BSW APC: BaNES, Swindon & Wiltshire (BSW) CCG, Avon & Wiltshire Mental Health Partnership NHS Trust (AWP), Royal United Hospitals Bath NHS Foundation Trust, Great Western Hospitals NHS Foundation Trust, Salisbury NHS Foundation Trust, Virgin Care, Swindon Community Health Services, Wiltshire Health & Care

SHARED CARE AGREEMENT

Midodrine (licensed) &/or Fludrocortisone (off-label) for orthostatic hypotension – Adults

Amber TLS – 3 Months

Principles of Shared Care

Shared care agreements provide a framework for the seamless transfer of care from a hospital or specialist service setting to general practice, where this is appropriate and in the patient's best interest. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP (or other primary care prescriber) concerned and the patient to share their care.

Patients and/or carers must be centrally involved in any decision-making process. They should be supported by good quality information that helps them to both come to an informed decision about engagement in a shared care arrangement and sets out the practical arrangements for ongoing supplies of medicines.

The existence of a shared care agreement does not necessarily mean that the GP has to agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

Responsibilities of Secondary Care Specialist

- Initiate treatment and prescribe for the length of time agreed (at least 3 months) – this should be a sufficient amount of time to allow optimisation of treatment and demonstrate that the patient's response is consistent.
- Assess the patient and establish the diagnosis, determine a management strategy and ensure appropriate follow-up in conjunction with the GP.
- Discuss the benefits, risks and side effects of treatment with the patient as well as the off-label nature of medicines used if the medication being used is not a licensed product (fludrocortisone).
- Review concurrent medications for potential interactions prior to initiation.
- Undertake the clinical assessment and relevant monitoring at baseline and during the initiation period.
- Communicate details of treatment to GP (in writing or via secure email) within the first month of treatment and ask the GP whether he or she is willing to participate in shared care.
- Discuss shared care arrangements with the patient/carer, obtain their consent and explain their responsibilities.
- Review the patient's condition and monitor response to treatment regularly where indicated.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Supply GP with clinic letter or discharge summary within 14 days of an outpatient review or inpatient admission, and inform GP if patient does not attend scheduled clinic appointments.
- Ensure that clear arrangements exist for GPs to obtain advice and support.
- Ensure that the patient knows what to do and who to contact if they experience adverse effects. Inform the patient that if they are taking midodrine, that there is a risk of urinary retention and the symptoms to watch out for and report.
- Report adverse events to the MHRA.
- Stop treatment where appropriate or provide GP with advice on when to stop.

Responsibilities of GP/Primary Care Prescriber

- Reply to the request as soon as practicable if **unable** to support shared care (in writing or via secure email).
- Prescribe medicine at the dose recommended after the initiation period and adjust doses as recommended.
- Undertake ongoing clinical assessment and relevant monitoring following initiation period.
- Review any new concurrent medications for potential interactions.
- Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
- Report to and seek advice from the specialist on any aspect of care that is of concern and may affect treatment.
- Report adverse events to the specialist and MHRA.
- Stop treatment on the advice of the specialist.

Responsibilities of Patient/Carer		
• Report to the specialist or GP if he or she does not have a clear understanding of the treatment. • Share any concerns in relation to treatment with medicine. • Report any adverse effects to the specialist or GP whilst taking the medicine. • Attend appointments for clinical review and monitoring.		
1. Summary of condition and treatment aims Include links to relevant clinical guidelines e.g. NICE	Orthostatic (or postural) hypotension is defined as - a sustained reduction of systolic blood pressure (BP) of at least 20 mmHg and/or diastolic BP of at least 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 may be idiopathic or may arise as a result of disorders affecting the autonomic nervous system (for example, Parkinson's disease, multiple system atrophy or diabetic autonomic neuropathy), from a loss of blood volume or dehydration, or because of certain medications such as antihypertensive drugs. Orthostatic hypotension is more common in older people, and estimates of prevalence range from 5% to 30% of people aged over 65 years (in the general population), up to 60% of people with Parkinson's disease, and up to 70% of people living in care homes. Some estimate that 50% of cases have a medication cause – these include, for example, diuretics, alpha blockers, nitrates, tricyclic antidepressants etc. Thus, 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, pharmacological treatment with midodrine or fludrocortisone alone or in combination, may be considered. The choice of starting fludrocortisone or midodrine will depend in part as to whether the patient's problem is primarily volume or autonomic neuropathy related, so a tailored approach is needed by the specialist.	
2. Details of medicine and indication Please state whether licensed or unlicensed (off-label) use. Note that shared care is generally unsuitable for off-label prescribing unless it is a widely recognised use (e.g. included in BNF)	This SCA covers the management of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate. • Midodrine Hydrochloride: Licensed Indication • Fludrocortisone Acetate Tablets (Florinef®): "Off-Label" indication Use of these medicines for other types of orthostatic hypotension or for neurocardiogenic syncope is not included in this SCA.	
3. Pharmaceutical aspects	Route of administration:	Oral
	Formulation:	Tablets
	Administration details:	With water
	Other important information:	

