Ampyra (dalfampridine) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Open, FlexRx Closed, FocusRx, GenRx Open, GenRx Closed, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
03-01-2024	01-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Ampyra® (dalfampridine)* Tablet	To improve walking in adult patients with multiple sclerosis (MS). This was demonstrated by an increase in walking speed	*generic equivalent available	1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Multiple Sclerosis	Multiple sclerosis (MS) is a disorder of the central nervous system (CNS) characterized by demyelization, inflammation, and degenerative changes. Most people with MS experience relapses and remissions of neurological symptoms, particularly early in the disease, and clinical events are usually associated with areas of CNS inflammation. Gradual worsening or progression, with or without subsequent acute attacks of inflammation or radiological activity, may take place early, but usually becomes more prominent over time. While traditionally viewed as a disease solely of CNS white matter, more advanced imaging techniques have demonstrated significant early and ongoing CNS gray matter damage as well.(2) Those diagnosed with MS may have many fluctuating and disabling symptoms (including, but not limited to, fatigue, pain, bladder and bowel issues, sexual dysfunction, movement and coordination problems, visual disturbances, and cognition and emotional changes.(8) There are currently four major types of MS: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).(2) Many patients with MS develop gait impairment, and some eventually require a cane or wheelchair. Gait impairment in MS can result from a multitude of issues such as spasticity, weakness, fatigue, sensory loss, visual loss, and vestibular dysfunction. Leg weakness and spasticity can result from MS lesions in the descending motor tracts of the brain and spinal cord. Ambulatory imbalance can be caused by lesions involving the cerebellar pathways. The International Symposium on Gait and balance in Multiple Sclerosis states that the causes of gait and balance dysfunction in patients with MS are multifactorial and therefore may benefit from a wide range of interventions. Evidence based recommendations from the 2nd International Symposium included balance rehabilitation, self-management, medications, functional electrical stimulation,

	robotics, sensory augmentation, gait training with error feedback, and fall prevention.(7) There is ample evidence to support the benefits of ongoing treatment for the majority of people with multiple sclerosis, there may be some situations in which clinicians and their patients might consider stopping treatment. Although freedom from subsequent relapse is impossible to guarantee, treatment cessation may be considered in patients who:(2) • Are over 60 years of age • Have experienced a progressive disease course for five years or longer • Have no accumulating T2 lesions or gadolinium enhancing lesions on MRI of the brain or spinal cord after a period of observation over several years. Earlier discontinuation, particularly in patients with active disease, may lead to increased disease activity. Clinical and MRI monitoring for recurrent disease activity is clearly warranted in those patients.(2)
Efficacy	The effectiveness of Ampyra (dalfampridine) was studied in two adequate and well controlled trials involving 540 patients. Patients in these two clinical trials had a mean Kurtzke Expanded Disability Status Scale (EDSS) score of 6. Patient inclusion criteria in both trials included the ability to walk 25 feet in 8 to 45 seconds at baseline. Both trials used a responder analysis as the primary endpoint. Responders were defined as patients who achieved faster walking speeds (measured by a timed 25-foot walk in seconds) in at least three of four visits during the study period compared to their fastest speed during the off-treatment period.(1) A retrospective analysis of a previous trial indicated that treatment responders experienced a 25% improvement in walking speed compared to baseline.(3) 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. 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. 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.(5) The Kurtzke Expanded Disability Status Scale (EDSS) quantifies the level of functioning that is used by health care providers diagnosing MS. The EDSS provides a total score on a scale that ranges from 0 to 10. EDSS 1.0 to 4.5 refer to patients with a high degree of ambulatory ability and subsequent levels 5.0 to 9.5 refer to the loss of ambulatory ability. An EDSS score of 7 indicates the patient is unable to walk beyond 5 meters even with aid, essentially restricted to wheelchair.(6)
Safety	Ampyra is contraindicated in:(1) • Patients who have a history of seizures • Patients with moderate to severe renal impairment (CrCl less than 50 mL/min) • Patients with a hypersensitivity to dalfampridine or 4-aminopyridine.

