NHS BSW ICB Primary care guidance for the treatment of postural hypotension

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

Background

Orthostatic (or postural) hypotension is defined as

- a sustained reduction of systolic blood pressure (BP) of ≥20 mmHg and/or diastolic BP of ≥10 mmHg or
- systolic BP fall >30 mmHg in hypertensive patients with supine systolic BP > 160 mmHg, when assuming a standing position or during a head-up tilt test of at least 60°.

Orthostatic hypotension results from an inadequate physiological response to postural changes in BP. In people with the condition, standing leads to an abnormally large drop in BP which can result in symptoms such as light-headedness, dizziness, blurring of vision, syncope and falls.

Orthostatic hypotension is more common in older people. It may be idiopathic or arise as a result of disorders affecting the autonomic nervous system (e.g. Parkinson's, multiple system atrophy or diabetic autonomic neuropathy), from a loss of blood volume or from dehydration. Some estimate that 50% of cases have a medication cause; these include antihypertensives, diuretics, alpha blockers, nitrates, tricyclic antidepressants etc. **Medication review as a first step is important**.

Non-pharmacological management options are recommended first-line if no medication cause is found (including increased water and salt ingestion) with BP monitoring. If these do not resolve symptoms, midodrine or fludrocortisone alone, or in combination, may be considered. The choice of starting fludrocortisone or midodrine depends on whether the problem is primarily volume or autonomic neuropathy related, so a tailored approach is needed by the specialist.

Drug treatment options:

- Midodrine Hydrochloride: Licensed Indication
- Fludrocortisone Acetate Tablets: "Off-Label" indication

Both are **AMBER** on BSW Formulary (*suitable for GP prescribing following specialist initiation or recommendation*)

Dose, frequency and titration

Titration to maximum tolerated and effective dose will be undertaken by the specialist:

Midodrine:

- Initially 2.5 milligrams TDS (ideally before rising, mid-morning and mid-afternoon). Titration is usually as follows:
- Week one: 2.5 milligrams TDS
- Week two: 5 milligrams TDS
- Week three: 7.5 milligrams TDS
- Week four: 10 milligrams TDS (maximum dose)

Effects can be seen from as little as half to one hour following doses and the increase in standing systolic pressure can be sustained for up to 6 hours or more. The last daily dose should be taken at least 4 hours before bedtime in order to prevent supine hypertension.

Fludrocortisone: Initially 100 micrograms each morning (50 microgram if >65 years). Dose titrated according to response up to a max of 400 micrograms each morning. Patients taking fludrocortisone should carry steroid treatment cards giving clear guidance on precautions to minimise risk and providing details of prescriber, drug, dosage and duration of treatment.

COMBINATION USE: If higher doses of midodrine or fludrocortisone are not tolerated due to side-effects, consider combination treatment as advised by a specialist.

Duration of treatment is subject to patients' response to treatment and tolerability.

Baseline investigations

- Initial lying and standing BP
- U&E, glucose, BP, HR, weight, FBC, Bone Mineral Density (Fludrocortisone only, use FRAX before DEXA (note that DEXA is inaccurate/uninterpretable in those > 80-85 years)), lipids

Additionally for fludrocortisone: assess for risk factors or pre-existing conditions that may be exacerbated by steroid therapy, such as diabetes, dyslipidaemia, CVD, GI disorders, affective disorders, or osteoporosis.

The specialist should advise patient to self-monitor and immediately report symptoms of supine hypertension e.g. palpitations, chest pain, shortness of breath, headache, blurred vision.

Patients who are still symptomatic after 4 weeks of treatment should be told to report back to their GP who may wish to seek advice from specialist teams, see contact details below.

NHS BSW ICB Primary care guidance for the treatment of postural hypotension

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

On-going investigations

- Monitor U&Es and LFTs and supine/standing BP as recommended by specialist.
- Monitor for signs of developing heart failure or volume overload.
- **Additionally for fludrocortisone (a potent mineralocorticoid):** monitor dosage and salt intake to avoid hypertension, oedema or weight gain. Salt restriction and/or potassium supplements may be necessary if advised by the specialist.

Treatment Pathway

Symptoms suggestive of orthostatic hypotension

Diagnosis confirmed by Head-Upright Tilt Testing (if possible)
Secondary and otherwise treatable causes should be excluded and medication reviewed.

Non-Pharmacological treatment:

- **Hydration advice: 250ml hourly fluid intake between 8am to 6pm**
- **>65 years and no systemic hypertension: Additional table salt in diet (NB: Caution in heart failure or volume overload)**

Pharmacological treatment (Choice of drug determined by Specialist)

Fludrocortisone (off-label):
100micrograms each morning (50micrograms if >65 yrs). Titrate dose according to response up to a maximum of 400micrograms each morning. Fludrocortisone works as a volume expander but is not licensed for this use.

Midodrine (licensed):
2.5mg TDS. The third dose of the day should be taken at least four hours before bedtime to avoid supine hypertension. Dose may be increased weekly up to 10mg TDS depending on response and tolerability.

