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

This prior authorization applies to Commercial, NetResults A series, SourceRx, 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. Criteria will approve doses that are at or below the maximum FDA labeled dose.

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

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 primary progressive MS or a 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, Ocrevus, Plegridy, Rebif, Tecfidera, Tysabri (IV), or Zinbryta for relapsing MS. Ocrevus for primary progressive MS]
         OR
         b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to all disease modifying agents appropriate for the patient's form of MS
      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

A. One of the following: 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

Agent	Contraindication(s)
Ampyra (dalfampridine)	• History of seizures • Moderate to severe renal impairment (CrCl < 50 mL/min [not an eGFR with this value]) • hypersensitivity to dalfampridine or 4-aminopyridine

FDA APPROVED INDICATIONS AND DOSAGE

FDA Indication[1]: To improve walking in patients with multiple sclerosis (MS). This was demonstrated by an increase in walking speed.

Dosing[1]: 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 (CrCl ≤50 mL/min).

Dalfampridine is also contraindicated in patients with a history of seizure and 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.[8]

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 $\geq$ 7.5 refers to patients with low to no ambulation and usually restricted to a bed or chair.[9]

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. The goal of disease-modifying treatment is to reduce the early and sub-clinical disease activity thought to contribute to long-term disability. Guidelines from the United States and Europe recommend DMAs for relapsing remitting multiple sclerosis as soon as possible following a first clinical event. Ocrelizumab has also been FDA approved for use in primary progressive multiple sclerosis (PPMS) beyond being approved for relapsing forms of multiple sclerosis (RMS). Once disease-modifying treatment is initiated, evidence suggests that treatment needs to be ongoing for benefits to persist. Non-adherence and gaps in treatment are associated with an increased rate of relapses and progression of disability.[5-7]

REFERENCES

1. Ampyra prescribing information. Acorda. September 2017.
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5. The Use of Disease Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. A Consensus Paper by the Multiple Sclerosis Coalition. March 2017.
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Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.