

Today's date

Plan name

Plan address

Re: (Claimant's name, claim #)

Dear Sir or Ms.:

This is an appeal for reconsideration of (\_\_\_\_***your denial of coverage/pre-authorization, limitation of coverage***\_\_\_\_\_) for Ampyra (dalfampridine) for my patient (\_\_\_\_***name***\_\_\_\_) who was diagnosed with multiple sclerosis in (\_\_\_\_*year*\_\_\_\_), and has a history of impaired mobility.

Ampyra received FDA approval in January 2010 "to improve walking ability in patients with multiple sclerosis (MS)". Ampyra is a medication for management of the symptom of impaired ambulation and has no effect on the natural history of the disease process. Consequently, it does not replace or duplicate the desired effect of drugs prescribed to slow the progression of Multiple sclerosis (such as interferon beta, glatiramer acetate, or natalizumab for example). At the present time there are no other FDA approved agents with a similar indication which may be used as alternatives.

Two phase III clinical trials of the drug were sponsored by Acorda Therapeutics. In the first, involving 301 people with any type of MS, walking speed increased by an average of 25% compared with placebo in those who had a response to the medication.<sup>1</sup>

Results from a later, second phase III study involving 240 people with MS announced in 2008 confirmed the benefits seen in the first trial, finding that a significantly greater proportion of people on the therapy had a consistent improvement in walking speed compared to those who took placebo. Among those taking Ampyra who improved in walking speed, there was also a statistically significant improvement in leg strength.<sup>2</sup>

Citations from these studies are included for your information.

Sincerely,

(name)

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**1** Goodman, AD. et.al., *Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial*, The Lancet (2009) 373:732-738.

**2** Goodman AD, Brown TR, Cohen JA, Krupp LB, Schapiro R, Schwid SR, Cohen R, Marinucci LN, Blight AR; Fampridine MS-F202 Study Group. *Dose comparison trial of sustained-release fampridine in multiple sclerosis*, Neurology. 2008 Oct 7;71(15):1134-41. Epub 2008 Jul 30.

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Abstract #1: Ampyra (fampridine SR)

Lancet. 2009 Feb 28;373(9665):732-8.

## **Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial.**

[Goodman AD](#), [Brown TR](#), [Krupp LB](#), [Schapiro RT](#), [Schwid SR](#), [Cohen R](#), [Marinucci LN](#), [Blight AR](#); [Fampridine MS-F203 Investigators](#).

Collaborators: [Agius M](#), [Arnason BG](#), [Bethoux FA](#), [Bever CT Jr](#), [Bowen JD](#), [Brown TR](#), [Dietrich DW](#), [Edwards K](#), [Freedman MS](#), [Freedman M](#), [Kachuck NJ](#), [Kaufman MD](#), [Keilson M](#), [Khan O](#), [Krupp LB](#), [Leist TP](#), [Lindsey JW](#), [Lublin FD](#), [Mass MK](#), [Mattson D](#), [McGowan D](#), [Naismith R](#), [O'Connell C](#), [Oger JJ](#), [Panitch H](#), [Picone MA](#), [Center GM](#), [Rammohan KW](#), [Schapiro RT](#), [Schwid SR](#), [Scott T](#), [Short C](#), [Thrower BW](#), [Vollmer TL](#).

University of Rochester, Rochester, NY, USA.

Comment in:

- [Lancet. 2009 Feb 28;373\(9665\):697-8.](#)

