Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

HWEICS Prescribing Support Document
Fludrocortisone and Midodrine for the treatment of orthostatic (or postural) hypotension

1. **Introduction**

The document aims to support prescribing of fludrocortisone and midodrine in adults with orthostatic (postural) hypotension across Herts and West Essex ICS.

HWE ICS approved indications for use:

Fludrocortisone and Midodrine are recommended as an option for treating orthostatic (postural) hypotension in line with the following pathway.

2. **Summary**

Orthostatic (or postural) hypotension is defined as a sustained reduction of **systolic** blood pressure of at least **20 mmHg** and/or **diastolic** blood pressure of at least **10 mmHg**, or Systolic blood pressure fall **>30 mmHg** in hypertensive patients with supine systolic blood pressure **> 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 blood pressure. In people with the condition, standing leads to an abnormally large drop in blood pressure, 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. It is estimated that about 0.2% of people aged over 75 years are admitted to hospital with problems relating to orthostatic hypotension.

This prescribing support document covers management of **severe orthostatic hypotension** due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate. This prescribing support document does not cover management of **Neurocardiogenic Syncope.**

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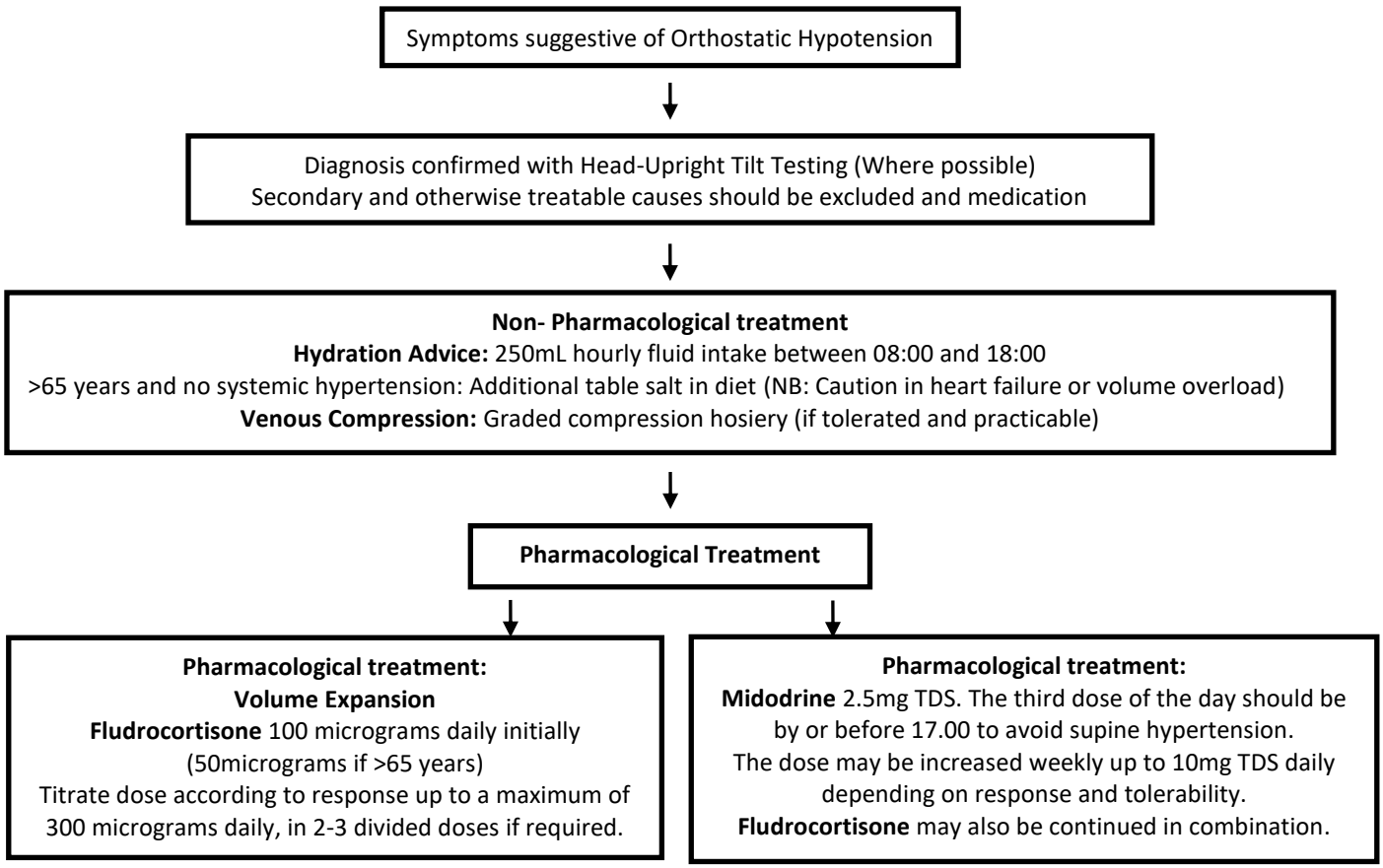
Treatment Pathway:



Fludrocortisone Acetate or treating orthostatic (postural) hypotension.

Clinical information

Fludrocortisone acetate is a synthetic mineralocorticoid with minimal glucocorticoid effects. It raises renal sodium reabsorption and increases blood volume. It has an elimination half -life of around 7 hours.

Fludrocortisone is quickly absorbed when taken orally, with peak plasma concentrations achieved within 45 minutes.

'Off label' indication

The use of fludrocortisone for neuropathic postural hypotension is '**off label'**. This is because it does not have a UK marketing authorisation for this indication.

It is recommended for use following diagnosis and non-pharmacological interventions such as hydration advice and venous compression.

Licensed indications

Fludrocortisone acetate is licensed for use in:

- Partial replacement therapy for primary adrenocortical insufficiency in Addison's disease and for the treatment of salt-losing adrenogenital syndrome.

Midodrine for treating orthostatic (postural) hypotension.

Clinical information

Midodrine is a pro drug, which is metabolised into its pharmacologically active metabolite, desglymidodrine in the body. Desglymidodrine is a sympathomimetic agent which acts on peripheral alpha-1-adrenoreceptor as an agonist at peripheral alpha-adrenergic receptors to increase peripheral arterial resistance, resulting in an increase in arterial blood pressure. The elimination half- life of desglymidodrine is 3 hours and duration of action of midodrine is approximately 4 hours. It is excreted mainly in urine.

Midodrine is not recommended for hypotension due to loss of blood volume or dehydration or medications such as anti-hypertensives. These causes should be excluded before considering midodrine treatment.

Licensed indications

Treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate.

RAG rating

AMBER initiation RAG rating

Fludrocortisone acetate and Midodrine has been assigned a '**AMBER initiation'** RAG rating in the Hertfordshire and West Essex ICS for the treatment of Orthostatic (postural) hypotension

> Recommended for prescribing but only considered suitable for initial prescribing by specialists in Community, Secondary and Tertiary care (as agreed) with prescribing (and monitoring, where applicable) continued by GPs. A shared care agreement is not required here but the patient's GPs must be supplied with sufficient information on the prescribed medication. Examples fitting this category are where dose stabilisation is needed, or where treatments are complex but the monitoring is not great enough to require amber protocol status.

3. **Criteria for prescribing in primary care**
   The following must apply before the GP is asked to accept on-going prescribing responsibility for Fludrocortisone and Midodrine.

Fludrocortisone or Midodrine should be initiated and titrated by a specialist who has undertaken the necessary testing to confirm a diagnosis of orthostatic (postural) hypotension.

How is Lying and Standing Blood Pressure Measured (LSBP)?

Th Royal College of Physicians have guides on how to measure lying and standing blood pressure as a part of a falls assessment which can be found here: fffap_how-to-measure-bp.pdf (rcp.ac.uk) fffap_lying-and-standing-bp-procedure.pdf (rcp.ac.uk)

What is Abnormal?: Postural hypotension is said to be present if: systolic blood pressure falls by ≥20mmHg on standing OR diastolic blood Pressure falls by ≥10mmHg on standing