REFERENCES

Number	Reference
1	Ampyra prescribing information. Acorda Therapeutics, Inc. November 2021.
2	Multiple Sclerosis Coalition. The Use of Disease Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. A Consensus Paper by the Multiple Sclerosis Coalition. June 2019.
3	Goodman AD, Brown TR, Cohen JA, et al. Dose comparison trial of sustained release fampridine in multiple sclerosis. *Neurology* 2008;71:1134-1141.
4	FDA. Medical review of fampridine. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022250s000_MedR.pdf.
5	Pikoulas TE and Fuller MA. Dalfampridine: A Medication to Improve Walking in Patients with Multiple Sclerosis. *The Annals of Pharmacotherapy* 2012;46:1010-15.
6	U.S. Department of Veterans Affair. Kurtzke Expanded Disability Status Scale. Available at: https://www.va.gov/MS/Professionals/diagnosis/Kurtzke_Expanded_Disability_Status_Scale.asp. Accessed November 2018.
7	Zackowdki KM, Cameron M, Wagner JM. Perspectives in Rehabilitation. 2nd International Symposium on Gait and Balance in Multiple Sclerosis: interventions for gait and balance in MS. Journal of Disability and Rehabilitation. Volume 36,2014 – Issue 13. Pages 1128-1132.
8	MS international federation. About MS - Symptoms. Accessed at MS Symptoms | Multiple Sclerosis (msif.org)

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Ampyra	dalfampridine tab er	10 MG	M ; N ; O ; Y	O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Ampyra	Dalfampridine Tab ER 12HR 10 MG	10 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Ampyra	dalfampridine tab er	10 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Ampyra	Dalfampridine Tab ER 12HR 10 MG	10 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ;

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   - A. The patient has a diagnosis of multiple sclerosis (MS) AND ALL of the following:
     1. ONE of the following:
        - A. The patient will be using a disease modifying agent for the treatment of MS (e.g., Aubagio, Avonex, Bafiertam, Betaseron, Briumvi, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Lemtrada, Mavenclad, Mayzent, Ocrevus, Plegridy, Ponvory, Rebif, Rituxan, Tascenso ODT, Tecfidera, Tysabri, Vumerity, Zeposia) in combination with the requested agent **OR**
        - B. The patient has an intolerance, hypersensitivity, or FDA labeled contraindication to ALL disease modifying agent drug classes used for the treatment of MS (see MS disease modifying agents drug class table) **OR**
        - C. The patient is currently being treated with the requested agent as indicated by ALL of the following:
          1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
          2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
          3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
        - D. The prescriber has provided documentation that ALL disease modifying agents FDA labeled for the treatment of MS cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND**
     2. Information has been provided that the patient has significant limitations attributable to slow ambulation **AND**
     3. The patient is ambulatory with a baseline (prior to therapy with the requested agent) timed 25-foot walk of 8 to 45 seconds **AND**
     4. Information has been provided that the patient has a current EDSS score less than 7 **OR**
   - B. The patient has another FDA approved indication for the requested agent and route of administration **AND**
2. ONE of the following:
   - A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   - B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**
5. If the requested agent is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following:

Module	Clinical Criteria for Approval

A. The patient has an intolerance or hypersensitivity to the generic equivalent that is not expected to occur with the brand agent **OR**
B. The patient has an FDA labeled contraindication to the generic equivalent that is not expected to occur with the brand agent **OR**
C. The prescriber has provided information to support the use of the requested brand agent over the generic equivalent **OR**

Brand	Generic Equivalent
Ampyra	dalfampridine

D. BOTH of the following:
    1. The prescriber has stated that the patient has tried the generic equivalent **AND**
    2. A generic equivalent was discontinued due to lack of effectiveness or an adverse event **OR**
E. The patient is currently being treated with the requested agent as indicated by ALL of the following:
    1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
    2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
    3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
F. The prescriber has provided documentation that the generic equivalent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

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

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization Review process **AND**
2. ONE of the following:
    A. The patient has a diagnosis of multiple sclerosis (MS) AND ALL of the following:
        1. Information has been provided that the patient has had stabilization or improvement from baseline (before treatment with requested agent) in timed walking speed or EDSS score with the requested agent **AND**
        2. The patient is ambulatory **AND**
        3. Information has been provided that the patient has a current EDSS score of less than 7 **AND**
        4. ONE of the following:
            A. BOTH of the following:
                1. The patient is currently treated with a disease modifying agent for the treatment of MS (e.g., Aubagio, Avonex, Bafiertam, Betaseron, Briumvi, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Lemtrada, Mavenclad, Mayzent, Ocrevus, Plegridy, Ponvory, Rebif, Rituxan,

