Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2107

# fampridine 10mg prolonged-release tablet (Fampyra®)

Biogen Idec Ltd

## Resubmission

05 October 2018

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

**ADVICE**: following a resubmission

**fampridine (Fampyra®)** is not recommended for use within NHSScotland.

**Indication under review:** For the improvement of walking in adult patients with multiple sclerosis with walking disability (EDSS [expanded disability status scale] 4-7).

In double-blind phase III studies fampridine, compared with placebo, improved walking ability in adults with multiple sclerosis and walking impairment.

The submitting company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

**Chairman**
**Scottish Medicines Consortium**

## Indication

For the improvement of walking in adult patients with multiple sclerosis with walking disability (EDSS [expanded disability status scale] 4-7).[1]

## Dosing Information

Fampridine 10mg, twice daily, taken 12 hours apart (one tablet in the morning and one tablet in the evening). Fampridine should not be administered more frequently or at higher doses than recommended. The tablets should be swallowed whole and taken without food.[1]

Treatment with fampridine is restricted to prescription and supervision by physicians experienced in the management of multiple sclerosis.[1]

**Starting and evaluating fampridine treatment**

- Initial prescription should be limited to two to four weeks of therapy as clinical benefits should generally be identified within two to four weeks after starting fampridine
- An assessment of walking ability, e.g. the Timed 25 Foot Walk (T25FW) or Twelve Item Multiple Sclerosis Walking Scale (MSWS-12), is recommended to evaluate improvement within two to four weeks. If no improvement is observed, fampridine should be discontinued.
- Fampridine should be discontinued if benefit is not reported by patients.[1]

**Re-evaluating fampridine treatment**

If decline in walking ability is observed physicians should consider an interruption to treatment in order to reassess the benefits of fampridine. The re-evaluation should include withdrawal of fampridine and performing an assessment of walking ability. Fampridine should be discontinued if patients no longer receive walking benefit.[1]

## Product availability date

20 July 2011

## Summary of evidence on comparative efficacy

Multiple sclerosis is an inflammatory condition that damages the myelin of the central nervous system and causes neurologic impairment and often severe disability.[2] Fampridine is a selective potassium channel blocker which is believed to help electrical impulses travel along the nerves to stimulate the muscles, making it easier to walk. It is the first treatment licensed to improve walking in patients with multiple sclerosis.[1] It was initially granted a conditional marketing authorisation in Europe on 20 July 2011 and this was converted to a standard marketing authorisation on 22 May 2017. [2,3]

Additional data supporting conversion of the marketing authorisation to a standard marketing authorisation, and presented in the resubmission, were from the double-blind phase III ENHANCE study. This recruited adults (18 to 70 years) with multiple sclerosis as defined in the revised McDonald criteria for at least three months, investigator-assessed walking impairment and an expanded disability status scale (EDSS) score of 4 to 7. Randomisation was stratified by EDSS score (≤6 or >6) at screening, and after a protocol amendment, also by prior aminopyridine use (yes or no). Patients were equally assigned to fampridine 10mg orally twice daily for 24 weeks or placebo.

The primary outcome was the proportion of patients who achieved a mean improvement from baseline of at least eight points on the twelve item multiple sclerosis waking scale (MSWS-12) score over 24-weeks. MSWS-12 rates patients' limitations of mobility due to multiple sclerosis during the preceding two weeks on a five-point Likert scale from not at all (1) to extremely (5) and assesses function (walking, running, climbing stairs, standing and balancing) and quality (distance, effort, need for support outdoor and indoor, speed, smoothness and required mental concentration). The total score is transformed to a scale ranging from 0 to 100, with higher scores showing a greater limitation. If a patient's baseline score was less than eight, they were considered to have achieved the primary outcome if their mean MSWS-12 score over 24-weeks was less than 0.5. The primary outcome was assessed in the intention to treat population, defined as all randomised patients who received at least one dose of study medication and had at least one post-baseline efficacy assessment, excluding patients from one centre with good clinical practice noncompliance issues. The primary outcome was achieved by significantly more patients in the fampridine group, compared with placebo, and results are detailed in table 1.[3]

