

# MIDODRINE

## Traffic light classification- Amber 2 Information sheet for Primary Care Prescribers

### Key points/interactions

- Midodrine should only be considered when non-pharmacological strategies with or without volume expanding drugs such as fludrocortisone have failed to alleviate the patient's symptoms.
- The most common side effects seen with midodrine are piloerection (goose bumps), pruritus and paraesthesiae (particularly of the scalp), urinary retention or urgency, and supine hypertension.
- Midodrine interacts with alpha adrenergic blocking drugs, and medicines which decrease the heart rate (e.g. digoxin and beta-blockers).
- Patients taking midodrine should avoid other drugs with sympathomimetic pressor effects, including OTC preparations containing pseudoephedrine.

### Licensed Indications

Midodrine is indicated in 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.

### Medicines Initiation

Midodrine should be initiated by a consultant geriatrician/cardiologist/neurologist or other specialist experienced in the management of neurocardiovascular instability. Midodrine should only be considered when non-pharmacological strategies with or without volume expanding drugs such as fludrocortisone have failed to alleviate the patient's symptoms. A diagnostic and management algorithm is included at [Appendix 1](#).

### Dose Regimen and Route of Administration

The initial titration of midodrine dosage (3 months) will be carried out by the initiating specialist  
Initial dose: 2.5 mg oral three times a day. The last daily dose should be taken **at least 4 hours before bedtime** in order to prevent supine hypertension. Midodrine may be taken with food.  
Depending on the results of supine and standing blood pressure recordings, this dose may be increased weekly up to a dose of 10 mg three times a day. This is the usual maintenance dosage and should not be exceeded.

### Duration of treatment

A careful evaluation of the balance of the response to treatment and the risks needs to be undertaken by the specialist before any dose increase and at least every 6 months.  
In young adults, it may be reasonable to expect the occurrence of postural symptoms to wane over time. For older adults the duration of treatment may also depend on the effects of co-morbid conditions on overall functional mobility such that the need for the drug is obviated.

### Monitoring Requirements and Responsibilities

The specialist will be responsible for the monitoring required during initial titration – usually first 3 months. This includes baseline renal and liver function and regularly reviewing lying and standing blood pressures during initial treatment (weekly for the first 4 weeks and monthly thereafter).

### Ongoing monitoring in primary care

Frequency of monitoring	Test to be done		
	<a href="#">Lying and standing blood pressure</a>	Renal function	LFTs
Minimum 6 monthly or if symptoms recur	✓	✓	✓

- **Lying and standing blood pressures (see [Appendix 2](#) for instructions).** It may be more convenient for patients and primary care staff to advise the purchase of a home blood pressure monitor and the recording of readings in a diary.

### Contraindications

- Severe organic heart disease (e.g. bradycardia, heart attack, congestive heart failure, cardiac conduction disturbances or aortic aneurysm).
- Hypertension.
- Serious obliterative blood vessel disease, cerebrovascular occlusions and vessel spasms.
- Acute or severe kidney disease. (Creatinine clearance of less than 30 ml/min).
- Serious prostate disorder.
- Urinary retention.
- Proliferative diabetic retinopathy.
- Phaeochromocytoma
- Hyperthyroidism.
- Narrow angle glaucoma.
- Pregnancy and breast feeding
- Hypersensitivity

### Precautions

- Risk of supine Hypertension: Patients should be advised to report symptoms of supine hypertension immediately. Symptoms may include cardiac awareness, pounding in the ears, headache, blurred vision, etc. If these occur, the patient should discontinue the drug and consult with the prescribing physician.
- Urinary Retention: Midodrine may induce an increase in the tone of the internal sphincter of the urinary bladder which may lead to urinary retention. Midodrine also may affect the bladder trigone which may result in a delayed response to bladder filling. Patients should be told to report promptly any indication of urinary retention (e.g. hesitancy or frequency of micturition) which may be a sign of urinary retention.
- Midodrine should be used with caution in patients with urinary tract outflow obstruction, neurogenic bladder or similar conditions, since midodrine is eliminated by the kidneys (risk of accumulation).
- Caution must be observed in patients with atherosclerotic disease.

