Multiple sclerosis (MS) is the most common cause of neurological disability in young-to-middle aged adults. Disease onset usually occurs between the ages of 20 to 50 years, and females are affected more often than males. MS is an inflammatory relapsing or progressive disorder of central nervous system (CNS) white matter. Pathologically, it is characterized by multifocal areas of demyelination, loss of oligodendrocytes, and astrocytosis with relative sparing of axons. Almost any neurological symptom can appear with the disease, which often progresses to significant functional and cognitive disability following a variable course.

In 1996 the United States National Multiple Sclerosis Society standardized four subtypes of MS.
- **Relapsing-remitting MS (RMMS):** Defined as “clearly defined disease relapses with full recovery or with residual sequelae and residual deficit upon recovery; periods between disease relapses characterized by a lack of disease progression.”
- **Primary progressive MS (PPMS):** Defined as “disease progression from onset with occasional plateaus and temporary minor improvements allowed.”
- **Secondary progressive MS (SPMS):** Defined as “an initial RRMS course followed by progression with or without occasional relapses, minor remissions, and plateaus.”
- **Progressive-relapsing MS (PRMS):** Defined as “progressive disease from onset, with clear acute relapses, with or without full recovery; periods between relapses characterized by continuing progression.”

The cause of MS has not been identified, but is generally considered to be some combination of genetic, environmental, and infectious factors resulting in abnormal immune system reactions to the myelin sheath. The most common symptoms of MS are fatigue, weakness, numbness, visual and cognitive dysfunction. Because of fatigue and weakness, approximately 90% of MS patients report difficulty ambulating and the majority of MS sufferers classify this issue as having a moderate-to-high impact on their productivity and quality of life.

There is no cure for MS. The primary aims of current therapy are returning function after an acute attack, preventing new attacks, and preventing disability. Corticosteroids IV, IM, or oral, are generally effective in the short term for relieving symptoms, but do not appear to have a significant effect on long-term recovery. Disease modifying drugs (DMDs) are considered modestly effective at reducing the number of attacks in RRMS.

Ampyra is a broad spectrum potassium channel blocker used to improve walking (gait ataxia) in patients with all subtypes of MS. The exact mechanism by which Ampyra exerts its therapeutic effect has not been established. In animal studies, Ampyra has been shown to increase conduction of action potentials in demyelinated axons through inhibition of potassium channels.

Gait ataxia in MS: Gait imbalance and difficulty in performing coordinated actions may occur as a result of impairment of cerebellar pathways. Walking impairment is typically due to truncal ataxia and may impair the patient’s ability to sit or stand unsupported. In addition, greater than 30% of patients have moderate to severe spasticity, especially in legs which can interfere with ambulation, work and self-care.

Approval of dalfampridine extended release tablets to improve walking speed in MS patients was based on the use of a novel endpoint in clinical trials: the Timed 25 Foot Walk test (T25FW), that is, the number of seconds it takes to walk 25 feet.

Approximately 30% of patients responded to therapy by demonstrating what is considered a clinically significant improvement of 20% or more on the T25FW.

The recommended starting and maintenance dose is 10 mg twice daily, approximately 12 hours apart and without regard to food.

Higher doses do not add benefit and may increase the risk of adverse events, including the labeled contraindications of seizures and renal dysfunction.
### Prior authorization criteria

Coverage for Ampyra is provided in accord with the following criteria:

1. For use in improving walking speed in patients with all forms of multiple sclerosis.
   AND
2. The patient has a baseline 25 foot walk test between 8 to 45 seconds.

Coverage is **not** provided if the patient has history of a seizure disorder or moderate to severe renal impairment (CrCl ≤ 50 ml/min).

**Coverage duration:**

Coverage is initially provided for 3 months.
Coverage may be renewed for 12 months in situations where the patient had a baseline 25 foot walking test between 8 and 45 seconds AND where the patient demonstrates at least a significant improvement in walking speed from baseline.

**Quantity Duration Limit:**

Coverage is provided for a quantity not to exceed sixty 10 mg tablets (600 mg) per month to accommodate 10 mg twice daily. Coverage for additional quantities is not provided.

### References

- **Olek, MJ. Epidemiology, risk factors, and clinical features of multiple sclerosis in adults.** In: UpToDate, Gonzalez-Scarano, F (Ed). UpToDate, Waltham, MA, 2010.