Ampyra), but the clinical significance of this change is unknown. No evidence for an impact on ADLs or IADLs was provided. In deciding whether to treat any given patient with dalfampridine (Ampyra), potential benefit must be weighed against possible harms associated with treatment.



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References

1. Dalfampridine (Ampyra™) extended-release tablets [package insert]. Hawthorne, NY: Acorda Therapeutics, Inc.; July 2012.
2. Blue Cross and Blue Shield Association. Dalfampridine (Ampyra®). TEC Specialty Pharmacy Combined Capacity (SPCC) Report #7, May 2010.

Policy History

Original Effective Date: 10/20/2010

Current Effective Date: 11/20/2013

10/14/2010 Medical Policy Committee review

10/20/2010 Medical Policy Implementation Committee approval. New policy.

11/03/2011 Medical Policy Committee review

11/16/2011 Medical Policy Implementation Committee approval. Changed the requirement of a 10% improvement from baseline walking speed in the criteria for normal renal function to a demonstrated improvement in walking.

11/01/2012 Medical Policy Committee review

11/28/2012 Medical Policy Implementation Committee approval. No change to coverage.

02/19/2013 Coding revised

11/07/2013 Medical Policy Committee review

11/20/2013 Medical Policy Implementation Committee approval. Added not medically necessary section to policy.

Next Scheduled Review Date: 11/2014

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. in accordance with nationally accepted standards of medical practice;
- B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

Appendix

Expanded Disability Status Scale (EDSS)

- 0.0 Normal neurological examination
- 1.0 No disability, minimal signs in one FS (functional systems)
- 1.5 No disability, minimal signs in more than one FS
- 2.0 Minimal disability in one FS
- 2.5 Mild disability in one FS or minimal disability in two FS
- 3.0 Moderate disability in one FS, or mild disability in three or four FS. Fully ambulatory
- 3.5 Fully ambulatory but with moderate disability in one FS and more than minimal disability in several others
- 4.0 Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability; able to walk without aid or rest some 500 meters
- 4.5 Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability; able to walk without aid or rest some 300 meters.
- 5.0 Ambulatory without aid or rest for about 200 meters; disability severe enough to impair full daily activities (work a full day without special provisions)
- 5.5 Ambulatory without aid or rest for about 100 meters; disability severe enough to preclude full daily activities
- 6.0 Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting
- 6.5 Constant bilateral assistance (canes, crutches, braces) required to walk about 20 meters without resting
- 7.0 Unable to walk beyond approximately five meters even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day
- 7.5 Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; May require motorized wheelchair
- 8.0 Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms
- 8.5 Essentially restricted to bed much of day; has some effective use of arms retains some self care functions
- 9.0 Confined to bed; can still communicate and eat.
- 9.5 Totally helpless bed patient; unable to communicate effectively or eat/swallow
- 10.0 Death due to MS

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