Shared Care Guideline
Midodrine – for orthostatic hypotension and neurocardiogenic syncope

Executive Summary

- Update of Guideline following licencing of drug.
- The responsibility for initiating midodrine will remain with the hospital consultant.
- Midodrine will be prescribed for orthostatic hypotension and neurocardiogenic syncope as per licensing.
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document here.

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

1. Scope

Trust-wide and general practice for patients with idiopathic orthostatic hypotension.

2. Aim

To provide guidance on the prescribing of midodrine for orthostatic hypotension in primary and secondary care.

3. Introduction

Midodrine is a directly acting alpha- agonist which acts almost exclusively on peripheral alpha-adrenergic receptors of the arterial and venous vasculature increasing vascular tone. Midodrine causes an increase in supine and standing blood pressure, diastolic and systolic.

Midodrine is used to treat idiopathic orthostatic hypotension and has shown to be useful in neurocardiogenic syncope.

Midodrine is initiated in secondary care with follow up and continued supplies in primary care.

Midodrine is licensed for the treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out.

4. Abbreviations

BNF	British National Formulary
BP	Blood Pressure
CPJPG	Cambridgeshire and Peterborough Joint Prescribing Group
DME	Department of Medicine for the Elderly
HR	Heart rate
OH	Orthostatic Hypotension
POTS	Postural Orthostatic Tachycardia Syndrome
SPC	Summary of Product Characteristics
MHRA	Medicines and Healthcare products Regulatory Agency
LFT	Liver Function Tests

5. Dose and Administration

The starting dosage in adults (and adolescents) is 2.5mg three times a day. Doses should be increased at weekly intervals in small increments until an optimal response is obtained or side effects limit further dose escalation. Most patients are controlled at 30mg a day or less. Maximum daily dose is 30mg (10mg three times a day).

The maintenance dose for neurocardiogenic syncope is 5mg three times a day. The suggested dosing schedule being:

- 5mg on rising in the morning
- 5mg at midday
- The final 5mg taken during the late afternoon but not after 18.00 hours

The final dose should be taken before 18.00 hours to reduce the occurrence of supine hypertension during sleep. If this is not possible then midodrine should be taken at least four hours before bedtime.

Midodrine can be administered without regard to food.

Midodrine should not be taken if the patient is going to be lying down for any period of time i.e. sunbathing.

There are no dose adjustments required in the elderly but as there are no specific studies which have focused on a possible dose reduction in the elderly population cautious dose titration is recommended. Administration should be stopped, and GP informed if blood pressure in either position increased above 180mmgHg/100mmHg or is considered clinically significant.

Patients will continue on midodrine treatment until the patient's consultant or GP considers that treatment is no longer appropriate. Further information can be found in *in the* Summary of Product Characteristics for Midodrine 5mg tablets and Bramox 2.5mg tablets.

Criteria for treatment initiation, continuation and discontinuation

Initiation:

- Orthostatic hypotension with severe symptoms/ limiting daily activities
- Neurogenic syncope
- POTS with significant impact on daily activities

Continuation:

- Objective improvement in signs (tilt test or postural blood pressure)
- Subjective improvement in symptoms

Discontinuation:

- Unacceptable side effects
- Unwilling to continue
- Lack of subjective/ objective response
- On advice of specialist or no longer appropriate.

6. Adverse Effects

Very common (≥ 1 in 10)

- Piloerection
- Dysuria

Common (≥ 1 in 100 and < 1 in 10)

- Nausea, vomiting
- Dyspepsia
- Stomatitis
- Paraethesia
- Supine hypertension: (blood pressure ≥ 180/110 mmHg) with daily doses of more than 30 mg
- Urinary retention
- Pruritis
- Pruiritis of scalp
- Chills
- Flushing
- Rash

Uncommon (≥ 1 in 1000 and < 1 in 100)

- Insomnia
- Bradycardia
- Ventricular arrhythmia
- Urinary urgency
- Restlessness, excitability and irritability

- Supine hypertension: (blood pressure ≥ 180/110 mmHg) with daily doses up to 7.5mg
- Abdominal pain
- Headache
- Tachycardia
- Palpitations

Rare (≥ 1 in 10000 and < 1 in 1000)

- Deranged LFT, hepatic function abnormal
- Dizziness or light headedness
- Visual disturbance
- Chest pain
- Cerebrovascular accident

Other adverse reactions include anxiety, confusion, diarrhoea and increased tear production.

7. Cautions

- Severe orthostatic hypotension with supine hypertension
- Severe disturbances of the autonomic nervous system
- Atherosclerotic disease
- Prostate disease
- Renal and hepatic function
- Heart rate

8. Contraindications

Absolute contraindications:

- Hypersensitivity to the active substance or to any of the excipients
- Hypertension
- Vasovagal hypotension
- Severe cardiac disorders e.g. hypertrophic obstructive cardiomyopathy
- Cardiac valvular disorders
- Thyrotoxicosis
- Phaeochromocytoma
- Acute nephritis, acute renal disease
- Urinary retention
- Hyperthyroidism
- Narrow angle glaucoma
- Pregnancy or breastfeeding
- Proliferative diabetic retinopathy
- Serious prostate disorder

Relative contraindications:

- Cor-pulmonale
- Renal impairment where a smaller starting dose may be required and titrated according to response
- Coronary heart disease.

9. Interactions

The hypertensive effects of midodrine can be enhanced by:

- Methyldopa
- Tricyclic antidepressants
- Antihistamines
- Corticosteroids
- Thyroid hormones

An exaggerated response to midodrine may be expected in:

- Patients who have received monoamine oxidase inhibitors within the previous 14 days
- Patient receiving other medications that metabolised by CYP2D6 enzyme e.g.
  - SSRI
  - Antiarrhythmics (including class 1A, 1B and 1C)
- Patients receiving other sympathomimetic agents e.g.:
  - Decongestants
  - Some appetite suppressants

Concomitant use of midodrine and agents that cause bradycardia e.g. cardiac glycosides and beta blockers may cause an exaggerated bradycardic response.

