

Highlights on Dalfampridine – New Therapy in All Types of Multiple Sclerosis

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Initially approved in the U.S. (2010) and then in the E.U. (2011), Ampyra (dalfampridine extended release) is indicated as a treatment to improve walking of patients suffering from multiple sclerosis, as demonstrated by the increasing speed in walking. This is the first drug specifically approved for the improvement of walking ability.

Dalfampridine extended release is an orally administered formulation of dalfampridine (fampridine, 4-aminopyridine), a potassium channel antagonist, and its main pharmacological properties are prolongation of the action potential and improved conduction in demyelinated axons, as well as potentiation of synaptic and neuromuscular transmission.

Oral dalfampridine ER 10 mg twice daily was used in three randomized, double-blind, placebo-controlled, multicentre trials in multiple sclerosis.

The primary efficacy variable in these studies was the percentage change from baseline in walking speed based on T25FW (Timed 25-Foot Walk) test. Time walk responders were defined as patients whose walking speeds were faster in at least three of four assessments during the double-blind treatment period than the maximum speed recorded at the five non-treatment assessments.

In two phase III trials the proportion of timed walk responders (primary endpoint) in the

dalfampridine ER-treated group (42,9% and 35%) was significantly ($p < 0.001$) higher than in the groups given placebo (9.3% and 8%) during the studies. Between-group differences in timed walk responder rates appeared to be independent of patient demographics, MS disease characteristics and the use of concomitant immunomodulators drugs (interferon, glatiramer acetate, natalizumab). No differences in effectiveness based on degree of impairment, age, gender, or body mass index were detected.

The most common side effects of Ampyra include: urinary tract infection, insomnia, dizziness, headache, nausea, back pain. Dalfampridine ER was generally well tolerated, with adverse events occurring $>5\%$ of treated patients. One of serious adverse event reported in trials and US prescribing information notes is that the incidence of seizures appeared to increase with increasing dalfampridine ER dosage in patients with MS. Because patients with renal impairment would require a dose lower than 10 mg twice daily and no strength smaller than 10 mg is available, Ampyra is contraindicated in patients with moderate to severe renal impairment.

Ampyra represents a new therapy approach to the treatment of MS symptoms and it could be prescribed in all forms of MS for the improvement in walking ability.

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