### Explicit Criteria for Review and Discontinuation of the Medicine

Adverse Event	Action
Symptoms of supine hypertension immediately such as chest pain, palpitations, shortness of breath, headache and blurred vision	Check lying and standing blood pressure. If supine hypertension present see below
Supine hypertension (systolic BP>160mmHg)	Usually dose related but check last dose is taken at least 4 hours before bedtime Consider dose reduction or withhold and discuss with specialist. If persistent despite dose reductions consider discontinuation in consultation with specialist
Urinary retention	Withhold and discuss with specialist team.
Acute or severe renal impairment	Withhold until discussed with specialist team. The active metabolite is almost exclusively cleared via the kidneys and thus toxicity is likely, check for urinary retention.
AST, ALT > twice upper limit of reference range	Withhold until discussed with specialist team
Lying or standing Blood pressure increases above 180/100 mm Hg or is considered clinically significant.	Withhold until discussed with specialist team.
Persistently labile blood pressure after the initial titration	Discontinue treatment

**In addition to absolute values for haematological or biochemical indices a rapid fall or rise or consistent downward or upward trend in any value should prompt caution and extra vigilance.**

For a full list of side effects refer to the BNF or Summary of Product Characteristics.

### **Clinically relevant medicine interactions and their management**

**Midodrine is unlikely to be listed in the interactions section on GP computer systems**, and hence co-prescribing of potentially interacting drugs may not be highlighted.

Interacting medicine	Management
Heart rate reducing drugs (e.g. digoxin, beta-blockers)	Risk of heart block with digoxin – avoid. Monitoring for signs and symptoms of bradycardia is recommended if midodrine is combined with other drugs that directly or indirectly reduce the heart rate.
Sympathomimetics and other vasopressor agents (e.g. TCAs, antihistamines, thyroid hormones etc.)	Avoid concomitant use- risk of pronounced hypertension
Corticosteroids	Risk of hypertension and glaucoma / raised IOP with concomitant use. Monitor
Alpha-adrenergic antagonists e.g. doxazosin, tamsulosin	Avoid, will block the effects of midodrine (an alpha 1 agonist)

Midodrine is the rapidly absorbed pro-drug of the pharmacologically active constituent desglymidodrine. Desglymidodrine is a sympathomimetic agent with a direct and selective effect on the peripheral  $\alpha$ 1-adrenergic receptors.

*For further information on contraindications, precautions, adverse effects and interactions refer to the BNF or [Summary of Product Characteristics](#).*

### **Information given to patient**

The Patient Leaflet in branded packaging ([click here](#)) gives detailed information for patients

### **An estimate of the potential medicine costs (and any additional costs) to primary care**

12 months treatment with midodrine 10mg twice daily is approximately £1100.

### **REFERENCES**

1. Bramox tablets SPC last updated on <https://www.medicines.org.uk/emc> 18/10/2018.
2. Shared Care Agreement for the use of midodrine for severe orthostatic hypotension. Brancaster Pharma Sept 2015.
3. NICE evidence summary new medicine [ESNM 61October 2015](#)