<table>
<tr><td>4. Usual dose and frequency (including details of dose adjustments, e.g. in renal impairment) and duration of therapy
Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results.
All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
The duration of treatment will be determined by the specialist, based on clinical response and tolerability.
Termination of treatment will be the responsibility of the specialist.</td><td colspan="2">Titration of the dose to max. tolerated and effective dose will be undertaken by the specialist:

Midodrine: Initially 2.5 milligrams TDS (ideally first thing in the morning (before rising), mid-morning and mid-afternoon). Titration is usually as follows:
Week 1: 2.5 milligrams TDS
Week 2: 5 milligrams TDS
Week 3: 7.5 milligrams TDS
Week 4: 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 which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the 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.

For all medicines in this SCA, duration of treatment is subject to patients' response to treatment and tolerability.</td></tr>
<tr><td rowspan="4">5. Baseline investigations and initial monitoring to be undertaken by specialist</td><td colspan="2">Baseline investigations</td></tr>
<tr><td colspan="2">For all medicines in this SCA:
• 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 potentially be exacerbated by steroid therapy, such as diabetes, dyslipidemia, CVD, GI disorders, affective disorders, or osteoporosis.</td></tr>
<tr><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>• Monitor lying and standing BP
• Monitor electrolytes weekly in the first month and 3 monthly thereafter.
• Specialist to advise patient to self-monitor and immediately report symptoms of supine hypertension such as chest pain, palpitations, shortness of breath, headache and blurred vision.
• Follow-up by secondary care is required for patients whom are still symptomatic at 4 weeks –This could be via telephone in the majority of cases.</td><td>• Primary care checks lying and standing BP at 2-4 weeks and seek further advice to titrate medication if still symptomatic.
• Secondary care to review the continuation of treatment at 6 months then at 12 months</td></tr>
<tr><td>6. Ongoing monitoring requirements to be undertaken by primary care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>For all medicines in this SCA: Monitor U&Es and LFTs and supine/standing BP. Monitor for signs of developing heart failure or volume overload.

Additionally for fludrocortisone: As fludrocortisone is a potent</td><td>• U&E, LFTs, lying and standing blood pressure 3-6 monthly
• Monitor for signs or symptoms of supine</td></tr>
</table>

	mineralocorticoid, the dosage and salt intake should be carefully monitored to avoid hypertension, oedema or weight gain. Salt restriction and/or potassium supplements may be necessary as advised by the specialist.	hypertension and for bradycardia at review and on an ad hoc basis. • Withdraw fludrocortisone slowly over several weeks to avoid the effects of adrenal suppression. Monitor pulse rate.

7. Action(s) to be taken by primary care if abnormal result(s)/ 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.

8. Cautions and contraindications

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.

Cautions – For all medicines in this SCA:

Supine hypertension:

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 (as 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 as 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.

Contraindications

All medicines in this SCA are contraindicated if there is hypersensitivity to the active substance or to any of the 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.

9. Significant medicine and food interactions and management

For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)

Midodrine interactions	
Sympathomimetics and other vasopressor agents	Avoid as a pronounced increase in blood pressure may occur.
Alpha-adrenergic antagonists	The effect of midodrine is blocked by α-adrenergic antagonists such as prazosin and phentolamine.
Heart rate reducing drugs	Monitoring is recommended if midodrine is combined with other drugs that directly or indirectly reduce the

