

Midodrine prescribing information sheet

V2

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Nottinghamshire Area Prescribing Committee

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 medicines 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 paresthesia (particularly of the scalp), urinary retention or urgency, and supine hypertension.
- Midodrine interacts with alpha adrenergic blocking medicines and medicines which decrease the heart rate (e.g., digoxin and beta-blockers). See interaction section for more information.
- Patients taking midodrine should avoid other medicines with sympathomimetic pressor effects, including OTC preparations containing pseudoephedrine.

Midodrine is the rapidly absorbed pro-medicine of the pharmacologically active constituent desglymidodrine. Desglymidodrine is a sympathomimetic agent with a direct and selective effect on the peripheral α 1-adrenergic receptors. This induces vasoconstriction of the venous system and increases peripheral arterial resistance resulting in an increase in arterial blood pressure.

Licensed Indication

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. Uses for other types of orthostatic hypotension are off label and not included within this information sheet.

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 medicines such as fludrocortisone have failed to alleviate the patient's symptoms. A diagnostic and management algorithm is included in [Appendix 1](#).

Dose Regimen

The recommended starting dose is 2.5 mg orally three times a day. The last dose of the day should be taken **at least 4 hours before bedtime** to prevent supine hypertension. Midodrine tablets should be taken with a drink of water and can be taken during mealtimes. Depending on the results of supine and standing blood pressure recordings, this dose may be increased weekly up to a maximum dose of 10 mg three times a day. This is the usual maintenance dosage and should not be exceeded.

Duration of treatment

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 co-morbidity affecting overall functional mobility such that midodrine may no longer be needed or appropriate.

Monitoring Requirements and Responsibilities

The specialist will be responsible for the monitoring required during initial titration, usually the first 3 months. This includes baseline renal and liver function and regularly reviewing supine and standing blood pressures during initial treatment. This would be weekly for the first 4 weeks and monthly thereafter. Patients may be advised to self-monitor and report readings back to the specialist during the titration phase. A careful evaluation of the response to treatment and the risks needs to be undertaken by the specialist before any dose increase and six monthly if required such as for patients with additional risk factors. Increased monitoring and review needs will be advised by the specialist. Once stable, the patient should be managed by GP in line with medication reviews.

Ongoing monitoring in primary care

Frequency of monitoring	Test to be done		
	Supine and standing blood pressure	Renal function	LFTs
Minimum 6 monthly or if symptoms recur	✓		
Annual	✓	✓	✓

- **Supine 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.
- 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.

Advice to patients regarding side effects

- The most common side effects seen with midodrine are piloerection (goose bumps), pruritus and paresthesia (particularly of the scalp), urinary retention or urgency and supine hypertension.
- Patients should be advised to report symptoms of supine hypertension immediately. Symptoms may include cardiac awareness, chest pain, palpitations, shortness of breath, pounding in the ears, headache, blurred vision, etc.
- Patients should be told to report promptly any signs of urinary retention e.g., hesitancy or frequency of micturition. This is because midodrine may induce an increase in the tone of the internal sphincter of the urinary bladder which may lead to urinary retention. It may also affect the bladder neck which may result in a delayed response to bladder filling.
- Patients on agents that directly/indirectly reduce the heart rate and experiencing any signs of bradycardia e.g. pulse slowing, increased dizziness, syncope, cardiac awareness should be advised to discontinue midodrine and consult with prescribing physicians.
- See more information in Explicit criteria for review and discontinuation of medicine.

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.
- Pheochromocytoma
- Hyperthyroidism.
- Narrow angle glaucoma.
- Pregnancy and breast feeding
- Hypersensitivity

Cautions

- Midodrine should be used with caution in patients with urinary tract outflow obstruction, neurogenic bladder or similar conditions, as midodrine is eliminated by the kidneys (risk of accumulation).
- Caution is advised in prostrate disorders due to the possibility of urinary retention.
- Caution must be observed in patients with atherosclerotic disease.
- Caution must be observed in patients with diabetes mellitus as this patient group may suffer from supine hypertension
- Use in patients who are at increased risk of glaucoma/increased intra ocular pressure, or those treated with mineralocorticoids/fludrocortisone should be avoided or monitored very closely.
- Slowing of the heart rate may occur, primarily due to vagal reflex therefore great caution should be taken when using midodrine together with other agents that directly or indirectly slow the heart.

