



Ampyra (dalfampridine)

Policy Number: 5.01.550
Origination: 06/2013

Last Review: 02/2014
Next Review: 02/2015

Policy

BCBSKC will provide coverage for Ampyra dalfampridine) when it is determined to be medically necessary because the following criteria are met.

When Policy Topic is covered:

The use of Ampyra may be considered **medically necessary** when being used to improve the mobility in a patient with multiple sclerosis (MS).

Ampyra is indicated to improve walking in patients with MS. This was demonstrated by an increase in walking speed.¹ Ampyra also led to improvements in the lower extremity manual muscle test (LEMMT) score, which measures strength in four muscle groups bilaterally.

When Policy Topic is not covered:

The use of Ampyra is considered **investigational** for all other indications.

Considerations

Ampyra requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

Ampyra is an oral potassium channel blocker that is indicated to improve walking in patients with multiple sclerosis (MS), as demonstrated by an increase in walking speed.¹ The recommended maximum dose is 10 mg twice daily (BID) given approximately 12 hours apart. No additional benefits were noted when given at doses greater than 10 mg BID and adverse events (AEs), including seizures, were more common at higher doses. The tablets should be taken whole and not divided, crushed, chewed or dissolved. Ampyra is contraindicated in patients with a history of seizures and moderate or severe renal impairment (creatinine clearance [CrCl] \leq 50 mL/min).¹ The risk of seizures in those with mild renal impairment (CrCl 50 to 80 mL/min) is unknown, but the plasma levels of Ampyra in such patients may approach those noted at a dose of 15 mg BID, a dose related to an increase risk of seizures. Also, Ampyra should not be taken with other forms of 4-aminopyridine (4-AP, fampridine), which is an immediate-release agent that sometimes is compounded, because the active ingredients are similar. The most common AEs noted with Ampyra (incidence \geq 2% and at a rate greater than placebo) were urinary tract infection, insomnia, dizziness, headache, nausea, asthenia, back pain, balance disorder, MS relapse, paresthesia, nasopharyngitis, constipation, dyspepsia, and pharyngolaryngeal pain. The safety and effectiveness in children aged $<$ 18 years have not been established. Many patients in the pivotal clinical trials (63%) utilized Ampyra in combination with immunomodulatory agents. A Risk Evaluation and Mitigation Strategy (REMS) program is available for Ampyra, which will educate prescribers about the proper use of the medication and promote awareness about adverse events (e.g., seizures).

Rationale

The effectiveness of Ampyra in improving walking in patients with MS was evaluated in two pivotal, well-controlled trials involving 540 patients. Patients in the two clinical trials had a mean disease duration of 13 years and a mean expanded disability status scale (EDSS) score of 6.¹ In both trials, the primary efficacy measure was walking speed (in feet per second) as measured by the Timed 25-foot Walk (T25FW), using a responder analysis.¹⁻³ A responder was defined as a patient who displayed faster walking speed for at least three visits out of a possible four during the double-blind period than the maximum value achieved in the five non-double-blind no treatment visits (four before the double-blind period and one after). The 12-item MS Walking Scale (MSWS-12) was also used and is a rating scale that captures patients' perspectives on their ambulatory disability; other secondary parameters were also assessed.

The first pivotal trial involving Ampyra was a randomized, double-blind, placebo-controlled, Phase III, parallel-group, multicenter, 21-week study (1 week post screening; 2-week, single-blind placebo run-in, 14 weeks, double-blind treatment; and 4-week no treatment follow-up) involving 301 patients with MS (aged 18 to 70 years) performed in the US and Canada.¹⁻² A total of 229 patients were given Ampyra 10 mg BID (every 12 hours) and 72 patients received placebo.¹⁻² MS patients included were those who were able to walk 25 feet in 8 to 45 seconds. Exclusion criteria were a history of seizures or evidence of epileptiform activity on a screening electroencephalogram (EEG) and onset of an MS exacerbation within 60 days.¹⁻² The mean patient age was 51 years and 68% of patients were female.² Most patients were White (93%) and the average EDSS score was 5.8. MS was classified as relapsing-remitting in 28%, primary-progressive in 15%, secondary-progressive in 53%, and progressive-relapsing in 4% of patients. Immunomodulatory therapy (e.g., Betaseron, Copaxone) was received by 71% in the placebo group and 66% in the Ampyra group. The mean baseline timed 25-foot walk speed was 2.1 feet per second. More patients given Ampyra 10 mg BID were responders (35% [n = 78/224]) compared with placebo (8% [n = 6/72]) ($P < 0.0001$).¹⁻² The average change from baseline in walking speed for the Ampyra-treated time walk responders was 25.2% or 0.51 feet/second vs. 4.7% or 0.10 feet/second for placebo. For Ampyra-treated responders, the increase in walking speed was maintained during the entire treatment period. For the Ampyra-timed walk nonresponders, the average change was 7.5% or 0.16 feet/second. The increase in walking speed in Ampyra nonresponders was minimal but significant vs. placebo at the earliest double-blind treatment visit. Patients who were timed walk responders had statistically significant changes from baseline in MSWS-12 score, more positive subject global impression (SGI) scores and had more improvement regarding the clinical global impression (CGI) scores vs. nonresponders. For Ampyra-treated timed walk responders, the lower extremity manual muscle test (LEMMT) score, which measures strength in four muscle groups bilaterally, was improved during the double-blind period for those given Ampyra compared with placebo ($P = 0.0002$). Also, the Ampyra-treated nonresponder group had improved leg strength, as assessed by the LEMMT score, compared with the placebo group ($P = 0.046$).² During the double-blind treatment period a statistically significantly larger percentage of patients receiving Ampyra 10 mg BID had increases in walking speed of at least 10%, 20%, or 30% from baseline compared with placebo.