### **AUTHORS**

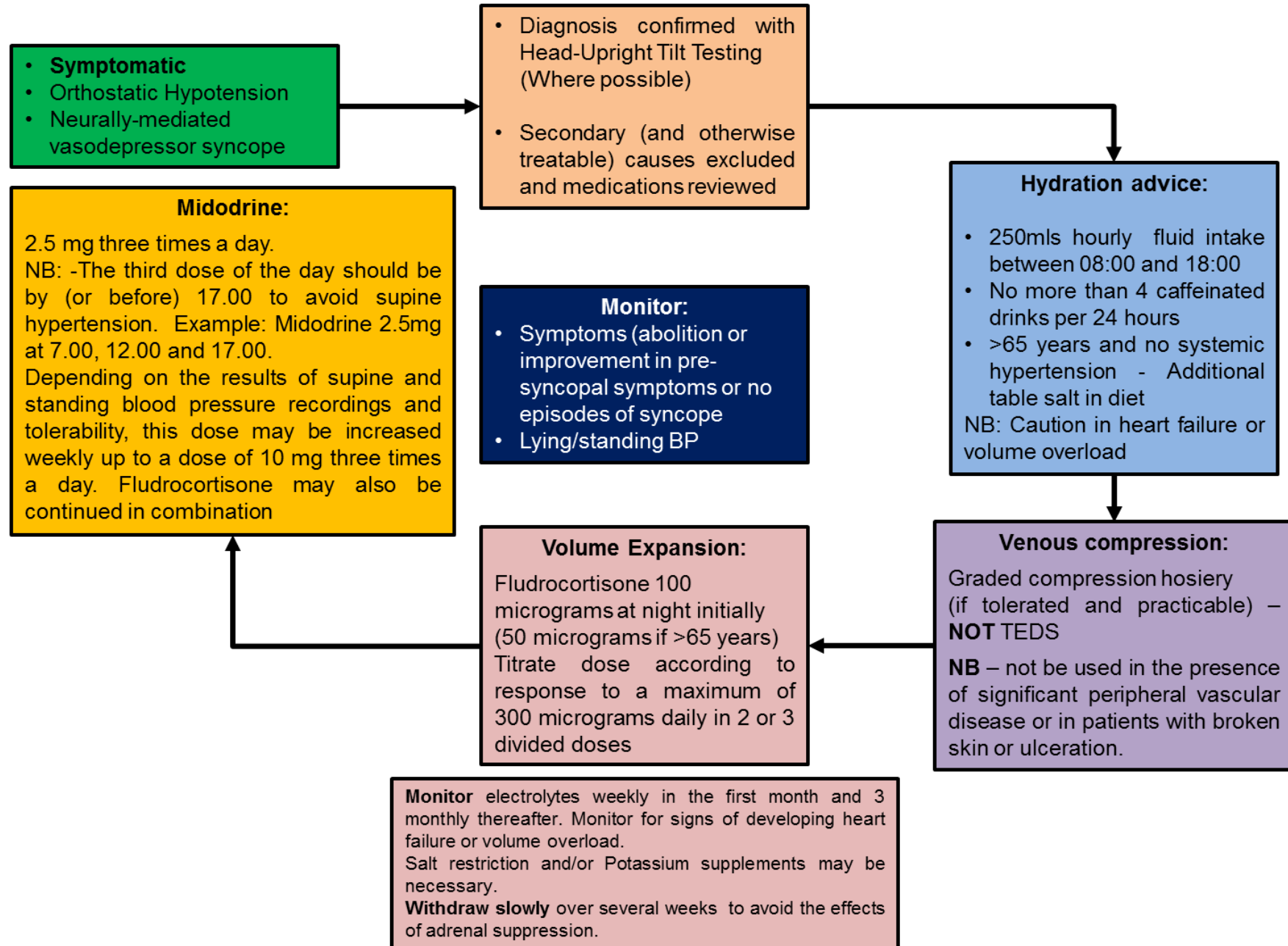
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Appendix 1 – Algorithm Summarising the Management of Orthostatic Hypotension



## Appendix 2 – Instructions for the measurement of lying and standing blood pressure

### How is Lying and Standing Blood Pressure Measured?

Automated equipment can be used but where measurements are difficult it will be necessary to use a manual sphygmomanometer. Ascertain if the patient is able and safe to stand. Illness may impair their ability to bear weight and severe symptoms resulting from a profound fall in blood pressure on standing could lead to a fall. Sitting blood pressure can be taken however this can reduce the sensitivity of the test

1. Ask the patient to lie on the bed.
  2. Wait at least 5 minutes.
  3. Apply the cuff securely such that its position will be unchanged when the patient stands up.
  4. Take Blood Pressure lying down.
  5. Ask or assist the patient to stand up or sit on the edge of the bed if the patient is unable to stand.
  6. Take BP immediately **AND** repeat after 3 minutes of standing/sitting on edge of bed.
- Stop if the patient is unable to stand/sit unsupported or is at risk of falling
  - Keep the patient standing/sitting for the full 3 minutes.

### **What is Abnormal?**

Postural hypotension is said to be present if:

- Systolic Blood Pressure falls by > 20mmHg on standing  
Diastolic Blood Pressure falls by >10mmHg on standing

**OR**