
fampridine 10mg prolonged-release tablet (Fampyra®)

Biogen Idec Ltd

06 March 2020

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 second resubmission

fampridine (Fampyra®) is accepted 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.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

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

The recommended dose is one 10mg tablet, 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.

Treatment with fampridine is restricted to prescription and supervision by physicians experienced in the management of MS.

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.

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. 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.²

Data were presented 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 walking 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

Two double-blind phase III studies (MS-F203 and MS-F204)² 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 European Medicines Agency (EMA) 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 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. Outcomes in bold indicate study primary outcome. 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; ABILHAND measures difficulty in performing manual activity; 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 1: EuroQol (EQ-5D) results in responders and non-responders in ENHANCE and MOBILE^{7, 8}

EQ-5D*	ENHANCE		MOBILE	
	Responder	Non-responder	Responder	Non-responder
Least square mean change from baseline	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 baseline levels.⁹

Summary of evidence on comparative safety

The EMA 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 Clinical experts consulted by SMC considered that fampridine fills an unmet need in this therapeutic area, namely for the small proportion of patients who will derive a meaningful improvement in walking impairment.

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, 3, 5} 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 EMA 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 minimum clinically important difference in MSWS-12. The EMA noted that the higher response rate for the primary analysis in the placebo group of ENHANCE (34% for MSWS-12 response) compared with the placebo groups in MS-F203 and MS-F204 (8.3% and 9.3% for T25FW response respectively) 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.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, that is 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 EMA concluded that maintenance of effect is 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 differences 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 differences 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

Clinical experts consulted by SMC considered that the introduction of this medicine may impact on service delivery as evaluation of treatment effect will require additional clinic and/or physiotherapy time.

Summary of comparative health economic evidence

A cost-utility analysis was submitted comparing prolonged-release fampridine plus best supportive care (BSC) to BSC alone, in patients with MS with walking disability (EDSS scores 4-7).

The economic model consisted of an initial decision tree, with responder and non-responder status determined at four weeks, followed by a cohort Markov model to simulate outcomes with and without fampridine treatment over the time horizon of five years. A four weekly model cycle was used and patients entered the model at a mean age of 48.9 years, based on the ENHANCE study. The Markov model contained three health states: response, non-response and death. Patients had a withdrawal rate from treatment following the initial four-week assessment, and a stopping rule included with patients discontinuing fampridine treatment if EDSS >7, which is proxied in the model by walking speed (as measured by the T25FW) dropping to zero. Over the base-case model time horizon it is assumed no patients would progress to EDSS score >7.

The key clinical data used in the model were taken from the ENHANCE study, which determined response rates for the first 24 weeks and the baseline patient demographics applied in the economic model, as well as adverse events. The MOBILE study, a pooled analysis of MS-F203EXT & MS-F204EXT studies, and the IMPACT study were also used to determine important model parameters including discontinuation rates, health state utilities, and disease progression (T25FW).

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. A pooled analysis of MS-F203EXT & MS-F204EXT studies was used to determine fampridine

initial 4-week withdrawal rate (0.73%) as well as T25FW for responders in both treatment arms, while the IMPACT study was used for T25FW for non-responders.

Utility estimates in the economic analysis were derived from the EQ-5D-5L data collected within the MOBILE study and mapped to the EQ-5D-3L using the Van Hout *et al.* (2012) algorithm¹¹. This was analysed by treatment arm, with the EQ-5D-5L data in the placebo arm of the MOBILE study used as a proxy for the BSC alone comparator. Data were applied at baseline and weeks 2, 4, 8, 12, 16, 20 and 24, for each treatment by responders and non-responders. Beyond 24 weeks, extrapolation over the model time horizon used the last recorded EQ-5D values from week 24 carried forward.

Costs included medicine acquisition, monitoring and response assessment for fampridine, background resource use, and adverse events. Administration costs associated with fampridine were assumed as zero due to it being an oral treatment. Resource use estimates for responder and non-responders included GP and outpatient visits, inpatient stays and emergency hospital visits. These were based on a published study¹², based on EDSS score, and assumed the same for both treatment arms.

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 NHS Scotland. The results with the PAS are shown in table 3.

