NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Midodrine for treating orthostatic hypotension

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of midodrine within its marketing authorisation for treating severe orthostatic hypotension.

Background

Orthostatic hypotension is defined as a drop in systolic blood pressure of at least 20mmHg and/or diastolic blood pressure of at least 10mmHg within three minutes of standing and can be recurrent[2]. Orthostatic (or postural) hypotension results from an inadequate physiological response to postural changes in blood pressure. In people with the condition, standing leads to an abnormally large drop in blood pressure, which can result in symptoms such as light‑headedness, dizziness, blurring of vision, syncope (temporary loss of consciousness) and falls. Orthostatic hypotension may arise as a result of disorders affecting the autonomic nervous system (for example, Parkinson's disease, multiple system atrophy or diabetic autonomic neuropathy), from a loss of blood volume or dehydration, or because of certain medications such as antihypertensive drugs or it may be idiopathic (of unknown cause). The severity (mild, moderate or severe) of orthostatic hypotension is defined by duration and type of symptoms.

The prevalence of orthostatic hypotension ranges from 5% to 11% but can affect up to 30% of adults over the age of 65 years[3]. Approximately 3,500 people in the UK have severe orthostatic hypotension due to autonomic dysfunction and other forms of treatment are inadequate[4]. The prevalence increases to 60% in people with Parkinson's disease and up to 70% of people living in nursing homes. It is estimated that about 0.2% of people over 75 years are admitted to hospital with problems relating to orthostatic hypotension[5].

The aims of treatment are too relieve symptoms of orthostatic hypotension and the choice of treatment depends on severity disease.
Non‑pharmacological management options are recommended first‑line (including compression stockings, blood pressure monitoring, increased physical exercise and increased water and salt ingestion). If these do not resolve symptoms, pharmacological treatment midodrine, alone or in combination with unlicensed fludrocortisone, may be considered. Other unlicensed treatments are available targeting the autonomic nervous system include phenylephrine, ephedrine, pseudoephedrine, droxidopa and phenylpropanoalamine, pyridostigmine, domperidone, non-steroidal anti-inflammatory drugs and erythropoietin.

The technology

Midodrine (Bramox, Brancaster Pharma Limited) is an alpha-adrenergic agonist which leads to an increase in blood pressure, decrease in venous capacity and lowers heart rates[6]. It is administered orally.

Midodrine has a marketing authorisation in the UK for 'adults for the treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate'.

Intervention(s)	Midodrine
Population(s)	Adults for the treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate
Comparators	• Established clinical management without midodrine
Outcomes	The outcome measures to be considered include: • achievement and maintenance of adequate blood pressure • alleviation of symptoms (including dizziness, fainting, palpitations, nausea) • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the

	marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Guidelines: 'Transient loss of consciousness ('blackouts') management in adults and young people' (2010) NICE clinical guideline 109. Review date October 2019 'Parkinson's disease: Diagnosis and management in primary and secondary care' (2006) NICE clinical guideline 35. Review currently in process. Publication expected April 2017 Related NICE Pathways: Diagnosing the cause of transient loss of consciousness (2015) NICE pathway http://pathways.nice.org.uk/pathways/transient-loss-of-consciousness/diagnosing-the-cause-of-transient-loss-of-consciousness
Related National Policy	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. All domains. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

How is severe orthostatic hypotension defined?

Have all relevant comparators for midodrine been included in the scope? Which treatments are considered to be established clinical practice in the NHS for orthostatic hypotension?

Have all appropriate outcomes been included in the scope?

Are there any other subgroups of people in whom midodrine is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider midodrine will fit into the existing NICE pathway, Diagnosing the cause of transient loss of consciousness?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which midodrine is licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider midodrine to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of midodrine can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

1. National Institute for Health and Clinical Excellence. Postural Hypotension in Adults: Midodrine. NICE advice (ESUOM5). February 2013
2. Patient. Hypotension. [accessed November 2015]
3. Patient. Hypotension. [accessed November 2015]
4. National Institute for Health and Clinical Excellence. Postural Hypotension in Adults: Midodrine. NICE advice (ESUOM5). February 2013
5. National Institute for Health and Clinical Excellence. Postural Hypotension in Adults: Midodrine. NICE advice (ESUOM5). February 2013
6. NIHR Horizon Scanning Research and Intelligence Centre Briefing Note [accessed November 2015]

Appendix B