Fludrocortisone

Areas of responsibility

Specialist responsibilities	
1.	Initiate fludrocortisone in patients with postural hypotension in line with recommended criteria
2.	Complete pre-treatment and initial monitoring: • Assessment for risk factors or pre-existing conditions that may potentially be exacerbated by glucocorticoid therapy, such as diabetes, dyslipidaemia, cardiovascular disease, gastrointestinal disorders, affective disorders, or osteoporosis. • Baseline urea and electrolytes, lying and standing blood pressure, BMI, HbA1c, triglycerides, physical assessment of fluid status, assessment of fracture risk in the context of any falls.
3.	Discuss treatment with fludrocortisone with the patient including; • Counselling points; to include but not limited to: • Advise on dosage and frequency. • Advise on common side effects with the patient/ carer and symptoms the patient may experience. • Advise patients of potential side-effects including adrenal suppression, oedema, immunosuppression, and psychiatric reactions • Advise patients to carry steroid treatment cards which give clear guidance on the precautions to be taken to minimise risk of adrenal crisis and contains treatment details. • Ongoing requirement for monitoring/review • Patients or their carers should be advised to seek help if side effects are suspected. • Advise patients to report any visual disturbance symptoms such as blurred vision which can occur with systemic corticosteroids. Consider referral to ophthalmologist for evaluation of causes if these occur. • Advise people who want and are able to monitor their blood pressure to use home blood pressure monitoring. Please see NHS pressure@home scheme and advise on blood pressure monitors using the British Heart Foundation Guide.
4.	Ensure that patient/carer is informed and made aware of their responsibilities (see 'Patient/carer responsibilities').
5.	Prescribe and titrate fludrocortisone prior to transferring prescribing to primary care. (see 'Criteria for prescribing in primary care')
6.	At the point of requesting the transfer to primary care, to provide advice to primary care prescribers which includes but is not limited to the following: - Clear diagnosis and information that has been discussed with patient and carer - Dosing regime - Additional monitoring requirements (if different to standard ongoing monitoring detailed in primary care prescriber responsibilities below) - Stopping/escalation (re-referral) criteria - Specialist team contact details for GPs to obtain advice and support

GP/primary care responsibilities	
1.	Review the request from the specialist and consider if sufficient information has been provided to take on the responsibility for prescribing fludrocortisone in adult patients and patient is on a stabilised dose.
2.	Prescribe fludrocortisone at the dose advised by the specialist team.
3.	Complete ongoing monitoring: • 6 monthly urea and electrolytes, 6 monthly check of resting BP to ensure systolic hypertension is not problematic, 6 monthly check for ankle oedema. (LSBP to be repeated if patient has persistent symptoms) • Monitor for signs of developing heart failure or volume overload • Salt restriction and/or potassium supplements may be necessary • Review need for treatment at 6 monthly intervals • Withdraw slowly over several weeks to avoid the effects of adrenal suppression.
4.	Advise people who want and are able to monitor their blood pressure to use home blood pressure monitoring. Please see NHS pressure@home scheme and advise on blood pressure monitors using the British Heart Foundation Guide.
5.	Check for possible drug interactions when newly prescribing or stopping concurrent medication.
6.	Seek advice from the specialist team when required regarding any concerns, for example: side effects or lack of efficacy.
7.	To deal with general health issues of the patient.
8.	To report any adverse events to MHRA

Patient/Carer responsibilities	
1.	Report to their GP if they do not have a clear understanding of or have any concerns with their treatment.
2.	Inform the GP of any changes in circumstances that could affect their treatment e.g. pregnancy
3.	Report any adverse effects or worsening of condition to the GP and/or specialist whilst taking fludrocortisone.
4.	Monitor blood pressure at home if able to as per GP/specialist recommendations at frequencies advised. Ensure an approved blood pressure monitor is used as per the British Heart Foundation Guide.
5.	Always carry their steroid treatment card and bring to medical appointments
6.	Attend review appointments with specialist and primary care as requested.
7.	Alert GP and/or specialist of any changes of circumstance which could affect management of disease
8.	Inform GP or specialist of any other medicines being taken including over-the-counter products such as decongestants

Further information

For full details, please refer to the current individual drug Summary of Product Characteristics (SPC) and BNF. Further information also available on the NICE evidence summary (2013)

Treatment for orthostatic hypotension:

The recommended daily dosage for this indication is as follows:

Initially, Fludrocortisone should be given at 100 micrograms daily. Patients over 65 years old should be initiated at 50 micrograms. The dose should then be titrated based on individual response, with a maximum of 300 micrograms daily, divided into 2-3 doses if required.

The duration of up titration and treatment is dependent on the patients' tolerability and overall response to the treatment.

