Ampyra™ (dalfampridine)
Prior Authorization with Quantity Limit Criteria

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

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.). According to the Blue Cross and Blue Shield Association Technology Evaluation Center's Specialty Pharmacy Combined Capacity (SPCC) Report on Ampyra, evidence does not support the use of dalfampridine in neurological conditions other than multiple sclerosis, such as spinal cord injury, myasthenia gravis, demyelinating peripheral neuropathies (such as Guillain-Barré syndrome), Alzheimer’s disease, and Lambert Eaton myasthenic syndrome.14

**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 (INFβ). Although the INFβ 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 INFβ. The INFβ 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 INFβ 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).8-13

For additional clinical information see Prime Therapeutics Formulary Monograph: Ampyra and Prime Therapeutics Formulary Chapter 9.6C, Miscellaneous CNS agents: Multiple Sclerosis; and also the BCBSA Specialty Pharmacy Combined Capacity (SPCC) Report #7: Dalfampridine – Extended Release Tablets (Ampyra).

**REFERENCES**


**Document History**

Original Prime Standard criteria approved via email vote by P&T UM Committee 05/2010
Initial Client Specific Review Client Specific Criteria approved by HCSC Corporate Clinical Committee 07/2010
Ampyra™ (dalfampridine) Prior Authorization with Quantity Limit

OBJECTIVE
The intent of the Ampyra (dalfampridine) Prior Authorization (PA) Criteria 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 (two tablets per day). The PA program will consider Ampyra appropriate for adult patients 18 years of age or older with multiple sclerosis treated by a neurologist, or another physician in consultation with a neurologist, who are receiving a disease modifying agent if indicated, who are ambulatory and able to walk 25 feet in 8 to 60 seconds or who have an Expanded Disability Status Score (EDSS) of greater than or equal to 4.5 but less than 7, with documentation of significant limitations of instrumental activities of daily living attributable to slow ambulation. Renewal criteria include documentation of at least a 20% improvement from baseline in timed walking speed or a stabilization or improvement in EDSS. The dose of Ampyra will be limited to the FDA-labeled dosage of 10 mg twice daily. Criteria in this program are consistent with the Blue Cross and Blue Shield Association Technology Evaluation Center, Specialty Pharmacy Combined Capacity (SPCC) Report #7: Dalfampridine – Extended Release Tablets (Ampyra).

Ampyra will not be covered in patients with any of the following exclusion criteria:
1. The patient has a seizure disorder, OR
2. The patient has moderate renal impairment (defined as a creatinine clearance (CrCl) of 30–50 mL/min) or severe renal impairment (defined as a CrCl ≤ 50 mL/min), OR
3. The patient is unable to walk 25 feet in 8–60 seconds with walking aids if needed, OR
4. The patient has minimal or no impairment of ambulation (corresponding to an EDSS of less than 4.5*), OR
5. The patient has severe impairment of ambulation and is essentially restricted to a wheelchair (corresponding to an EDSS of 7* or higher) OR
6. Contraindications to prescribing

*The Expanded Disability Status Score (EDSS) quantifies disability in eight functional systems: pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, and other. EDSS scores 1.0 to 4.5 refer to people with multiple sclerosis who are fully ambulatory. EDSS scores 5.0 to 9.5 are defined by increasing impairment to ambulation.

TARGET DRUGS AND PROGRAM QUANTITY LIMIT

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<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Per Day Limit</th>
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<tr>
<td>10 mg tablet</td>
<td>62406030007420</td>
<td>M, N, O, or Y</td>
<td>2 tablets</td>
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PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