The pivotal studies in the conditional marketing authorisation and the previous submission were two double-blind phase III studies (MS-F203 and MS-F204).[2] These recruited adults (18 to 70 years) with multiple sclerosis as defined by McDonald criteria who were able to complete two trials of the timed 25-foot walk (T25FW) test in 8 to 45 seconds. In both studies randomisation was stratified by study centre. Patients were assigned in a 3:1 ratio in F203 and in a 1:1 ratio in F204 to fampridine 10mg orally twice daily or placebo for 14 weeks and nine weeks in the respective studies, followed by a two to four week period of no treatment. The primary outcome in both studies was the proportion of T25FW responders, where response was defined as a faster walking speed on at least three of the four on-treatment visits compared with the maximum speed for any of the five off-treatment visits (four before and one at two weeks after double-blind treatment). This was assessed in the intention to treat population, which comprised randomised patients with at least one on-treatment T25FW and MSWS-12 assessment. In both studies the primary outcome was achieved by significantly more patients in the fampridine group, compared with placebo, and results are detailed in table 1.[2,4,5]

The double-blind phase II MOBILE study recruited patients similar to the ENHANCE study, with multiple sclerosis as defined in the revised McDonald criteria for at least three months and EDSS score of 4 to 7. They were randomised equally to fampridine 10mg orally twice daily or placebo for 24 weeks. The study was exploratory and had no pre-specified primary outcome. Median improvement from baseline in MSWS-12, timed up and go (TUG) speed, Berg balance scale (BSS) and 29-item multiple sclerosis impact scale (MSIS-29) physical scores appeared greater with fampridine, compared with placebo, although no statistical comparison was detailed. Categorical analyses of MSWS-12 and TUG are presented in table 1.[6] The second European Medicines Agency (EMA) review noted that post-hoc analyses of the MOBILE study using patient global impression of change (PGIC) and other anchor and distribution based analyses estimated the minimum clinically important difference (MCID) on MSWS-12 at eight points and 15% improvement for TUG.[3]

**Table 1: Primary and secondary outcomes of ENHANCE, MS-F203 and MS-F204 studies.[1-3]**

| | Fampridine | Placebo | Difference (95% CI) |
|---|---|---|---|
| **ENHANCE** | **N=315** | **N=318** | |
| ≥8 improvement in MSWS-12 | 43%* | 34% | RD: 10% (3% to 17.8%) |
| ≥15% improvement in TUG | 43%* | 35% | RD: 9% (0.9% to 17.5%) |
| Change in MSIS-29 physical | -8.00* | -4.68 | LSM: -3.31 (-5.13 to -1.50) |
| Change in BBS | 1.75 | 1.34 | LSM: 0.41 (-0.13 to 0.95) |
| Change in ABILHAND | 1.49 | 0.75 | LSM: 0.74 (-0.38 to 1.86) |
| **MOBILE** | **N=68** | **N=64** | |
| ≥8 improvement in MSWS-12 | 48%* | 28% | |
| ≥15% improvement in TUG | 47%* | 30% | |
| **MS-F203** | **N=224** | **N=72** | |
| T25FW response | 35%* | 8.3% | RD: 26% (18% to 35%) |
| Change in MSWS-12 | -2.84 | -0.01 | 2.83 |
| Change in LEMMT | 0.13* | 0.05 | 0.08 |
| Change in Ashworth | -0.18* | -0.09 | 0.10 |
| **MS-F204** | **N=119** | **N=118** | |
| T25FW response | 43%* | 9.3% | RD: 34% (23% to 44%) |
| Change in MSWS-12 | -2.77* | 0.87 | 3.65 |
| Change in LEMMT | 0.10 | 0.05 | 0.05 |
| Change in Ashworth | -0.17* | -0.07 | 0.10 |

* statistically significant versus placebo. MSWS-12 = 12-item multiple sclerosis walking scale; TUG = timed up and go; MSIS-29 = 29-item multiple sclerosis impact scale; BBS = Berg balance scale; LEMMT = lower extremity manual muscle test; Ashworth test measures muscle spasticity. LSM = least square mean; RD = risk difference.

Quality of life assessed by short-form (SF-36), health resources utilisation, utility and visual analogue scale (VAS) of EuroQol EQ-5D-3L in ENHANCE and EQ-5D-5L in MOBILE indicated little change from baseline and minimal differences between treatment groups.[3,6] Post-hoc subgroup analysis of MOBILE and ENHANCE indicated improvements in EQ-5D utility score and VAS within fampridine MSWS-12-responders compared with non-responders, as detailed in table 2.[7,8]