### **Abstract**

**BACKGROUND:** Clinical studies suggested that fampridine (4-aminopyridine) improves motor function in people with multiple sclerosis. This phase III study assessed efficacy and safety of oral, sustained-release fampridine in people with ambulatory deficits due to multiple sclerosis. **METHODS:** We undertook a randomised, multicentre, double-blind, controlled phase III trial. We randomly assigned 301 patients with any type of multiple sclerosis to 14 weeks of treatment with either fampridine (10 mg twice daily; n=229) or placebo (n=72), using a computer-generated sequence stratified by centre. We used consistent improvement on timed 25-foot walk to define response, with proportion of timed walk responders in each treatment group as the primary outcome. We used the 12-item multiple sclerosis walking scale to validate the clinical significance of the response criterion. Efficacy analyses were based on a modified intention-to-treat population (n=296), which included all patients with any post-treatment efficacy data. The study is registered with ClinicalTrials.gov, number NCT00127530. **FINDINGS:** The proportion of timed walk responders was higher in the fampridine group (78/224 or 35%) than in the placebo group (6/72 or 8%; p<0.0001). Improvement in walking speed in fampridine-treated timed walk responders, which was maintained throughout the treatment period, was 25.2% (95% CI 21.5% to 28.8%) and 4.7% (1.0% to 8.4%) in the placebo group. Timed walk responders showed greater improvement in 12-item multiple sclerosis walking scale scores (-6.84, 95% CI -9.65 to -4.02) than timed walk non-responders (0.05, -1.48 to 1.57; p=0.0002). Safety data were consistent with previous studies. **INTERPRETATION:** Fampridine improved walking ability in some people with multiple sclerosis. This improvement was associated with a reduction of patients' reported ambulatory disability, and is a clinically meaningful therapeutic benefit.

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Abstract #2: Ampyra (fampridine SR)

Neurology. 2008 Oct 7;71(15):1134-41. Epub 2008 Jul 30.

## **Dose comparison trial of sustained-release fampridine in multiple sclerosis.**

[Goodman AD](#), [Brown TR](#), [Cohen JA](#), [Krupp LB](#), [Schapiro R](#), [Schwid SR](#), [Cohen R](#), [Marinucci LN](#), [Blight AR](#); [Fampridine MS-F202 Study Group](#).

Collaborators: [Arnason BG](#), [Bethoux FA](#), [Bever CT](#), [Bowen JD](#), [Cross AH](#), [Ford CC](#), [Kachuck NJ](#), [Kaufman MD](#), [Krupp LB](#), [Leist TP](#), [Lindsey JW](#), [Lublin FD](#), [Mass MK](#), [Metz L](#), [Miller A](#), [O'Connor PW](#), [Picone MA](#), [Rammohan KW](#), [Rizzo MA](#), [Schapiro RT](#), [Schwid SR](#), [Smith CH](#), [Thrower BW](#), [Vollmer TL](#).

Multiple Sclerosis Center, Chief Neuroimmunology Unit, Department of Neurology, University of Rochester Medical Center, 601 Elmwood Ave., Room 6-8521, Box 605, Rochester, NY 14642, USA. [andrew\\_goodman@urmc.rochester.edu](mailto:andrew_goodman@urmc.rochester.edu)

Comment in:

- [Neurology. 2008 Oct 7;71\(15\):1130-1.](#)

### **Abstract**

**OBJECTIVE:** To examine the efficacy and safety of three different doses of sustained-release fampridine in people with multiple sclerosis (MS). **METHOD:** This multicenter, randomized, double-blind, placebo-controlled, parallel-group study recruited 206 participants at 24 centers in the United States and Canada. After a single-blind, 2-week placebo run-in, participants were randomly assigned to receive fampridine (10, 15, or 20 mg twice daily) or placebo for 15 weeks. The primary efficacy variable was percent change in walking speed based on the timed 25-foot walk. **RESULTS:** Trends for increased walking speed were consistent across dose groups vs placebo, but not significant, on the prospective analysis. An increase from baseline in lower extremity strength during the 12-week stable-dose period was seen in the groups receiving 10- and 15-mg doses, compared with placebo ( $p = 0.018$  and  $0.003$ ). There were no significant changes in other secondary assessments. Post hoc analysis revealed subsets of participants in each dose group with walking speeds during the treatment period that were consistently faster than during the nontreatment period. There were significantly more "consistent responders" in the drug-treated groups than in the placebo group (36.7% compared with 8.5%). Consistent responders showed significantly greater improvement in self-assessed ambulation on the 12-Item MS Walking Scale than did nonresponders. Fampridine was generally well tolerated. Severe and serious adverse events were more frequent at the highest dose. **CONCLUSIONS:** This phase 2 study suggests that a subgroup of patients, when treated with fampridine, experiences a clinically relevant improvement in walking ability, which is sustained for at least 14 weeks.