The effect of midodrine will be blocked by alpha-adrenergic antagonists such as prazosin.

Further information about dose and administration, adverse effects, cautions, contraindications and interactions can be found in the Summary of Product Characteristics for Midodrine 5mg tablets and Bramox 2.5mg tablets

10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

- BP, HR, subjective monitoring and tilt test.
- If an adverse event or abnormal laboratory test result is encountered, then the hospital specialist should be informed immediately.

11. Shared Care Responsibilities

a. Hospital specialist:

- Initially prescribe the treatment regimen.
- Provide an initial one-month supply of midodrine.
- Provide and discuss with the patient or carer:
    - Potential benefits and side effects
    - Possible drug interactions
    - The need to be aware of what actions to take if adverse events are suspected
- Send a letter to the GP requesting shared care for the patient.
- Monitor subjective improvement BP, HR and if appropriate tilt test at each clinic appointment until stable unless agreed by the GP that the GP will escalate the dose
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Provide back- up advice for the GP.
- Inform GP of patients who do not attend clinic appointments and advise regarding arrangements for further follow up.
- To provide any advice to the patient/carer when requested.
- Report adverse events to the MHRA via the yellow card scheme.

b. General Practitioner:

- Agreement to shared care guideline by the GP.
- Continue the supply of midodrine after treatment has been initiated by the hospital consultant
- Monitor the patient's progress every six months following initiation or earlier if the patient's condition changes, by the specialist or GP if indicated, including BP, HR, subjective improvement and if appropriate tilt test (if possible, to perform in the practice)
- It is advisable to monitor the renal and hepatic function routinely but not specifically
- Report any adverse events to the hospital specialist. If any unusual or serious adverse event is reported or if an abnormality is detected in any laboratory result which may be relevant to midodrine treatment, the relevant hospital team should be contacted immediately.
- Discontinue treatment (where necessary) on advice of specialist.
- Refer to the product information regarding potential interactions/ cautions.
- Request advice from the hospital specialist when necessary.

c. Patient or parent/carer:

- Consent to treatment with midodrine.
- Take medication as advised by the specialist and comply with follow up arrangements.
- Share any concerns regarding treatment with midodrine.

- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects or warning symptoms to the hospital specialist or GP.
- Notify the GP of any use or intended use of over the counter or herbal medicines.
- Arrange for ongoing supply (give GP surgery seven days' notice).

12. Contact numbers for advice and support

Cambridge University Hospitals NHS Foundation Trust

Specialist	Post	Telephone
Dr Jane Wilson	Consultant Geriatrician	01223 217785
Medicines information		01223 217502

Royal Papworth Hospital NHS Trust

Specialist	Post	Telephone
Dr G Mellor	Consultant Cardiologist (Papworth Clinical Lead for Midodrine Shared Care)	01223 639527
Dr S Agarwal	Consultant Cardiologist	01223 639557
Dr D Begley	Consultant Cardiologist	01223 639558
Dr S Fynn	Consultant Cardiologist	01223 639542
Dr P Heck	Consultant Cardiologist	01223 639547
Dr C Martin	Consultant Cardiologist	01223 639552
Dr M Virdee	Consultant Cardiologist	01223 639537
Bridget Humphreys	Arrhythmia Specialist Nurses	01223 638102
Tracey Welch	Arrhythmia Specialist Nurses	01223 638103
Michele-Roberto Rella/ Stephanie Williams	Cardiology Lead Pharmacists	01223 638179
Patient Medicines Helpline Service		01223 638777

North West Anglia NHS Foundation Trust

Specialist	Post	Telephone
Dr Riaz Mappilakkandy	Consultant Physician	01733 678000
Dr J Porter	Consultant Cardiologist	01733 673815
Dr John Thorpe	Consultant Neurologist	01733 673549

13. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service Equality and Diversity statement.

14. Disclaimer

It is **your** responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

15. Document Management

Ratification Process	**Details**
Authored by:	Cambridge University Hospitals NHS Foundation Trust
Ratified by:	Cambridgeshire and Peterborough Joint Prescribing Group
Date ratified:	July 2023
Review date:	July 2026
Version number:	3

The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics for Midodrine 5mg tablets or www.medicines.org.uk

Shared Care Guideline GP Template Letter

Shared Care Guideline Title - Template Letter

{GP ADDRESS}

Dear Dr,

{PATIENT DETAILS}

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. He/she has [description of diagnosis]. I have therefore initiated [medication name] and am writing to ask you to participate in the shared care for this patient.
This medication and indication has been accepted as suitable for shared care by the Cambridgeshire and Peterborough Integrated Care System. I agree to the secondary care responsibilities set out in the shared care agreement for this medication. I am therefore requesting your agreement to share the care of this patient.

Medication name: Midodrine

Current dose: {insert dose}

Date medication started: {Insert date}

Date after which GP to start prescribing: {Insert date}[1]

{Insert if applicable - Last bloods were taken on {Insert date} and these show {Insert blood test details} within the normal range. The latest results are attached below.}
{Insert if applicable - The dose has been titrated and is stable.}
I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted and the need for monitoring, how monitoring will be arranged, and the roles of the consultant/nurse specialist, GP and the patient in shared care.
I confirm the patient has understood and is satisfied with this shared care arrangement.
Yours sincerely

{Consultant name}

[1]This should be the date when the last prescription was issued. It is expected that patients will request a repeat prescription sometime after this date.