Module	Clinical Criteria for Approval

Tascenso ODT, Tecfidera, Tysabri, Vumerity, Zeposia) **AND**

2. The patient will continue a disease modifying agent for the treatment of MS in combination with the requested agent **OR**

B. The patient has an intolerance, hypersensitivity, or FDA labeled contraindication to ALL disease modifying agent drug classes used for the treatment of MS (see MS disease modifying agents drug class table) **OR**

C. The patient is currently being treated with the requested agent as indicated by ALL of the following:

1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**

D. The prescriber has provided documentation that ALL disease modifying agents FDA labeled for the treatment of MS cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR**

B. The patient has another FDA approved indication for the requested agent AND has had stabilization or clinical improvement with the requested agent **AND**

3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**
5. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following:

A. The patient has an intolerance or hypersensitivity to the generic equivalent that is not expected to occur with the brand agent **OR**

B. The patient has an FDA labeled contraindication to the generic equivalent that is not expected to occur with the brand agent **OR**

C. The prescriber has provided information to support the use of the requested brand agent over the generic equivalent **OR**

Brand	Generic Equivalent
Ampyra	dalfampridine

D. BOTH of the following:

1. The prescriber has stated that the patient has tried the generic equivalent **AND**
2. A generic equivalent was discontinued due to lack of effectiveness or an adverse event **OR**

E. The patient is currently being treated with the requested agent as indicated by ALL of the following:

1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**

F. The prescriber has provided documentation that the generic equivalent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or

Module	Clinical Criteria for Approval
	maintain reasonable functional ability in performing daily activities or cause physical or mental harm **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **Length of Approval**: Initial: 6 months for MS and 12 months for another FDA approved diagnosis. Renewal: 12 months

CLASS AGENTS

Class	Class Drug Agents
CD20 monoclonal antibody	
CD20 monoclonal antibody	KESIMPTA*Ofatumumab Soln Auto-Injector
CD20 monoclonal antibody	OCREVUS*Ocrelizumab Soln For IV Infusion
CD52 monoclonal antibody	
CD52 monoclonal antibody	LEMTRADA*Alemtuzumab IV Inj
Fumarates	
Fumarates	BAFIERTAM*Monomethyl Fumarate Capsule Delayed Release
Fumarates	TECFIDERA*Dimethyl Fumarate Capsule Delayed Release
Fumarates	VUMERITY*Diroximel Fumarate Capsule Delayed Release
Glatiramer	
Glatiramer	COPAXONE*Glatiramer Acetate Soln Prefilled Syringe
Glatiramer	GLATOPA*Glatiramer Acetate Soln Prefilled Syringe
IgG4k monoclonal antibody	
IgG4k monoclonal antibody	TYSABRI*Natalizumab for IV Inj Conc
Interferons	
Interferons	AVONEX*Interferon Beta-
Interferons	BETASERON*Interferon Beta-
Interferons	EXTAVIA*Interferon Beta-
Interferons	PLEGRIDY*Peginterferon Beta-
Interferons	REBIF*Interferon Beta-
Purine antimetabolite	
Purine antimetabolite	MAVENCLAD*Cladribine Tab Therapy Pack
Pyrimidine synthesis inhibitor	
Pyrimidine synthesis inhibitor	AUBAGIO*Teriflunomide Tab
Sphingosine 1-phosphate (SIP) receptor modulator	
Sphingosine 1-phosphate (SIP) receptor modulator	GILENYA*Fingolimod HCl Cap
Sphingosine 1-phosphate (SIP) receptor modulator	MAYZENT*Siponimod Fumarate Tab
Sphingosine 1-phosphate (SIP) receptor modulator	PONVORY*Ponesimod Tab

Class	Class Drug Agents
Sphingosine 1-phosphate (SIP) receptor modulator	TASCENSO*fingolimod lauryl sulfate tablet disintegrating
Sphingosine 1-phosphate (SIP) receptor modulator	ZEPOSIA*Ozanimod Cap Pack