	heart rate.
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 interactions	
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.
Antihypertensives, including diuretics	Corticosteroids antagonise the effects of antihypertensives and diuretics. The hypokalaemic effect of diuretics, including acetazolamide, is enhanced.
CYP3A inhibitors	Co-treatment with CYP3A inhibitors, including cobicistat-containing products may increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects.
Digitalis glycosides	Co-administration may enhance the risk of digitalis toxicity
Oestrogens, including oral contraceptives	Corticosteroid half-life and concentration may be increased and clearance decreased.
Hepatic Enzyme Inducers (e.g. aminoglutethemide, barbiturates, carbamazepine, phenytoin, primidone, rifabutin, rifampicin)	There may be increased metabolic clearance of Fludrocortisone. Observe for possible diminished effect of steroid, and adjust the dosage accordingly.
Ketoconazole	Corticosteroid clearance may be decreased, resulting in increased effects.
NSAIDS	Corticosteroids may increase GI bleeding and ulceration associated with NSAIDS. They can reduce serum salicylate levels reducing their efficacy. Stopping corticosteroids when on high-dose NSAIDS may result in salicylate toxicity.
Thyroid drugs	Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in adrenocorticoid dosage.
Vaccines	Neurological complications and lack of antibody response may occur when patients taking corticosteroids are vaccinated.

	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 on contra-indications, warnings, side-effects and drug interactions.
10. Adverse effects Include details of incidence, identification, importance.	**Adverse Effects** **Midodrine:** • Most common side effects: 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:** • Most common side effects: hypertension, sodium and water retention, potassium loss and increased calcium excretion. High doses can cause Cushing's syndrome. • Gastro-intestinal effects: dyspepsia, abdominal distension, acute pancreatitis, oesophageal ulceration and candidiasis • Musculoskeletal effects: muscle weakness, vertebral and long bone fractures, tendon rupture • Endocrine effects: menstrual irregularities and amenorrhoea, hirsutism, weight gain, hypercholesterolaemia, hyperlipidaemia, negative nitrogen and calcium balance, increased appetite; increased susceptibility to and severity of infection, reactivation of dormant tuberculosis • Neuropsychiatric effects: psychological dependence, insomnia, aggravation of schizophrenia, aggravation of epilepsy, increased intracranial pressure with papilloedema in children • Ophthalmic effects: glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning and exacerbation of ophthalmic viral or fungal disease, increased intra-ocular pressure, exophthalmos; • Other side effects: impaired healing, petechiae, ecchymoses, facial erythema, suppression of skin test reactions, urticaria, hyperhidrosis, skin atrophy, bruising, telangiectasia, myocardial rupture following recent myocardial infarction, congestive heart failure, leucocytosis, hyperglycaemia, thromboembolism, nausea, malaise, hiccups, headache, vertigo.
11. Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	**For all medicines in this SCA:** • Patients should be told to report symptoms of supine hypertension immediately such as chest pain, palpitations, shortness of breath, headache and blurred vision. • Avoid administration in the late evening. The last daily dose should be taken at least 4 hours before bedtime in order to prevent high BP. The risk of high BP occurring during the night can be reduced by elevating the head of the bed. • 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
12. Pregnancy and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both	Not applicable.

the GP and the specialist.				
13. Specialist contact information	**RUH Neurology**			
	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	
	GWH Care of the Elderly			
	Dr Nicola Watson	Nicola.watson12@nhs.net	Sec: 01793 605108 Dr Watson: 01793 607349	
	GWH Neurology			
	Dr Hinze/Dr Yiin	Consultant neurologists	Gwh.neurologyrefs@nhs.net	01793 605099
	Dr Lennox/Dr Paul/Dr Thompson			01793 604767
	Dr Zuromskis/ Dr Bajoriene			01793 605105
	Dr Mazzucco/Dr Morrish/Dr Sarangmat			01793 605114
	SFT Care of the Elderly			
	Dr Hugo Powell	Consultant	hugo.powell@nhs.net	
	Dr Jonny Drayson	Consultant	jonny.drayson@nhs.net	
	SFT Neurology			
	Dr Boyd Ghosh	Consultant neurologists	Sft.admin.neurology@nhs.net	01722 429233
	Dr Chinar Osman			
	Dr Joanna Lovett			
14. Additional information For example, process for when Specialist or GP changes roles; specific issues related to patient age/ capacity/ specific monitoring.	**Annual treatment costs (at maximum dose) February 2021 Drug Tariff:** • Midodrine (10mg TDS): £1644 • Fludrocortisone (300mcg in split doses): £480 (off-label)			
15. References	British National Formulary. London: British Medical Association and The Royal Pharmaceutical Society of Great Britain; Accessed Jan 2021 via: https://www.evidence.nhs.uk/formulary/bnf/current NICE evidence summary [ESUOM20]: Postural hypotension in adults: fludrocortisone, October 2013, Accessed Jan 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 Jan 2021 via: https://www.nice.org.uk/advice/esnm61/chapter/Key-points-from-the-evidence Summary of product characteristics: Midodrine. Accessed 18/1/21. https://www.medicines.org.uk/emc/product/2265/smpc Summary of product characteristics: Fludrocortisone. Accessed 18/1/21. https://www.medicines.org.uk/emc/product/11457			
16. To be read in conjunction with the following documents	• NHS England: Responsibility for Prescribing Between Primary & Secondary/ Tertiary Care. Ref 07573, Version 1.0, Published January 2018. Accessed via: https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/ • Click or tap here to enter text.			