**Table 2: EuroQol (EQ-5D) results in responders and non-responders in ENHANCE and MOBILE[7,8]**

| EQ-5D* | ENHANCE | | MOBILE | |
|---|---|---|---|---|
| **Least square mean change from baseline** | **Responder** | **Non-responder** | **Responder** | **Non-responder** |
| | **N=133** | **N=179** | **N=33** | **N=35** |
| Utility | 0.070 | 0.022 | 0.064 | -0.073 |
| Visual Analogue Scale | 5.9 | 1.6 | 2.86 | -3.38 |

* EQ-5D-3L in ENHANCE and EQ-5D-5L in MOBILE; Responders achieved at least a mean eight point improvement from baseline over 24 weeks on Twelve Item Multiple Sclerosis Walking Scale (MSWS-12)

Patients who completed the MS-F203 and MS-F204 studies could enter the extension studies, MS-F203EXT (n=269) and MS-F204EXT (n=214). Following the two to four week off-treatment period, all patients commenced fampridine 10mg orally twice daily. Mean treatment exposure was 39 and 26 months in the respective studies. Mean improvement from baseline in walking speed in patients considered fampridine-treated timed walk responders in the double-blind studies was lost during the two to four week off-treatment period. By eight weeks, the mean improvement in walking speed was 0.24 feet/second (from a baseline of 2.11 feet/second) in MS-F203EXT and 0.27 feet/second (from a baseline of 2.33 feet/second) in MS-F204EXT. However, at the end of the extension studies, the mean walking speed was similar to or slightly below baseline levels.[9]

## Summary of evidence on comparative safety

The second EMA safety review concluded that safety findings from ENHANCE were consistent with the known safety profile of fampridine in previous clinical studies and post-marketing experience. Review of ENHANCE with respect to important risks of seizures, serious hypersensitivity, urinary tract infections and interactions did not reveal any new safety findings. Also, there were no unexpected adverse events and no new safety signals with potential impact to the benefit-risk assessment of fampridine.[3]

Within the respective fampridine and placebo groups adverse events were reported by 66% (207/316) and 60% (190/319) in the ENHANCE study and 84% (294/348) and 72% (137/191) of patients in pooled data from MS-F203 and MS-F204 studies. These were treatment-related in 18% and 13% in ENHANCE and 26% and 18% in MS-F203/F204; serious in 8% and 7% in ENHANCE and 6.3% and 1.6% in MS-F203/F204; and lead to treatment discontinuation in 7% in both groups in ENHANCE and 3.2% and 2.1% in MS-F203/F204.[3,10]

In pooled data from MS-F203 and MS-F204 the most common adverse events in the fampridine and placebo groups respectively were; fall (16% versus 18%), urinary tract infection (15% versus 10%), insomnia (9.2% versus 2.6%), dizziness (8.3% versus 2.6%), headache (6.9% versus 3.1%), asthenia (6.6% versus 4.7%), nausea (6.6% versus 2.1%), upper respiratory tract infection (6.0% versus 7.9%), balance disorder (5.7% versus 1.6%), back pain (5.5% versus 1.6%), multiple sclerosis relapse (5.5% versus 3.7%), fatigue (5.2% versus 3.1%) and arthralgia (2.9% versus 5.2%). There were two reports of seizures, one in the fampridine group (a focal seizure involving the right extremity in the context

of severe sepsis associated with community-acquired pneumonia) and one in the placebo group (presumed complex partial seizure).[10]

In the ENHANCE study the most common adverse events in the respective fampridine and placebo groups were infections and infestations (31% and 28%, including urinary tract infection [18% and 12%], nasopharyngitis [5% and 6%] and upper respiratory tract infection [5% and 3%]), nervous system disorders (27% and 21%, including multiple sclerosis relapse [11% and 10%], headache [5% and 5%], dizziness [3% and 2%] and insomnia [4% and <1%]) and musculoskeletal / connective tissue disorders (18% and 13%, including back pain [5% and 3%], arthralgia [4% and 2%] and pain in extremity [3% and 3%]). Adverse events of special interest included asthenia (3% and 2%), fatigue (3% and 3%), muscle spasticity (3% and <1%), muscular weakness (3% and <1%), muscular spasm (1% and <1%) and gait disturbances (2% and 2%) in the respective groups.[3]

In the extension studies (MS-F203EXT and MS-F204EXT) the most common adverse events were urinary tract infections, falls, multiple sclerosis relapses, arthralgia and peripheral oedema and no new safety signals were identified. Four patients had seizure-related adverse events and all had previously received fampridine in the double-blind studies.[9]

## Summary of clinical effectiveness issues

Fampridine is the first medicine licensed to improve walking in adults with multiple sclerosis and walking disability.[1]