Explicit Criteria for Review and Discontinuation of the Medicine

Adverse Event	Action
Symptoms of supine hypertension such as chest pain, palpitations, shortness of breath, headache, and blurred vision	Check supine and standing blood pressure. If supine hypertension present, see below
Supine hypertension (systolic BP>160mmHg and < 180mmHg).	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
Supine or standing blood pressure increases above 180/100 mm Hg or any increase that is considered clinically significant.	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
Urinary retention	Withhold until discussed with specialist team.
Persistently labile or severely fluctuating blood pressure after the initial titration	Discontinue treatment
Change in mobility e.g. bedbound or prognosis that means midodrine is no longer essential e.g. end of life	Discontinue treatment
Intolerable side effects	Withhold until discussed with specialist team

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 medicines may not be highlighted. The list below is not exhaustive. For a full list, see manufacturers guidance available [here](#))

Interacting medicine	Management
Digitalis preparations e.g. digoxin	Avoid as heart block may occur
Heart rate reducing medicines (e.g. beta-blockers)	Monitoring for signs and symptoms of bradycardia is recommended if midodrine is combined with other medicines that directly or indirectly reduce the heart rate.
Sympathomimetics and other vasopressor agents (e.g. Tricyclic antidepressants), monoamine oxidase inhibitors, antihistamines, thyroid hormones etc.), over the counter decongestants	Avoid concomitant use - risk of pronounced hypertension
Corticosteroids	Risk of hypertension when used in combination. If midodrine is being used in combination with mineralocorticoids or glucocorticoids (e.g. fludrocortisone) there is an increase in the risk of glaucoma/IOP and should be monitored carefully.
Alpha-adrenergic antagonists e.g. doxazosin, tamsulosin	Avoid as they will block the effects of midodrine (an alpha 1 agonist)

