



**BlueCross BlueShield
of Alabama**

**Ampyra™ (dalfampridine)
Prior Authorization
with Quantity Limit Criteria
Program Summary**

This prior authorization applies to Commercial, NetResults A series, NetResults F series, and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Ampyra (dalfampridine) Prior Authorization (PA) program is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies and according to dosing recommended in product labeling. The PA program will consider Ampyra appropriate for patients with multiple sclerosis who are treated by or whose prescribers have consulted with a specialist in the area of the patients' diagnoses, who have documented significant limitations attributable to slow ambulation, who are receiving a disease modifying agent if indicated, who are ambulatory, and who do not have any FDA labeled contraindications to therapy. The criteria will also allow for a patient who has any FDA approved diagnosis that is not already addressed in the criteria set and who has no contraindications to therapy. The dosing requested for initial therapy for all approvable indications must be at or below the program limit unless it is below the FDA labeled limit and cannot be dose optimized. Renewal criteria include documentation of stabilization or improvement of the baseline walking speed or baseline EDSS score. The renewal dose of Ampyra will have the same restrictions as initial criteria.

TARGET DRUGS AND PROGRAM QUANTITY LIMIT

Brand (generic)	GPI	Multisource Code	Quantity Per Day Limit
Ampyra (dalfampridine)			
10 mg tablet	62406030007420	M, N, O, or Y	2 tablets

Agent	Contraindication(s)
Ampyra (dalfampridine)	<ul style="list-style-type: none"> History of seizures Moderate to severe renal impairment (CrCl < 50 mL/min [not an eGFR with this value]) Hypersensitivity to dalfampridine or 4-aminopyridine

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL

Ampyra will be approved when ALL of the following are met:

1. ONE of the following:
 - A. ALL of the following:
 - i. The patient has a diagnosis of multiple sclerosis (MS)

AND

 - ii. If the patient has relapsing form of MS, ONE of the following:
 - a. The patient is receiving concurrent therapy with a disease modifying agent [e.g. Aubagio, Avonex (IM), Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Lemtrada (IV), Novantrone, Plegridy, Rebif, Tecfidera, or Tysabri (IV)]

OR

- b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a disease modifying agent

AND

- iii. The prescriber is a specialist in the area of the patient's diagnosis (e.g. neurologist) or has consulted with a specialist in the area of the patient's diagnosis

AND

- iv. There is documentation of significant limitations attributable to slow ambulation

AND

- v. BOTH of the following:

- a. The patient is ambulatory

AND

- b. The prescriber has documented the patient's baseline timed 25 foot walk AND EDSS score

OR

- B. The patient has another FDA approved diagnosis

AND

- 2. The patient does not have any FDA labeled contraindications to therapy with the requested agent

AND

- 3. One of the following:

- A. The requested quantity (dose) is less than or equal to the program quantity limit

OR

- B. All of the following

- i. The requested quantity (dose) is above the set limit

AND

- ii. The requested quantity (dose) requested is at or below the FDA labeled dose

AND

- iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

Length of Approval: 6 months for MS and 12 months for another FDA approved diagnosis

Renewal Criteria

- 1. The patient has been previously approved for therapy through Prime Therapeutics Prior Authorization Review process

AND

- 2. If the patient has the diagnosis of multiple sclerosis, then the patient has demonstrated a stabilization or improvement from baseline in timed walking speed (timed 25 foot walk) or EDSS score

AND

- 3. The patient does not have any FDA labeled contraindications to therapy with the requested agent

AND

- 4. ONE of the following:

- a. The requested quantity (dose) is less than or equal to the program quantity limit

OR

- b. All of the following
 - i. The requested quantity (dose) is above the set limit
AND
 - ii. The requested quantity (dose) requested is at or below the FDA labeled dose
AND
 - iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

Length of Approval: 12 months

FDA APPROVED INDICATIONS AND DOSAGE

FDA Indication¹: To improve walking in patients with multiple sclerosis (MS). This was demonstrated by an increase in walking speed.

Dosing¹: The maximum recommended dose of dalfampridine is one 10 mg tablet twice daily. The maximum dose should not be exceeded. Doses above the maximum were not shown to confer additional benefit in clinical trials but did increase the incidence of adverse events, including seizures. Doses should be separated by 12 hours.