Combination use of midodrine and fludrocortisone:
If higher doses of midodrine or fludrocortisone are not tolerated due to side-effects, consider combination treatment as advised by a specialist.

Adverse effects (only most common are listed):

- **Midodrine**: Piloerection, itchy scalp, paraesthesia, paraesthesia of the scalp, urinary retention, supine hypertension, increased supine hypertension, and pruritus. Panic/anxiety occurs in about 5% of patients.
- **Fludrocortisone**: Hypertension, sodium and water retention, potassium loss and increased calcium excretion. High doses can cause Cushing's syndrome

This list is not exhaustive. The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information.

Cautions and contra-indications

Contraindications (see SPC or BNF for further information)

Both medicines are contraindicated if there is hypersensitivity to the active substance or to any excipients listed in their SPC.

Additionally for midodrine:

Contraindicated in aortic aneurysm; blood vessel spasm; bradycardia; cardiac conduction disturbances; cerebrovascular disease including stroke (relative C/I); congestive heart failure (relative C/I); hypertension; hyperthyroidism; myocardial infarction; narrow-angle glaucoma; phaeochromocytoma; proliferative diabetic retinopathy; serious obliterative blood vessel disease; serious prostate disorder; urinary retention.

Additionally for fludrocortisone:

Contraindicated in systemic infections unless specific anti-infective therapy is employed.

Cautions: (see SPC or BNF for further information)

For both medicines:

Regular monitoring of supine and standing BP is necessary due to the risk of supine hypertension. Patients should report symptoms of supine hypertension immediately (as detailed above). If supine hypertension occurs, which is not overcome by reducing the dose, treatment must be stopped; DO NOT stop fludrocortisone abruptly. The risk of supine hypertension occurring during the night can be reduced by elevating the head (e.g. multiple pillows).

Additionally for midodrine:

Use with caution in hepatic impairment, atherosclerotic cardiovascular disease (especially with symptoms of intestinal angina or claudication of the legs); elderly (manufacturer recommends cautious dose titration); prostate disorders (midodrine may cause urinary retention). Use caution when midodrine is used concomitantly with cardiac glycosides and other agents that directly or indirectly reduce heart rate; slowing of the heart rate may occur after midodrine administration, due to vagal reflex.

Additionally for fludrocortisone:

As with all systemic corticosteroids, use with caution in renal impairment, congestive heart failure; diabetes mellitus (including a family history of); diverticulitis; epilepsy; glaucoma (including a family history of or susceptibility to); history of steroid myopathy; history of tuberculosis or X-ray changes (frequent monitoring required); hypertension; hypothyroidism; infection (particularly untreated); long-term use; myasthenia gravis; ocular herpes simplex (risk of corneal perforation); osteoporosis (in children); osteoporosis (post-menopausal women and the elderly at risk) (in adults); peptic ulcer; psychiatric reactions; recent intestinal anastomoses; recent myocardial infarction (rupture reported); severe affective disorders (particularly if history of steroid-induced psychosis); thromboembolic disorders; ulcerative colitis.

Interactions:

Midodrine:

- Glycosides: Simultaneous use of digitalis preparations may potentiate heart rate reducing effect and heart block may occur.
- Corticosteroid preparations: Midodrine may enhance the hypertensive effects of corticosteroids. Patients treated with midodrine in combination with mineralocorticoids or glucocorticoids (e.g. fludrocortisone) may be at increased risk of glaucoma/increased intraocular pressure; monitor carefully.

Fludrocortisone:

- Oral anticoagulants: Corticosteroids may potentiate or decrease anticoagulant action
- Antidiabetics: Corticosteroids may increase blood glucose; monitor diabetic control, esp. when corticosteroids are initiated, discontinued, or dose is changed.
- Hepatic Enzyme Inducers (e.g. CBZ/phenytoin/rifampicin): There may be increased metabolic clearance of Fludrocortisone. Observe for possible diminished effect of steroid, and adjust the dosage accordingly.

This list is not exhaustive. The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information.