Table 2: Base case results fampridine versus best supportive care (BSC) at PAS prices

Analysis	Treatment	Incremental QALYs	ICER (cost/QALY)
With PAS for fampridine	Fampridine versus BSC	0.16	£13,156
BSC, best supportive care; ICER, incremental cost-effectiveness ratio; LY, life year; PAS, patient access scheme; QALY, quality adjusted life year			

In one-way sensitivity analysis the ICER was most sensitive to the utility values assumed to carry forward from week 24 to the 5 year time horizon and also the withdrawal rate of BSC, when varying by 95% confidence intervals. A range of scenario analyses were explored, with the potentially most plausible scenarios presented in

Table 34. The scenario analyses which had the greatest upward impact on the ICER were the use of utility values using the EQ-5D-3L data from the ENHANCE study or where treatment-specific utility differences were removed.

Table 3: Selected scenario analyses (fampridine + BSC versus BSC) at PAS price

	Scenario	Incremental QALYs	ICER (with PAS)
	Base case	0.16	£13,156
1	Utilities based on EQ-5D-3L valuation set (based on ENHANCE)	0.08	£25,690
2	Week 16 utilities applied from week 24	0.19	£11,042
3	Utility values applied for non-responders with no difference assumed in non-responder utility value by treatment arm (based on MOBILE)*	0.07	£28,942

4	Utility values applied for both responders and non-responders with no difference in utility values assumed by treatment arm (based on MOBILE)*	0.04	£58,792
5	Utility values applied for non-responders with no difference assumed in non-responder utility value by treatment arm (based on EQ-5D-3L from ENHANCE)*	0.06	£36,066
6	Increase the time horizon to 10 years	0.28	£10,722
7	Direct costs decrease by 25%	0.16	£16,116
8	Societal perspective for costs	0.16	£12,587
*Baseline utility set to the same utility for all patients, based on BSC non-responders			

The main weaknesses with the analysis are:

- The ICER results are upwardly sensitive to using the EQ-5D-3L from ENHANCE (£25,690/QALY) versus the EQ-5D (3L or 5L) data from MOBILE (Table 34). The company asserted that the EQ-5D-3L is not sensitive enough to capture changes in quality of life in patients treated with fampridine due to the limited number of response categories in the questionnaire. It remains uncertain whether the EQ-5D-3L, or EQ-5D-5L mapped to the EQ-5D-3L predicts a more reliable estimate of utility outcomes or whether differences in utility data are in part due to the MOBILE study having a better response than the ENHANCE study.
- Utility values are modelled separately for responders and non-responders in each treatment arm. The submitting company justified this assumption with recourse to trial data showing not just more responders with fampridine than BSC but also that there is a greater absolute difference from baseline in the MSWS-12 between fampridine responders and BSC responders. While this is noted, it remains an area of uncertainty and leads to increased ICERs when applying the same utility values by treatment arm for responders and non-responders.
- Beyond week 24 in the model, the company estimated long-term utilities by carrying the last observed value (week 24) forward and assuming these utility values apply for the remainder of the time horizon. This approach is not aligned with the modelled time-horizon, which is longer than the observation period, therefore the degree to which this approach reflects utility in the patient population beyond 24 weeks is uncertain. The ICER is sensitive to the EQ-5D data time point applied over the model time horizon (see Table 4).
- The model combines a range of data sources and the compatibility of these data sources in terms of outcome measures (using MSWS-12 for efficacy and T25FW for progression) and patient characteristics is uncertain.
- There is some imbalance in the treatment and control groups at baseline in the key data source for the base case utility weights (the MOBILE study). The mean time since diagnosis was 12.4 years in the control (BSC) group and 10.9 years in the treatment (fampridine) group. This could lead to bias with patients perhaps being healthier, with less time to progression, in the fampridine arm than BSC.

The Committee also considered the benefits of fampridine in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for the absence of other treatments of proven benefit was satisfied.

After considering all the available evidence and after application of the appropriate SMC modifier, the Committee accepted fampridine for use in NHSScotland.

*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 11.4% 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. Walking problems and consequent loss of independence is one of the greatest fears of people diagnosed with MS. 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. Symptom management treatments could make a real difference to the day to day lives of people living with mobility challenges.
- 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. If walking speed is improved, further doses can be taken at home minimising time and cost of travelling to a hospital clinic.

Additional information: guidelines and protocols

In October 2014 NICE published Clinical Guideline 186 Multiple sclerosis in adults: management.¹³ 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, for example 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.

Additional information: comparators

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

Additional information: List price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
fampridine	10mg orally twice daily	4,706

Cost from BNF online on 04 December 2019. Cost does not take patient access scheme into consideration.

Additional information: budget impact

The submitting company estimated there would be 9,767 patients eligible for treatment in year 1 rising to 10,004 patients in year 5 based on expected patients with EDSS 4-7, to which confidential estimates of treatment uptake were applied.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

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

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This assessment is based on data submitted by the applicant company up to and including 14 February 2020.

**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.