4-Aminopyridine (4-AP) and 3, 4-Diaminopyridine (3, 4-DAP)

4-Aminopyridine is an experimental drug that may reduce symptoms in some people with MS, particularly those who are more sensitive to heat. 4-AP blocks potassium channels on the surface of nerve fibers and may improve conduction of electrical impulses through nerves whose protective myelin sheath has been damaged or destroyed by MS.

Studies Show Drug Helps Some People
Early clinical trials of 4-AP, given either intravenously or orally, showed that the drug provided temporary improvement in symptoms such as weakness, imbalance, and decreased vision—in small numbers of MS patients.

In a somewhat larger study, involving 68 MS patients over a three-month period, 27% reported improvement in symptoms while they were taking 4-AP, compared to only 2% (1 patient) who reported improvement while taking a placebo, an inactive substance used as a control in testing new drugs. In addition, 10 patients on 4-AP significantly improved their rating on a neurologic function scale called the Expanded Disability Status Scale, or EDSS, while none of the patients taking a placebo improved their EDSS rating.

Patients with more neurologic impairment and those more sensitive to heat were more likely to be helped by 4-AP. Although this was a controlled, double-blind study—neither the patients nor the investigators knew who was taking 4-AP or who was taking the placebo—41 patients correctly guessed that they had received 4-AP rather than the placebo.

Side Effects Can Be Troublesome
Side effects in this trial included dizziness, numbness and tingling, and instability while walking. Less common side effects included nausea, vomiting, and abdominal pain. Some of these side effects, however, also occurred among patients taking the placebo.

Serious side effects of 4-AP treatment included generalized convulsions, confusion, and one case of liver inflammation (chemical hepatitis).

Timed-Release Formula
A small-scale (36 subjects), controlled trial using a timed-release formulation of 4-AP (Fampridine-SR, developed by Acorda Therapeutics), was recently completed in which subjects were given gradually higher doses. Although the higher doses were not well-tolerated, even with the timed-release formula, people on lower doses
showed some improvement in walking speed and leg strength. No benefit was found for fatigue. Side effects included dizziness, insomnia, and numbness and tingling; at the higher doses, two subjects had seizures.

In a double-blind, placebo-controlled dosing study, 206 people with MS were randomized to receive either Fampridine (10 mg, 15 mg, or 20 mg) or an inactive placebo for 12 weeks. The results indicated a trend (an effect that does not quite reach statistical significance) toward improved walking speed in the groups receiving Fampridine, as well as a significant increase in leg strength. Side effects included dizziness, insomnia, and nausea, with two people in the 20-mg group having seizures (one related to an accidental overdose).

To look further at the safety and effectiveness of Fampridine, investigators at approximately 30 centers in the United States and Canada are enrolling participants in a 21-week clinical trial. This placebo-controlled trial, which will not include the 20 mg dose, will evaluate walking ability in 240 people with MS.

**Related Compound Not as Effective**
A related compound, 3, 4-diaminopyridine, has been reported to provide similar improvements in symptoms, but 3, 4-DAP is less able to get into the brain than 4-AP. One clinical trial showed that 3, 4-DAP was less effective than 4-AP and produced more side effects, such as nausea and abdominal pain.

---

**See also…**

**Sourcebook**
- Clinical Trials
- Expanded Disability Status Scale (EDSS)
- Placebo Response

**Society Web Resources**
- Spotlight: MS and Mobility [www.nationalmssociety.org/Mobility](http://www.nationalmssociety.org/Mobility)
- Spotlight: Rehabilitation in MS [www.nationalmssociety.org/Rehab](http://www.nationalmssociety.org/Rehab)
- Spotlight: Treatments [www.nationalmssociety.org/Treatments](http://www.nationalmssociety.org/Treatments)

The National Multiple Sclerosis Society is proud to be a source of information about multiple sclerosis. Our comments are based on professional advice, published experience, and expert opinion, but do not represent individual therapeutic recommendations or prescription. For specific information and advice, consult your personal physician.

To contact your chapter, call **1-800-FIGHT-MS** (1-800-344-4867) or visit the National MS Society web site: [www.nationalmssociety.org](http://www.nationalmssociety.org).

© 2005 The National Multiple Sclerosis Society. All rights reserved.

Last updated October 2005