Current treatments for multiple sclerosis include symptom control of complications, modification of acute relapses with corticosteroids and disease-modifying treatments (e.g. beta-interferons, glatiramer and natalizumab).[2] In the phase III studies use of these medicines was generally balanced across the treatment groups and there were restrictions on initiation and modification of therapies with the potential to affect assessment of study outcomes.[2-4] Within the respective fampridine and placebo groups, immunomodulators were taken by 40% and 39% of patients in ENHANCE, 66% and 71% in MS-F203 and 69% and 70% in MS-F204.[2,3]

In the phase III ENHANCE study and similar phase II MOBILE study the proportion of patients with a mean improvement from baseline over 24 weeks of at least eight points in MSWS-12 (which assesses 12 domains of mobility impairment) was significantly greater with fampridine compared with placebo (43% versus 34% and 48% versus 28% in the respective studies).[3] In the phase III MS-F203 and MS-F204 studies the primary assessment of walking ability, sustained increase in T25FW speed, was achieved by significantly more patients given fampridine compared with placebo (35% versus 8.3% and 43% versus 9.3% in the respective studies).[2] The second EMA review concluded that the ENHANCE study confirmed that fampridine improves walking ability in a proportion of patients, however the effect is modest.[3]

The EMA noted that the primary outcome in MS-F203/204 assessed persistence of any increase in T25FW speed during the 9 to 14 week study periods, without consideration of magnitude of effect, and was further limited by a failure to assess other characteristics of walking quality, including balance, co-ordination and stamina or endurance. The latter was highlighted as being particularly relevant to patients as it can increase range of action. T25FW response as defined in the study was considered a pharmacodynamic, rather than clinically relevant, outcome.[2] The primary outcome in the subsequent ENHANCE study, mean improvement from baseline over 24 weeks of at least eight

points on MSWS-12, was accepted by the EMA as clinically meaningful. This was supported by analyses of the MOBILE study to define eight points as a MCID in MSWS-12. The EMA noted that the higher response rate for the primary analysis in the placebo group (34%) of ENHANCE compared with the placebo groups in MS-F203 (8.3%) and MS-F204 (9.3%) may be due to the subjective nature of the MSWS-12 questionnaire compared with the objective T25FW test.[3]

In the ENHANCE study results of the primary outcome were supported by significant differences in secondary outcomes including TUG response (achieving at least a 15% improvement in the time to rise from sitting, walk three meters and return to sitting) and in MSIS-29 physical score change from baseline, which assesses the physical impact of multiple sclerosis. Numerical, non-significant, improvements were observed with fampridine for Berg balance scale (BBS) and ABILHAND, which measures difficulty in performing manual activity.[3] In MS-F203 and MS-F204 improvements in measures of muscle strength (lower extremity manual muscle test [LEMMT]) and spasticity (Ashworth test) were considered small by the EMA, although statistical significance was observed in some analyses.[2]

Quality of life measures were not significantly different between treatment groups in ENHANCE or MOBILE.[3] Evidence to support improvements in quality of life (EQ-5D) are only available from post-hoc analysis in responders.[7,8] It was noted in the submission that EQ-5D-3L is likely to be insensitive to changes in quality of life in patients with multiple sclerosis ambulation problems due to the structure and scoring system, i.e. within the assessment of mobility there are three options: “no problems”, “some problems walking about” or “confined to bed”. The EQ-5D-5L scale may be more sensitive, as it has two additional options “slight problems walking about“ and “severe problems walking about”.

The initial EMA review concluded that maintenance of effect was unclear, as the decline in walking speed over time in the extension studies MS-F203EXT and MS-F204EXT could be due to progression of disease or lack of maintenance of effect.[2]

In the ENHANCE study subgroup analyses of the primary outcome by age, sex and body mass index were consistent with the primary analysis. In patients with less disability at baseline (baseline MSWS-12 score less than median) the difference in proportions and odds ratio were larger than those for the overall population, whereas in those with greater disability (baseline MSWS-12 score greater than median or EDSS>6.0) the difference in proportions and odds ratio were smaller than in the overall population. Subgroup analyses by type of multiple sclerosis indicated that response rates in relapsing-remitting multiple sclerosis (RRMS) were greater than the overall study population, whereas those in all other types of multiple sclerosis (secondary progressive [SPMS], primary progressive [PPMS] and primary relapsing [PRMS]) were lower. Results were consistent with the primary analysis for all forms of multiple sclerosis, except for the small group with PRMS, where a lower response rate was observed with fampridine compared with placebo. It has been suggested that the results in PRMS group and the small treatment difference within the PPMS group may be due to small sample sizes in the subgroups and also greater disability and likelihood of progression in these types of multiple sclerosis.[3]