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

Information given to patient

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

REFERENCES

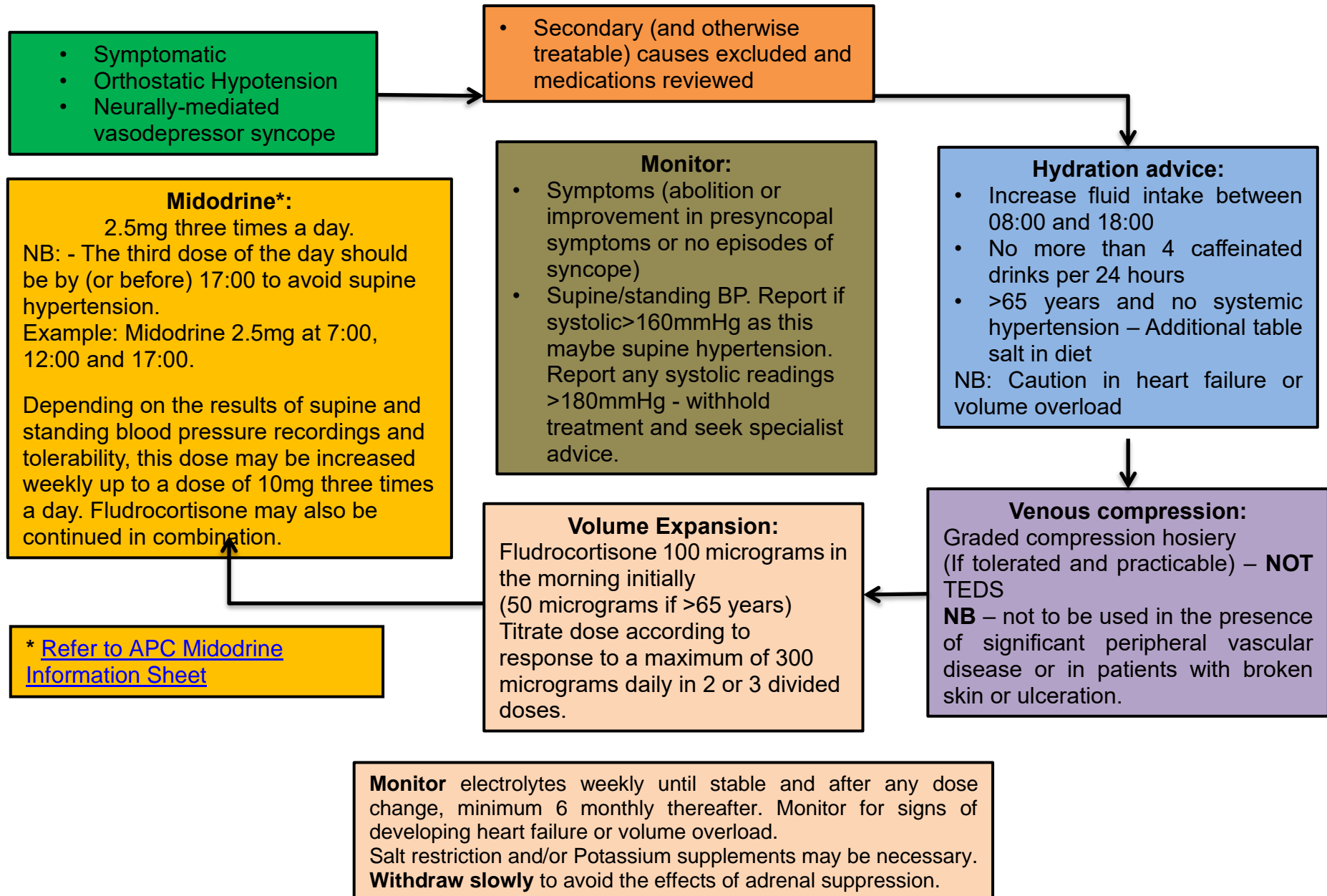
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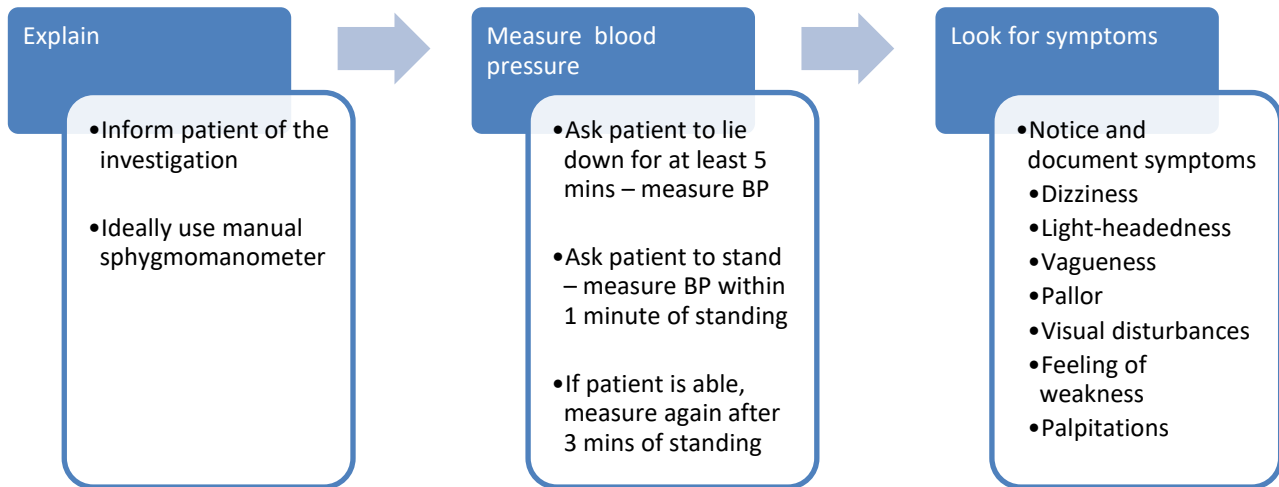
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Appendix 1 – Management of Orthostatic Hypotension Algorithm



Appendix 2 – Supine and Standing Blood Pressure Measurement

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.



- Ask or assist the patient to stand up or sit on the edge of the bed if the patient is unable to stand
- 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

Postural hypotension is said to be present if:

- Systolic Blood Pressure falls (SBP) by ≥ 20 mmHg on standing (with or without symptoms)
- SBP falls to below 90mmHg on standing (even if the drop is less than 20mmHg with or without symptoms)
- Diastolic Blood Pressure falls by ≥ 10 mmHg on standing with symptoms (although clinically much less significant than a drop in systolic BP)

Report any systolic readings > 160 mmHg as this may indicate supine hypertension. Report any systolic readings > 180 mmHg to prescribing physician for discussion with specialist team and withhold treatment.