In the second pivotal trial, Ampyra was assessed in a randomized placebo-controlled, double-blind, parallel-group, 14-week study (1 week post-screening, 2 weeks of single-blind, placebo run-in, 9 weeks of double-blind treatment and 2 weeks of no-treatment follow-up) involving 239 patients with MS (aged 18 to 70 years) in the US and Canada. Patients received Ampyra 10 mg BID (n = 120) or placebo (n = 119).^{1,3} The inclusion and exclusion criteria were similar to the previous study,¹⁻² but patients with severe renal impairment were excluded.¹ The mean EDSS scores were 5.6 for placebo vs. 5.8 for Ampyra.^{1,3} Most patients were White (91%) and female (68%). The primary MS disease classification groups were relapsing-remitting (35%) and secondary-progressive (50%). The baseline mean timed 25-feet walk speed was 2.2 feet per second.³ Approximately 69% of patients were receiving immunomodulator therapy.³ The response rate, the primary efficacy endpoint, was 42.9% (n = 51/119) in the Ampyra-treated group and 9.3% (n = 11/118) for the placebo-treated group ($P < 0.0001$).^{1,3} The average improvement in the LEMMT score for the Ampyra responders was statistically significant vs. placebo ($P = 0.028$).³ The average percentage change from baseline in T25FW speed for Ampyra-

treated responders and placebo were 24.7% or 0.51 feet per second and 7.7% or 0.17 feet per second, respectively (P < 0.001 for the Ampyra-treated responders vs. placebo). During the double-blind treatment period, a statistically significantly greater percentage of patients given Ampyra 10 mg BID experienced increases in walk speed of at least 10%, 20%, or 30% from baseline vs. placebo.¹

References

1. Ampyra™ extended-release tablets [package insert]. Hawthorne, NY: Acorda Therapeutics, Inc.; January 2010.
2. Goodman AD, Brown TR, Krupp LB, et al, on behalf of the Fampridine MS-F203 Investigators. Sustained-release oral fampridine in multiple sclerosis: a randomized, double-blind, controlled trial. *Lancet.* 2009;373:732-738.
3. Goodman AD, Brown TR, Edwards KR, et al, on behalf of the MSF204 investigators. A phase 3 trial of extended-release oral dalfampridine in multiple sclerosis. *Ann Neurol.* 2010;68:494-502.

Other References Utilized

- Chwieduk CM, Keating GM. Dalfampridine extended-release in multiple sclerosis. *CNS Drugs.* 2010;24(10):883-891.
- Goodman AD, Cohen JA, Cross A, et al. Fampridine-SR in multiple sclerosis: a randomized, double-blind, placebo-controlled, dose-ranging study. *Mult Scler.* 2007;13:357-368.
- McDonald S, Clements JN. Dalfampridine: a new agent for symptomatic management of multiple sclerosis. *Am J Health Syst Pharm.* 2011;68:2335-2340.

Billing Coding/Physician Documentation Information

N/A Ampyra is considered a pharmacy benefit.

Additional Policy Key Words

Policy Number:

Related Topics

N/A

Policy Implementation/Update Information

06/2013 New policy titled Ampyra

02/2014 Reviewed – no changes made

This Medical Policy is designed for informational purposes only and is not an authorization, an explanation of benefits, or a contract. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there is any exclusion or other benefit limitations applicable to this service or supply. Medical technology is constantly changing and Blue Cross and Blue Shield of Kansas City reserves the right to review and revise medical policy. This information is proprietary and confidential and cannot be shared without the written permission of Blue Cross and Blue Shield of Kansas City.