Pharmacotherapeutic report on Fampridine (Fampyra®) for the indication 'improvement in MS patients' walking ability', summary

Approved on 17 December 2012 by the Medicinal Products Reimbursement Committee (CFH)

Medicine. (=4 aminopyridine (4-AP)=dalfampridine). 10-mg tablet with prolonged release (PR). 4-Aminopyridine and dalfampridine are other names for fampridine; in the USA fampridine is marketed under the name dalfampridine.

Registered indication. "improvement in walking of adult patients with multiple sclerosis with walking disability (EDSS 4-7)." The European Registration Authority (EMA) has registered fampridine 'conditionally'. This means that we shall have to wait for further pointers about its mechanism of action, particularly about other advantages alongside the effects on speed of walking and in relation to the early identification of responders. This will be investigated in a study. The EMA will assess new information over this product every year and the SmPC will be adjusted where necessary.

Posology. 10 mg twice daily. Initial prescription should be limited to 2 weeks of therapy as clinical benefits should generally be identified within 2-weeks after starting. If a timed walking-test, e.g., the Timed 25-Foot Walk (T25FW) does not indicate any improvement after 2 weeks, treatment should be discontinued.

Mechanism of action. Fampridine blocks the potassium-channels, thereby reducing the leakage of ionic current through these channels. This prolongs repolarisation and enhances action potential formation in demyelinated axons and neurological function. Presumably, by enhancing action potential formation, more impulses might be conducted in the central nervous system.

Summary of the therapeutic value

Intended effects. In comparison with placebo, no clinically relevant positive effect of fampridine-PR on ability to walk has been demonstrated for the entire population with walking disability (EDSS 4-7). In short-term studies lasting 14-15 weeks, in comparison with placebo, fampridine-PR has a statistically, but small effect on the speed with which one-third of the patients could walk a short distance (7.8 m) as fast as possible. There is no evidence that these responders are able to walk longer distances or that this effect is maintained after 3 months. Nor has any favourable effect been demonstrated of fampridine on other significant aspects of walking (coordination, balance, fatigue, radius of action). Furthermore, the studies with fampridine do not indicate whether (or which proportion of) the patients were also being treated with exercise/physical therapy, although research reveals that exercise therapy/physical therapy has a favourable effect on mobility. There are no direct comparative studies with pharmacy-compounded fampridine (4-AP) and/or with physical therapy/exercise therapy; indirect comparison did not prove possible. In comparison with pharmacy-compounded fampridine (4-AP), fampridine-PR contains the same active substance and a difference in favourable effect is not plausible; a clinically relevant, favourable effect has not been sufficiently demonstrated for either of them.

Unintended effects. The most frequent adverse effects are urinary tract infection; central side effects such as insomnia, anxiety, dizziness, headache, balance disorders, paraesthesia, tremor; dyspnoea, pharyngolaryngeal pain, gastrointestinal disorders, back pain, asthenia. Fampridine has a narrow therapeutic window: a relatively small increase in exposure leads in particular to a large increase in CNS adverse effects (convulsions). Some adverse effects can have a negative effect on walking. The suggestion that the formulation with extended release gives fewer adverse effects than pharmacy-compounded fampridine is a theoretical supposition. This supposition is plausible but has not been substantiated with research data.

Experience. Experience with fampridine-PR is limited and less extensive than with pharmacy-compounded fampridine (=4-AP).

Applicability. Fampridine cannot be administered to patients with epilepsy. There is a lack of data on elderly patients and patients with cardiovascular disorders.

Ease of use. An advantage of fampridine-PR is that it is administered only twice daily in comparison with the 4x daily administration of pharmacy-compounded fampridine.

Final conclusion.

The therapeutic value of fampridine is the same as that of pharmacy-compounded fampridine (=4-AP) in improving the walking ability of adult patients with multiple sclerosis (EDSS 4-7). Fampridine-PR has a lower therapeutic value in comparison with exercise therapy/physical therapy in improving the walking ability of adult patients with multiple sclerosis (EDSS 4-7). There is no proven place for fampridine in the therapy, neither for fampridine-PR, nor for pharmacy-compounded fampridine (=4-AP).

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