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

1. The patient is an adult 18 years of age or older **AND**
2. The patient has a diagnosis of multiple sclerosis **AND**
3. The patient does not have a diagnosis of spinal cord injury, myasthenia gravis, demyelinating peripheral neuropathies (such as Guillain-Barré syndrome), Alzheimer's disease, and Lambert Eaton myasthenic syndrome. **AND**
4. The patient is receiving concurrent therapy with a disease modifying agent (e.g. Avonex, Betaseron, Copaxone, Extavia, Novantrone, Rebif, or Tysabri) if indicated **AND**
5. The prescriber is a neurologist or has consulted a neurologist **AND**
6. There is documentation of significant limitations of instrumental activities of daily living attributable to slow ambulation **AND**
7. **ONE of the following:**
   a. The patient is ambulatory with a baseline timed 25 foot walk between 8 to 60 seconds with walking aids if needed **OR**
   b. The patient has an EDSS of greater than or equal to 4.5 but less than 7 **AND**
8. The patient does not have a history of seizures **AND**
9. The patient does not have moderate to severe renal impairment (CrCl [creatinine clearance] less than 50 mL/min; not an eGFR with this value) **AND**
10. **ONE of the following:**
    a. The patient is being started on initial therapy with Ampyra **OR**
    b. The patient has been receiving Ampyra therapy for at least 3 months and **ONE of the following:**
       i. The patient has demonstrated at least a 20% improvement from baseline in timed walking speed (timed 25 foot walk) **OR**
       ii. The patient has documented stability of or improvement in EDSS score **AND**
11. The prescribed dosage is 10 mg twice daily

**Length of Approval:**

Initial use: 3 months
Renewal: 12 months
**Ampyra™ (dalfampridine) Prior Authorization with Quantity Limit**

**ELECTRONIC EDIT**

The overall process for a prior authorization will not allow the targeted drugs (table above) to adjudicate through the claims system. When a patient requests a targeted drug the system will reject the claim with the message indicating that prior authorization is necessary.

**PRIOR AUTHORIZATION CRITERIA QUESTION SET**

**Initial and Renewal Evaluation**

1. Is the patient an adult 18 years of age or older?
   - If yes, continue to 2. If no, deny.
   - 2. Does the patient have a diagnosis of multiple sclerosis?
      - If yes, continue to 3. If no, deny.
   - 3. Does the patient have a diagnosis of spinal cord injury, myasthenia gravis, demyelinating peripheral neuropathies (such as Guillain-Barré syndrome), Alzheimer's disease, or Lambert Eaton myasthenic syndrome?
      - If yes, deny. If no, continue to 4.
   - 4. Is concurrent therapy with a disease modifying agent (e.g. Avonex, Betaseron, Copaxone, Extavia, Novantrone, Rebif, or Tysabri) indicated in this patient?
      - If yes, continue to 5. If no, continue to 6.
   - 5. Is the patient receiving concurrent therapy with a disease modifying agent (e.g. Avonex, Betaseron, Copaxone, Extavia, Novantrone, Rebif, or Tysabri)?
      - If yes, continue to 6. If no, deny.
   - 6. Is the prescriber a neurologist or has the prescriber consulted with a neurologist on treatment of this patient?
      - If yes, continue to 7. If no, deny.
   - 7. Does the patient have documentation of significant limitations of instrumental activities of daily living (e.g., meal preparation, household chores) attributable to slow ambulation? [intermittent occupational tasks that are not required as a daily part of job functioning are not considered instrumental activities of daily living.]
      - If yes, continue to 8. If no, deny.
   - 8. Is the patient ambulatory with a baseline timed 25 foot walk between 8 to 60 seconds?
      - If yes, continue to 10. If no, continue to 9.
   - 9. Does the patient have an Expanded Disability Status Score (EDSS) of greater than or equal to 4.5 but less than 7?
      - If yes, continue to 10. If no, deny.
   - 10. Does the patient have a history of seizures?
      - If yes, deny. If no, continue to 11.
   - 11. Does the patient have moderate to severe renal impairment (CrCl [creatinine clearance] less than 50 mL/min; note, NOT an eGFR with this value)?
      - If yes, deny. If no, continue to 12.
12. Has the patient already been treated with Ampyra (dalfampridine) for at least 3 months?
   If yes, continue to 13. If no, continue to 15.

13. Does the patient demonstrate a current timed walking speed (timed 25 foot walk) which is at least a 20% improvement from the baseline timed walking speed (timed 25 foot walk)?
   If yes, continue to 15. If no, continue to 14.

14. Does the patient demonstrate a stabilization of or improvement in EDSS scores?
   If yes, continue to 15. If no, deny.

15. Is the prescribed dosage 10 mg twice daily?
   If yes, approve: for 3 months for initial therapy; for 12 months for renewal of therapy.
   If no, deny.