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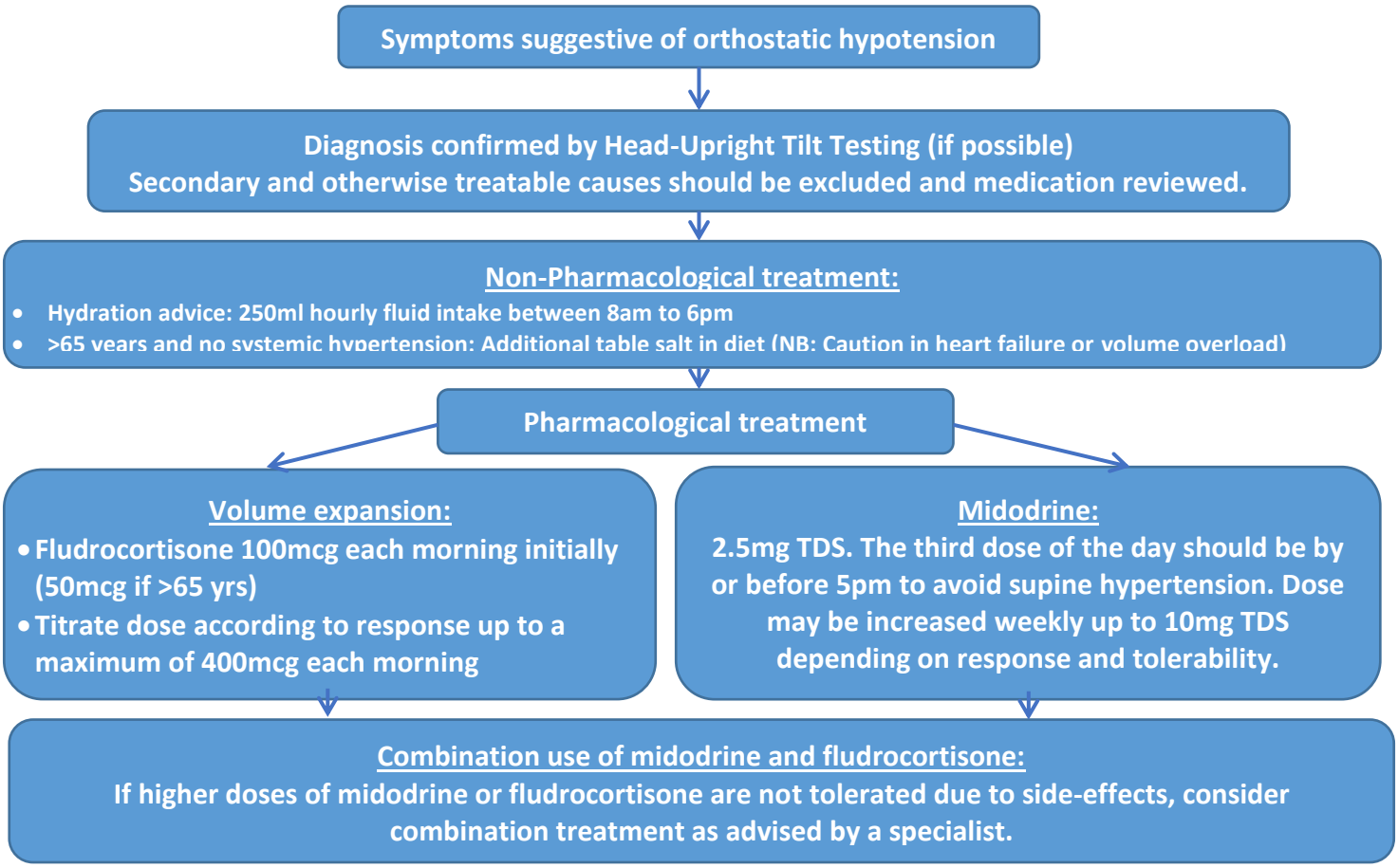
Treatment pathway:



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