NHS BSW ICB Primary care guidance for the treatment of postural hypotension

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

Actions to be taken if abnormal results/adverse effects

Review and discontinuation of Midodrine by GP	
Symptoms of supine hypertension such as chest pain, palpitations, shortness of breath, headache, blurred vision	Check lying and standing BP. If supine hypertension present, see below.
Supine hypertension (systolic BP>160mmHg) (hypertension in the supine position, e.g. at night).	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 reduction, consider discontinuation in consultation with specialist.
Urinary retention	Withhold and discuss with specialist.
Acute or severe renal impairment	Withhold until discussed with specialist. The active metabolite is almost exclusively renally cleared and thus toxicity is likely. Check for urinary retention.
AST, ALT >twice upper limit of reference range	Withhold until discussed with specialist.
Lying or standing BP increases >80/100mmHg or is considered clinically significant	Withhold until discussed with specialist.
Persistently labile BP after initial titration	Discontinue treatment/discuss with specialist.
Review and discontinuation of Fludrocortisone by GP	
Symptoms of supine hypertension such as chest pain, palpitations, shortness of breath, headache, blurred vision	Check lying and standing BP. If supine hypertension present, see below.
Supine hypertension (systolic BP>160mmHg) (hypertension in the supine position, e.g. at night).	Usually dose related. Consider dose reduction or following discussion with specialist. If persistent despite dose reduction, consider discontinuation in consultation with specialist.
Symptoms of adrenal suppression: nausea, D&V, abdominal pain, anorexia/weight loss, headache (usu. In the morning), fever, weakness/fatigue, malaise, myalgia, arthralgia, psychiatric symptoms (mood and behaviour changes).	Seek specialist advice. Withdrawal of corticosteroids after prolonged therapy must always be gradual and should be tapered according to dose and duration of treatment to avoid acute adrenal insufficiency (see BNF). A steroid card and patient information leaflet should be supplied by the specialist to every patient when a systemic corticosteroid is prescribed.
Hypokalaemia	Consider prescribing potassium supplements
Persistently labile BP after initial titration	Discuss with specialist for advice.

Advice to patients and carers:

- Patients on midodrine 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.
- Patients taking fludrocortisone should carry steroid treatment cards which give clear guidance on the precautions to be taken to minimise risk and which provides details of prescriber, drug, dosage and the duration of treatment.

Useful NICE patient information about the use of fludrocortisone for postural hypotension can be found here (Oct 2013): https://www.nice.org.uk/advice/esuom20/resources/fludrocortisone-for-low-blood-pressure-on-standing-postural-hypotension-pdf-17488116421

NHS BSW ICB Primary care guidance for the treatment of postural hypotension

Bath and North East Somerset, Swindon and Wiltshire Integrated Care Board

BSW Specialist contact information:

RUH Neurology	E-mail/address	Telephone	
Dr N Giffin	Nicola.giffin@nhs.net		X5456
Dr P Lyons	Paul.lyons@nhs.net		X4433
Dr G Chohan	g.chohan@nhs.net		X5378
RUH Care of the Elderly			
Dr Sara Evans	sara.evans1@nhs.net	Sec: 01225 821028	
Dr Chris Dyer	chris.dyer1@nhs.net		
HCRG Falls clinic	Care Coordination Centre	0300 247 0200	
GWH Care of the Elderly			
Dr Nic Watson	Nicola.watson12@nhs.net	Sec: 01793 605108 Dr Watson: 01793 607349	
GWH Neurology			
Dr Hinze/Dr Yiin	Send all requests for advice and guidance through choose and book	01793 605099	
Dr Lennox/Dr Paul/Dr Thompson		01793 605114	
Dr Zuromskis/ Dr Bajoriene		01793 605105	
Dr Mazzucco/Dr Morrish/Dr Sarangmat		01793 605114	
SFT Care of the Elderly			
Dr Hugo Powell	hugo.powell@nhs.net		
Dr Jonny Drayson	jonny.drayson@nhs.net		
SFT Neurology			
Dr Boyd Ghosh	Sft.admin.neurology@nhs.net	01722 429233	
Dr Chinar Osman			
Dr Joanna Lovett			
Dr Thomas Cox			

NOTE: GPs can use 'cinapsis' app to request consultant Geriatrician support with initiation from GWH and RUH

Annual treatment costs (at maximum dose) May 2023 Drug Tariff:

- Midodrine (10mg TDS): £902
- Fludrocortisone (300mcg in split doses): £254 (off-label)

References:

- British National Formulary. London: British Medical Association and The Royal Pharmaceutical Society of Great Britain; Accessed Oct 21 via: https://www.evidence.nhs.uk/formulary/bnf/current
- NICE evidence summary [ESUOM20]: Postural hypotension in adults: fludrocortisone, October 2013, Accessed Oct 2021 via: https://www.nice.org.uk/advice/esuom20/chapter/Key-points-from-the-evidence
- NICE Evidence summary [ESNM61]: Orthostatic hypotension due to autonomic dysfunction: midodrine, October 2015, Accessed Oct 2021 via: https://www.nice.org.uk/advice/esnm61/chapter/Key-points-from-the-evidence
- Summary of product characteristics: Midodrine. Accessed Oct 21 via: https://www.medicines.org.uk/emc/product/2265/smpc
- Summary of product characteristics: Fludrocortisone. Accessed Oct 21 via: https://www.medicines.org.uk/emc/product/11457

Written by (Author Name, Organisation & Role):	Dr Rachel Hobson, Lead Clinical effectiveness Pharmacist, NHS BSW CCG
Contributors:	Neurology & Care of the Elderly teams at RUH/GWH/SFT
Document history:	V1 - First approved BSW APC October 2021
	V2 - Minor review May 2023 to replace logo and correct broken embedded hyperlinks and contact details.
Review Date:	05/2025