Fampridine (Fampyra®) for the improvement of walking in adult MS patients with Expanded Disability Status Scale (EDSS) 4-7 and severely impaired walking ability (Timed 25 Foot Walk Test (T25FWT) ≥6 seconds)

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 6 August 2019

Zorginstituut Nederland carried out an assessment of the medicinal product fampridine (Fampyra®) for the improvement of walking in adult MS patients with EDSS 4-7 and severely impaired walking ability (T25FWT ≥6 seconds) and concluded as follows.

In a letter dated 11 June 2019 (CIBG-19-08254), the Minister of Health, Welfare and Sport (VWS) asked *Zorginstituut Nederland* for advice on reimbursement of the medicinal product fampridine (Fampyra®) for use in a subgroup of MS patients with EDSS 4-7. The *Zorginstituut* has completed its assessment.

Previous assessments
A negative reimbursement advice was given for fampridine (Fampyra®) in 2012 and 2018, due to insufficient evidence of the effectiveness of fampridine on improving walking in adult patients with MS with an EDSS score of 4-7.

Current reimbursement request
Beginning of 2019, on request of the Minister of VWS, *Zorginstituut Nederland* spoke with the MS specialists (MS working group of the Dutch Society for Neurology [NVN]) and the manufacturer Biogen about possible reimbursement of fampridine (Fampyra®) for a subgroup of the above-mentioned MS patients, for whom fampridine may be effective. The subgroup includes adult MS patients with EDSS 4-7 *and* severely impaired walking ability, defined as a walking speed of 6 seconds or longer on the *Timed 25 Foot Walk test* (T25FWT ≥ 6 seconds). The MS working group of the NVN recommended a trial treatment strategy for these patients. Only patients who demonstrate at least a 20% improvement on the T25FWT after two weeks of the trial treatment are allowed to continue the treatment with reimbursement via the standard health care package. Moreover, re-assessment will take place annually. During re-assessment, the treatment with fampridine will be terminated for at least 48 hours, after which the T25FWT will be carried out. Only patients who achieve at least 6 seconds on the T25FWT will receive a 2-week trial treatment, after which the T25FWT will be repeated. Patients must demonstrate at least a 20% improvement in this T25FWT (in comparison with the first T25FWT) to be able to continue treatment with fampridine with reimbursement from the standard health care package. The manufacturer has based its reimbursement request on the recommendations of the specialists. Furthermore, the manufacturer has designed a repayment arrangement under which a large percentage of the list-price of fampridine (Fampyra®) will be refunded to patients who participated in an earlier study of fampridine in the Netherlands on 20 March 2019. If the reimbursement decision is positive, the personal contribution will be reimbursed retrospectively. This arrangement will continue to, at the latest, 31 August 2019. All parties, including *Zorginstituut Nederland*, will make every effort to arrive at a substantive assessment and advice by this date.

Assessment of interchangeability
No product is included in the Medicine Reimbursement System (GVS) with which fampridine (Fampyra®) is interchangeable. Based on this, fampridine (Fampyra®)

cannot be placed on List 1A. The *Zorginstituut* has assessed whether fampridine (Fampyra®) is eligible for inclusion on List 1B.

Therapeutic value
Fampridine (Fampyra®) has a therapeutic added value for the improvement of walking in adult MS patients with an EDSS-score of 4-7 *and* severely impaired walking ability (T25FWT ≥6 seconds) in comparison with placebo, both added to best supportive care, taking into account the trial treatment strategy as recommended by the specialists (MS working group of the NVN). Fampridine thus complies with established medical science and medical practice for this subgroup of MS patients. The *Zorginstituut* was advised by the Scientific Advisory Committee (WAR).

Budget impact analysis
The *Zorginstituut* concludes that including fampridine (Fampyra®) on List 1B of the GVS for the current subgroup will result in additional costs to the pharmacy budget of approximately €3.7 million in the third year after inclusion in the standard package. If the costs of an extra consultation with a neurologist are included, then the additional costs will still be €3.7 million in the third year (the additional costs for the neurologist are mainly incurred in the first year after inclusion in the standard package). Uncertainty exists regarding the number of patients who will use fampridine, but the *Zorginstituut* estimates that ultimately more than 2100 patients will be involved.

Advice
Zorginstituut Nederland advises that fampridine (Fampyra®) for improving the walking ability of adult MS patients with EDSS 4-7 *and* severely impaired walking ability (T25FWT ≥6 seconds) should be included on List 1B and List 2 of the Health Insurance Decree and to attach the following conditions. Its inclusion on List 1B will result in the above-mentioned additional costs.

Conditions for fampridine (Fampyra®)
Only for an insured person aged 18 years or older with multiple sclerosis, with *Expanded Disability Status Scale* of 4 to 7 (EDSS 4-7) *and* a severely impaired walking ability based on a *Timed 25 Foot Walk Test Score* of at least 6 seconds (T25FWT ≥6 seconds), who fulfils the conditions of the trial treatment strategy:

1. At the start, a two-week trial treatment with this product;
2. After an initial trial treatment, an improvement of at least 20% is achieved in the T25FWT;
3. If treatment is continued, the trial treatment is repeated at least once a year, whereby treatment with this product is terminated for at least 48 hours, after which the first T25FWT is carried out, and after a renewed two-week trial treatment, an improvement of at least 20% is achieved in this T25FWT (in comparison with the first T25FWT).

After 2 years, together with the parties, the *Zorginstituut* will re-assess these List 2 conditions on the third point, to determine whether this condition is still necessary within the framework of appropriate use.

If the reimbursement of fampridine starts on 1 September 2019, it will not be possible for all patients who are currently using fampridine to have started a trial treatment before 1 September 2019. These patients must receive a trial treatment within one year, as described in the List 2 conditions. For these patients, treatment with fampridine will be terminated for at least 48 hours, after which the T25FWT will take place. Only patients who achieve at least 6 seconds on the T25FWT will receive a 2-week trial treatment, after which the T25FWT will be repeated. There must be at least a 20% improvement in this T25FWT (in comparison with the first T25FWT) to be able to continue treatment with fampridine with reimbursement from the standard health care package.

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The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.