FAMPYRA® (prolonged-release fampridine tablets)

ENABLE Clinical Trial Fact Sheet

FAMPYRA Overview
FAMPYRA (prolonged-release fampridine tablets) is a formulation of the drug fampridine (4-aminopyridine, 4-AP or dalfampridine). FAMPYRA has been developed to improve mobility problems and address walking impairment in adult patients with multiple sclerosis (MS). In MS, damaged myelin exposes channels in the membrane of axons allowing potassium ions to leak, weakening the electrical current sent through nerves. Studies have shown that fampridine can increase conduction along damaged nerves, which results in improved walking ability.

This prolonged-release formulation was developed and is being commercialized in the U.S. by Acorda Therapeutics, Inc. (NASDAQ: ACOR) under the trade name AMPYRA® (dalfampridine) Extended Release Tablets, 10 mg. Biogen Idec has licensed the rights from Acorda to develop and commercialize FAMPYRA in all markets outside the United States. In the European Union, FAMPYRA is indicated for the improvement of walking in adult patients with MS with walking disability (Expanded Disability Status Scale [EDSS] score of 4.0-7.0).

ENABLE Study Design
ENABLE is an open-label, single-arm, prospective, 48-week, multicenter, Phase 4 study to assess the effects of FAMPYRA on health-related quality of life (HRQoL) outcomes in MS patients with walking impairment. The study enrolled 901 patients with a mean EDSS score of 5.2, indicating that on average patients in this study had mobility disability that impaired their daily activities and required walking assistance. Patients in the study had been diagnosed with MS for a mean of 12.1 years and 63 percent had progressive MS, which is characterized by steadily worsening neurologic function.

Enrolled patients completed the Timed 25-Foot Walk (T25FW) at baseline and weeks two and four, and completed the MS Walking Scale (MSWS-12) at baseline and week four. Approximately three-quarters of FAMPYRA-treated patients showed improvement after four weeks (n=704) and entered the treatment arm of the study. The primary endpoint was the change from baseline in the 36-Item Short-Form Health Survey (SF-36®) 18 physical component summary (PCS) score in patients clinically assessed as having a treatment response. The SF-36 is one of the most widely used measures of HRQoL. Outcomes were assessed at weeks 12, 24, 36 and 48.

![Table of outcomes](image-url)
Enable Study Results: Patient Benefits After One Year of Fampyra Treatment

Summary of Results
Results from ENABLE show treatment with FAMPYRA is associated with sustained, statistically significant improvements in long-term HRQoL outcomes, physical function and the ability to perform daily activities, as well as psychological outcomes, in people living with MS who have walking disability. The observed HRQoL benefits were detected as early as 12 weeks and continued through 48 weeks of treatment. These data indicate that FAMPYRA may provide early and sustained benefits that extend beyond improved walking ability and may enhance overall quality of life for MS patients who are living with this chronic disabling disease.

Health Related Quality of Life Improvements
- The main outcomes from ENABLE show treatment with FAMPYRA was associated with benefits on HRQoL as early as 12 weeks and through 48 weeks of treatment:
  - Statistically significant and clinically meaningful improvements on HRQoL were observed in FAMPYRA-treated patients at 12 weeks (4.3; p<0.0001) through 48 weeks (3.3; p<0.0001), as measured by the change from baseline in the PCS score of the SF-36
    - Improvements are considered clinically meaningful if a patient’s score improved by two points
  - Physical component scores from the Multiple Sclerosis Impact Scale (MSIS-29) also showed improvement from baseline in FAMPYRA-treated patients as early as week 12 (-13.00; p<0.0001) through week 48 (-9.28; p<0.0001)
    - Negative numbers on the MSIS indicate improvement
  - No significant differences from baseline in SF-36 and MSIS-29 physical component scores were observed in patients not treated with FAMPYRA

Physical Function Improvements
- Patients taking FAMPYRA for one year reported improvements across a broad range of physical functions and daily activity limitations, specifically on physically-demanding tasks and the ability to perform physical tasks without difficulty:
  - The PRIMUS ALS score significantly improved from baseline to week 12 and through week 48 in patients on treatment
  - The top five individual MSIS-29 physical component subscale items that improved the most from baseline to week 48 among patients on treatment were:
    - Stuck at home more than they would like to be
    - Ability to complete physically demanding task
    - Having to cut down time on work or other activities
    - Taking longer to do things
    - Feeling of heaviness in the arms or legs

Safety
An interim safety summary of the ENABLE study as of 15 July 2013 showed that by responder status, 518 of 704 responders (73.6%) and 64 of 129 non-responders (49.6%) reported AEs. Adverse events occurring in ≥5% of total subjects were insomnia, headache, nausea, MS relapse, urinary tract infection (UTI), nasopharyngitis, fall, and dizziness. Two subjects receiving FAMPYRA reported an adverse event of “convulsion” and two others reported “grand mal convulsion.” The percentage of subjects who have discontinued study treatment due to AEs was 4.8% overall. There were no new safety signals or unexpected safety findings identified from the review of the interim safety data from this study.