

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

MIDODRINE FOR THE TREATMENT OF SEVERE ORTHOSTATIC HYPOTENSION DUE TO AUTONOMIC DYSFUNCTION IN ADULTS– **RECOMMENDED FOR RESTRICTED USE**

Name: generic (trade)	What it is	Indication	Date decision last revised	Decision Status	NICE / SMC Guidance
Midodrine Bramox®	Peripheral alpha adrenergic agonist	Treatment of severe orthostatic hypotension due to autonomic dysfunction in adults	June 2016	Final	<b>NICE</b> – Evidence Summary New Medicines (ESNM 61) Oct 2015 <b>SMC</b> – Accepted for use within license (Sept 2015)

**HMMC Recommendation: Midodrine for the treatment of adults with severe orthostatic hypotension due to autonomic dysfunction in adults- **RECOMMENDED for restricted use as a third line treatment option:****

- **First line: non-pharmacological measures, e.g. review of anti-hypertensive medication, use of compression garments, increasing water/salt intake and physical manoeuvres.**
- **Second line: off-label fludrocortisone**
- **Initiation and titration should be undertaken by an appropriate specialist or on the advice of a specialist.**
- **Treatment may be continued in primary care if specialist initiated, following specialist guidance on titration and monitoring.**
- **Treatment should only be continued when there is clear benefit (e.g. reduced falls).**

**EFFICACY**

- 2 RCTs ([Low et al. 1997](#) and [Jankovic et al. 1993](#)) found that midodrine 10 mg 3 times daily increased standing blood pressure statistically significantly more than placebo, 1 hour after the dose was taken.
- Improvements in patient- and investigator-rated symptoms were seen with midodrine compared with placebo in both RCTs. However, the symptom measurement scales were not reported to have been validated.

**SAFETY**

- According to the summary of product characteristics, the most common adverse effects of midodrine are piloerection, pruritus of the scalp and dysuria, occurring in more than 1 in 10 people.
- Adverse effects occurring in between 1 in 10 and 1 in 100 people include paraesthesia, headache, nausea, dyspepsia, stomatitis, pruritus, rash, chills, flushing, urinary retention and supine hypertension.

**COST**

- Midodrine at its maximum daily dose of 10mg three times a day approximately costs £1,643 per pt per year.
- The cost of the licensed product is lower than that of unlicensed products used across Hertfordshire.
- The manufacturer of [Bramox®](#), Brancaster Pharma Limited, considers that up to around 3500 people in the UK may be eligible for midodrine treatment under the terms of the marketing authorisation.
- Fludrocortisone (Florinef®) used off label, would cost £365 per patient per year at a dose of 100microgram per day.

**PATIENT FACTORS**

- No published evidence is available for outcomes such as quality of life, falls or ability to carry out daily activities.
- Because of the risk of supine hypertension, regular monitoring of supine and standing blood pressure is necessary. Patients should be told to report symptoms of supine hypertension immediately, such as chest pain, palpitations, shortness of breath, headache and blurred vision, and should be monitored for these adverse effects by their doctor (see [summary of product characteristics](#)).

## **Assessment against Ethical Framework**

### **Evidence of Clinical Effectiveness**

- The evidence review is primarily based on 2 randomised controlled trials comparing midodrine with placebo for orthostatic hypertension. The main limitation of the 2 RCTs is the focus on disease-oriented outcomes (changes in standing blood pressure), as opposed to patient-oriented outcomes such as quality of life, falls or ability to carry out daily activities.
- A summary of three systematic reviews and meta-analyses were also considered. Overall, they concluded that the quality of the evidence supporting the use of midodrine in orthostatic hypotension is limited by the lack of robust clinical data.

### **Cost of treatment and Cost Effectiveness**

- May 2016 Drug Tariff price: midodrine 2.5mg tablets, 100 pack, £55.05; 5mg tablets, 100pack, £75.05.
- Midodrine approximately costs £1,643 per patient per year at a maximum dose of 10mg three times a day.
- Based on Epect data (April 2015-Nov 2015), if licensed midodrine 2.5mg and 5mg tablets had been available, a total cost saving of £8484.89 for HVCCG and £6550.10 for E&NH could have been realised.
- The manufacturer of Bramox<sup>®</sup>, Brancaster Pharma Limited, considers that up to around 3500 people in the UK may be eligible for midodrine treatment under the terms of the marketing authorisation.
- Midodrine hydrochloride (Bramox<sup>®</sup>) is accepted as a cost effective treatment for use within NHS Scotland. The availability of midodrine hydrochloride (Bramox<sup>®</sup>) will allow the prescribing of a licensed medicinal product, with a resultant small net budget impact, based on estimates from primary and secondary prescribing and expenditure data from 2013/14. Fludrocortisone (Florinef<sup>®</sup>) used off label, would cost £365 per patient per year at a dose of 100microgram once daily.

### **The needs of the population**

- For the small cohort of patients in whom corrective factors have been inadequate, the needs of the population are considered to be moderate, as no other licensed preparation is currently available, although there are off label and unlicensed treatment options.

### **The needs of the community**

- The impact on the community is expected to be low. The cost of the licensed product is lower than that of the unlicensed products previously prescribed so the net resource impact is expected to be small.

### **Policy Drivers**

- North Central London Joint Formulary Committee – Approved for initiation in secondary care by specialist (e.g. Autonomic Unit) and transfer to primary care when stabilised. (<http://www.ncl-jfc.org.uk/recommended-medicines.html>)
- SMC- Midodrine has been accepted for use within license (decision document Sept 2015).
- Beds and Luton- Not formally reviewed yet (email communication May 2016).
- West Essex CCG- non-formulary (email communication May 2016).
- Mid Essex CCG- Approved for use second line after fludrocortisone, for specialist initiation and for transfer to primary care after 3 months (decision document Oct 2015).
- Addenbrookes Hospital- Available under shared care which is currently being reviewed with the availability of the licensed product (email communication May 2016).

### **Equity:**

No impact anticipated

### **References**

- NICE Evidence Summary New Medicines (ESNM 61): Orthostatic hypotension due to autonomic dysfunction: midodrine (Oct 2015) <https://www.nice.org.uk/advice/esnm61/chapter/Key-points-from-the-evidence>
- [https://www.scottishmedicines.org.uk/files/advice/midodrine\\_hydrochlorine\\_Bramox\\_Abbreviated\\_FINAL\\_Sept\\_2015\\_for\\_website.pdf](https://www.scottishmedicines.org.uk/files/advice/midodrine_hydrochlorine_Bramox_Abbreviated_FINAL_Sept_2015_for_website.pdf)
- [http://www.ukmi.nhs.uk/applications/ndo/record\\_view\\_open.asp?newDrugID=6679](http://www.ukmi.nhs.uk/applications/ndo/record_view_open.asp?newDrugID=6679)
- <http://www.hsric.nihr.ac.uk/topics/midodrine-bramox-for-orthostatic-hypotension/>
- <http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1446187110351.pdf>
- <http://www.mims.co.uk/drugs/cardiovascular-system/circulatory-disorders/bramox>
- [http://www.nhsbsa.nhs.uk/PrescriptionServices/Documents/PPD%20Drug%20Tariff/May\\_2016.pdf](http://www.nhsbsa.nhs.uk/PrescriptionServices/Documents/PPD%20Drug%20Tariff/May_2016.pdf)