Dalfampridine is eliminated through the kidneys primarily as unchanged drug. Because patients with renal impairment would require a dose lower than 10 mg twice daily and no strength smaller than 10 mg is available, dalfampridine is contraindicated in patients with moderate to severe renal impairment.¹

Dalfampridine is also contraindicated in patients with a history of seizure and contraindicated in patients with a history of hypersensitivity to dalfampridine or 4-aminopyridine.

CLINICAL RATIONALE

Dalfampridine (Ampyra)

Dalfampridine was studied in two phase III, double blind trials. Both trials used a responder analysis as the primary endpoint. A retrospective analysis of a previous trial indicated that treatment responders experienced a 25% improvement in walking speed compared to baseline.² In trial MS-F203, a total of 35% of patients in the dalfampridine group were responders compared to 8% in the placebo group ($p < 0.001$; OR 4.75; 95% CI 2.08-10.86).³ The average improvement in walking speed for responders was a 25.5% increase from baseline compared to 4.7% for the placebo group.³ In trial MS-F204, responder rates were significantly higher in the dalfampridine group (43%) compared to the placebo group (9%) ($p < 0.01$).⁴ The mean improvement from baseline walking speed in responders was 21.45% to 26.80% compared to 7.07% to 8.78% in the placebo group.⁴

An FDA analysis using the entire study group (not just responders) found that neither trial demonstrated statistically significant differences in change in walking speed at visit 6 compared to baseline or average walking speed during the treatment phase of the trial.⁴ The FDA calculated that changes in walking speed would improve the 25 foot walk time for dalfampridine patients compared to placebo by 0.88 seconds and 0.5 seconds in trials MS-F203 and MS-F204, respectively.⁴ FDA analyses found that there was no significant difference between groups in either trial for the SGI score.⁴ SGI is a measurement of patient perceived improvement of disease. The FDA analysis did not compare differences in walking endpoints or SGI for the responder group compared to placebo.

Evidence is lacking on how to identify patients that are likely to respond to dalfampridine without a trial of the drug. Dalfampridine is approved to improve walking speed in patients with MS and has not been shown to be effective in improving strength in other neurologic conditions (spinal cord injury, etc.). Evidence supports criteria similar to that used in Phase 3 clinical trials which includes patients diagnosed with MS who have difficulty walking as defined by a timed 25 foot walk between 8 and 45 seconds.¹⁵

A widely used method to measure the disability status for people with multiple sclerosis (MS) is known as the expanded disability status scale (EDSS). The purpose of this scale is to quantify the level of disability that could be used by health care providers diagnosing MS and monitor changes of disability. The EDSS score ranges from 0 to 10. The first level 1.0 to 4.4 refers to people with high degree of ambulation. Second level from 4.5 to 7.5 refers to

patients with impairment to walk. Third level ≥ 7.5 refers to patients with low to no ambulation and usually restricted to a bed or chair.¹⁶

Acorda Therapeutics established the Ampyra First Step Program, which allows patients to receive a free trial of Ampyra. The program allows patients to receive a 2 month supply if they meet the following criteria: cannot have filled an Ampyra prescription within the last 12 months, do not have any history of seizures and do not have moderate or severe kidney impairment, are not allergic to dalfampridine (the active ingredient in Ampyra), and are not a Medicare/Medicaid recipient. Patients must consult a physician prior to receiving the free trial.

Disease-Modifying Agents

Disease modifying agents (DMAs) for the treatment of multiple sclerosis (MS) reduce the number and severity of relapses, reduce the number of new lesions appearing on magnetic resonance imaging, and probably reduce long-term progression of MS.⁵⁻⁷ Guidelines from the United States and Europe recommend treatment for relapsing-remitting MS be initiated with either glatiramer or interferon beta (INF β). Although the INF β agents differ in route of administration (intramuscular or subcutaneous) and in dosing frequency, studies have not shown clinical differences in efficacy between the different types of INF β . The INF β agents are considered appropriate for patients at high risk of developing clinically definite MS, or those who already have relapsing remitting MS or secondary progressive MS and are experiencing relapses. There is a probable dose or frequency of dosing response curve associated with use of INF β agents. Glatiramer is considered an appropriate option for any patients with relapsing remitting MS. Natalizumab is recommended for patients with relapsing forms of MS who have had an inadequate response to, or are unable to tolerate, other MS therapies.⁵⁻⁷ To date no treatment is approved for treatment of primary progressive multiple sclerosis (PPMS).⁸⁻¹⁴

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