In the ENHANCE study, among patients given fampridine, any improvement on the MSWS-12 at week 2 or 4 showed strong positive predictive value and negative predictive value for the response of at least an eight-point mean improvement over 24-week treatment period. This has been added to criteria defining responders detailed in the summary of product characteristics.[3]

## Summary of comparative health economic evidence

A cost-utility analysis was presented comparing prolonged-release fampridine with best supportive care in patients with MS with walking disability (EDSS scores between 4.0 and 7.0). A health care perspective was taken in the base case and a societal perspective was explored in a sensitivity analysis. A relatively short time horizon of 5 years was used as this was considered sufficient to capture most of the relevant costs and outcomes.

A simple decision tree, determining responder and non-responder status at four weeks, followed by a cohort Markov model, was used to simulate outcomes with and without fampridine treatment. The Markov model contained four health states: responding to fampridine treatment, withdrawn from fampridine treatment, continuing with best supportive care and death. The company also suggested patients should stop fampridine treatment if EDSS >7 which is proxied in the model by walking speed (as measured by the T25FW) dropping to 0.

The key clinical data used in the model were taken from the ENHANCE study, the MOBILE study, a pooled analysis of the MS-F203EXT and MS-F204EXT studies, and the IMPACT study. Important model parameters estimated from these data are the responder rates, definition of response, health state utilities values, disease progression and treatment withdrawal.

The definition of response and responder rates used in the base case analysis were taken from the ENHANCE study with response defined as a ≥8 point improvement on the MSWS-12 over 24 weeks. The model also used the T25FW data from IMPACT and pooled MS-F203EXT and MS-F204EXT studies to determine disease progression for BSC/patients who withdrew from fampridine, and fampridine responders respectively. Treatment withdrawal rates used in the model for fampridine responders were also based on the pooled MS-F203EXT and MS-F204EXT study data.

Health-related quality-of-life data collected using the EQ-5D-5L survey questionnaire from the MOBILE study provided the key utility weights in the model. These data were used in preference to the EQ-5D-3L data collected in ENHANCE as the EQ-5D-3L was considered insensitive to patient relevant changes in quality of life for patients treated with fampridine.

Medicine and administration costs for fampridine were included. Monitoring costs included a single physician visit at 4 weeks and the analysis assumed there were no other additional monitoring costs. Additional resource use by patients including outpatient visits in various specialties and primary care were estimated for each treatment group based on data from a published study.

A Patient Access Scheme (PAS) was proposed by the submitting company and was assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. SMC would wish to present the with-PAS cost-effectiveness estimates that informed the SMC decision. However, owing to commercial in confidence concerns regarding the PAS, SMC is unable to publish these results. As such, only the without-PAS figures can be presented.

The base case analysis presented by the submitting company produced an incremental cost-effectiveness ratio (ICER) of £44,734 without PAS.

The company presented an alternative base case which used the EQ-5D-3L data from ENHANCE to estimate utility values. This analysis produced an ICER of £149,659 without PAS.

Additional selected sensitivity analysis are presented in table 3 below.

**Table 3: Sensitivity analyses (without PAS for fampridine)**

| Scenario | ICER |
|---|---|
| Map the EQ-5D-5L data from MOBILE on to the EQ-5D-3L valuation set for utilities | £92,961 |
| Response rates, and utility weights, from the ENABLE study | £188,375 |
| Response rates from ENHANCE, and utility weights from the ENABLE study | £195,868 |
| Response rates using MS-F203 study | £53,561 |
| Allow BSC patients in the model to experience response (treatment specific utilities from MOBILE) | £39,359 |
| Allow BSC patients in the model to experience response (treatment independent utilities from MOBILE) | £123,367 to £137,328 |
| Increase the time horizon to 10 years | £48,780 |

The main weaknesses with the analysis are:

- The model is sensitive to using the EQ-5D-3L from ENHANCE versus the EQ-5D-5L data from MOBILE as demonstrated by the increase in the ICER in the company's alternative base case analysis. The company suggested that the EQ-5D-3L is not sensitive to capture changes in quality of life in patients treated with fampridine due to the limited number of response categories in the questionnaire. However, whether the EQ-5D-5L is a more appropriate measure of health related quality of life in this disease context is a source of uncertainty. In addition, the EQ-5D-5L valuation set which is used to derive utility values may be considered less established than the EQ-5D-3L valuation set. The company provided further sensitivity analysis which mapped the EQ-5D-5L data from MOBILE on to the EQ-5D-3L valuation set and the results are available in Table 3 above.
- Further to this, the results are sensitive to the use of alternative sources of health related utility data such as the ENABLE study. This suggests that there is some uncertainty around the generalisability of any one estimate to the Scottish population.
- The economic model did not allow patients who received BSC to respond to treatment although some patients responded in the placebo arm of the ENHANCE study. The company subsequently provided sensitivity analyses where BSC patients could respond and the results are available in Table 3 above.
- The model uses a range of data sources and the compatibility of these data sources in terms of outcome measures and patient characteristics is uncertain. The definition of response used in the economic model also may not reflect clinical practice.
- In the key source for the base case utility weights (MOBILE study) there is some imbalance in the treatment and control groups at baseline. The mean time since diagnosis was 12.4 years in the control group and 10.9 years in the treatment group. Further to this, baseline utility for patients randomised to fampridine was higher than BSC irrespective of future response category.

Due to the above uncertainties the economic case has not been demonstrated.

*Other data were also assessed but remain confidential.**

## Summary of patient and carer involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from The MS Society and Multiple Sclerosis Trust, both organisations are registered charities.

- The MS Society has received <0.5% pharmaceutical company funding in the past two years, including from the submitting company. Multiple Sclerosis Trust has received 11.8% pharmaceutical company funding in the past two years, including from the submitting company.

- MS is one of the most common disabling neurological conditions affecting young adults. Walking problems affect a large proportion of people with MS and can have a major impact on all aspects of work, social and family life, and lead to loss of independence. Loss of mobility can also compound other MS symptoms such as fatigue (due to the effort of walking) and incontinence (because it becomes difficult to reach the toilet in time), and can cause increased risk of falls, and social isolation through becoming housebound.

- Apart from walking aids, there are no medical symptom management treatments available to help improve walking speed for people with MS. The standard level of care would be access to a physiotherapist.

- Fampridine is currently the only licensed medicine for mobility problems in people with MS. A small clinical improvement in walking ability may be perceived to have a substantial benefit for the person with MS. Improved mobility and walking speed could lead to an increase in independence which may reduce social isolation and reliance on family members and carers. Additionally, patients have reported that an improvement in their mobility also improved other symptoms, including fatigue and co-ordination, which had a positive impact on their general quality of life.

- Patients will know if they are responding, shortly after they start fampridine allowing them to avoid unnecessary long term treatment if it is not effective.

## Additional information: guidelines and protocols

In October 2014 the National Institute of Heath and Care Excellence (NICE) published Clinical Guideline number 186: multiple sclerosis in adults: management. This noted that reduced mobility is a common consequence of the gradual decline in function associated with multiple sclerosis. This can arise from multiple causes such as visual deficit, disordered balance, co-ordination problems, spasticity and muscle weakness. Walking problems suffered by people living with multiple sclerosis can have a significant impact on all aspects of their life, whether recreational activities, usual activities of daily living or in the workplace. Non-pharmacological methods to improve mobility are recommended in the guidance, e.g. supervised exercise programmes involving resistance and cardiovascular training. The guideline noted that fampridine has beneficial effects on subjective improvement in muscle strength and walking speed. However it recommended that fampridine should not be used to treat lack of mobility in people with multiple sclerosis because it was found not to be a cost effective treatment.[11]

## Additional information: comparators

No other medicines are licensed for the same indication as fampridine.

## Cost of relevant comparators

| Medicine | Dose Regimen | Cost per year (£) |
|---|---|---|
| **Fampridine** | **10mg orally twice daily** | **4,706** |

*Costs from eVadis on 3 May 2018. Costs do not take any patient access schemes into consideration.*

## Additional information: budget impact

The company estimated there would be 9,709 patients eligible for treatment in year 1 rising to 9,944 patients in year 5 to which confidential uptake rates were applied.

SMC is unable to publish the without PAS budget impact due to commercial in confidence issues.

*Other data were also assessed but remain confidential.**

**References**


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This assessment is based on data submitted by the applicant company up to and including 14 September 2018.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

**Advice context:**

*No part of this advice may be used without the whole of the advice being quoted in full.*

*This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.*