Cambridge University Hospitals NHS Foundation Trust
Papworth Hospital NHS Foundation Trust
Hinchingbrooke Health Care NHS Trust
NHS Cambridgeshire and Peterborough Clinical Commissioning Group
Peterborough and Stamford Hospitals NHS Foundation Trust

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 licencing.
- Please note that midodrine only has a shelf life of 8 weeks from opening
- 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. Further information about the general responsibilities of the hospital specialist and GP can be found here

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 now holds a UK product license hence prompting an update of the guidance. It 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.

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 ie 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.

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 the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1441947213533.pdf

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
- Pruritus of scalp
- Dysuria

Common (≥ 1 in 100 and < 1 in 10)
- Nausea
- Dyspepsia
- Stomatitis
- Paraesthesia
- Headache
- Supine hypertension
- Urinary retention
- Pruritus
- Chills
- Flushing
- Rash

Uncommon (≥ 1 in 1000 and < 1 in 100)
- Insomnia
- Bradycardia
- Urinary urgency
- Restlessness, excitability and irritability

Rare (≥ 1 in 10000 and < 1 in 1000)
- Tachycardia
- Palpitations
- Deranged LFT

Other adverse reactions include anxiety, confusion, abdominal pain, vomiting and diarrhea.

Further information can be found in the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1441947213533.pdf

7. Cautions

Further information can be found in the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1441947213533.pdf

8. Contraindications

Absolute contraindications:
- Hypertension
- Severe cardiac disorders e.g. hypertrophic obstructive cardiomyopathy
- Cardiac valvular disorders
- Thyrotoxicosis
- Phaeochromocytoma
- Acute nephritis
- Urinary retention
- Hyperthyroidism
- Narrow angle glaucoma
- Pregnancy or breastfeeding

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

Further information can be found in the Summary of Product Characteristics
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1441947213533.pdf

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
- 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 can be found in the Summary of Product Characteristics – http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1441947213533.pdf

9. 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.

10. 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.
- 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).

11. 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

Papworth Hospital NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Dr A Grace	Consultant Cardiologist	01480 364362
Patient Services Cardiac	Secretary to Dr Grace	01480 364920
B Thomson S Williams	Cardiac Directorate Pharmacist Cardiac Directorate Pharmacist	01480 364762 01480 364762
Pharmacy Medicines Information Service		01480 364179
Pharmacy Medicines Helpline		01480 364739 (Answerphone)

Peterborough and Stamford Hospitals NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Dr SH Guptha	Consultant Physician	01733 673885
Dr J Porter	Consultant Cardiologist	01733 673815
Dr John Thorpe	Consultant Neurologist	01733 673549
Medicines information		01733 677303

Hinchingbrooke Health Care NHS Trust		
Specialist	**Post**	**Telephone**
Dr Colin Borland	Consultant Physician	01480 418015
Medicines information		01480 416142

12. Equality and Diversity Statement

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

13. Disclaimer

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

14. Document Management

Document ratification and history	
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Approved by:	Papworth Hospital NHS Foundation Trust Drugs and Therapeutics Committee
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Approved by:	Ann Ritchie Pharmacist Team Manager - Procurement and Formulary Peterborough and Stamford Hospitals NHS Foundation Trust
Date approved:	10th June 2016
Approved by:	Stephen Cook Chief Pharmacist Hinchingbrooke Health Care NHS Trust
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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
http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1441947213533.pdf