Contra-indications and cautions:

Contra-indicated with:

- Hypersensitivity to the drug's active substance or excipients
- Systemic infections - unless specific anti-infective therapy given

Cautions:

Please refer to BNF and SPC for complete and up to date list of cautions

Special attention and frequent monitoring are needed for patients with specific conditions like recent intestinal anastomoses, diverticulitis, severe affective disorders, chronic nephritis, osteoporosis, peptic ulcers, myasthenia gravis, systemic fungal infections, acute psychoses, glomerulonephritis, hypertension, glaucoma, steroid myopathy, epilepsy, or liver failure.

Adrenal Suppression:

- Prolonged therapy with Fludrocortisone Acetate can lead to adrenal atrophy, persisting for years post-discontinuation.
- Gradual withdrawal is crucial to prevent acute adrenal insufficiency, tapering over weeks or months based on dosage and treatment duration.
- Patients on long-term therapy may require additional corticosteroids during times of stress and even up to a year post-treatment. Reintroduction of corticosteroids might be necessary after prolonged therapy.

Anti-inflammatory/Immunosuppressive Effects:

- Suppression of inflammation and immune function increases susceptibility to infections, potentially masking symptoms of severe infections such as septicaemia and tuberculosis.
- Chickenpox, shingles, and measles pose grave risks, advising patients to avoid exposure and seek immediate medical attention if exposed.
- Measles: Prophylaxis with normal immunoglobulin may be needed

Other Considerations:

- Since Fludrocortisone acetate is a potent mineralocorticoid both the dosage and salt intake should be carefully monitored to avoid the development of hypertension, oedema or weight gain. Periodic checking of serum electrolyte levels is advisable during prolonged therapy.

- Corticosteroid effects can be intensified in hypothyroid patients and reduced in hyperthyroid patients.

- Diabetes may worsen, requiring increased insulin dosage, and latent diabetes may emerge.
- All corticosteroids increase calcium excretion, which may predispose to osteoporosis or aggravate pre-existing osteoporosis.
- Patients with rare hereditary conditions such as galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption should avoid Fludrocortisone Acetate.
- Aspirin should be used cautiously with corticosteroids in patients with hypoprothrombinaemia

Side effects:

Please refer to SPC for complete and up to date list of side effects.

Very common side-effects (≥ 1/10): Hypokalaemia, cardiac disorders congestive, hypertension
Common side effects (≥ 1/100 to < 1/10): Headache, muscular weakness, oedema, swelling.
Uncommon (≥ 1/1,000 to < 1/100): hypokalaemia alkalosis, decreased appetite, delusional perception, hallucination, seizures, loss of consciousness, cardiomegaly, diarrhoea, muscle atrophy, blood potassium decreased.

The occurrence of side effects can be reduced by administering the lowest effective dosage for the shortest duration necessary. Most side effects are reversible upon cessation of the drug.

Action and Advice

Review and discontinuation of medication

Adverse Event:	**Recommended action**
Hypokalaemia	Consider prescribing potassium supplementation
Symptoms of supine hypertension including chest pain, palpitations, shortness of breath, headache and blurred vision	Consider dose reduction as symptoms often dose related. If symptoms continue following dose reduction, discuss discontinuation with specialist
Persistent labile blood pressure – following initial titration	Refer to specialist for further assistance
Symptoms of adrenal suppression including weakness/ fatigue, malaise, nausea, vomiting, diarrhoea, abdominal pain, headache (usually in the morning) fever, anorexia/weight loss, myalgia, arthralgia, psychiatric symptoms	Patients receiving systemic corticosteroids must be provided with an information leaflet. Patients must be informed about potential risks, including infections, adrenal suppression, psychiatric reactions, and corticosteroid withdrawal. **Seeking specialist advice** is recommended. Gradually tapering off corticosteroids over weeks or months is essential to prevent acute adrenal insufficiency.
Mood and behaviour changes	
Serious gastro-intestinal, musculoskeletal, and ophthalmic effects requiring medical assistance	

Pregnancy and Lactation

Pregnancy

It may be decided to continue a pregnancy in a woman requiring replacement mineralocorticoid therapy, despite the risk to the foetus. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.

There is evidence of harmful effects in pregnancy in animals. There may be a small risk of cleft palate and intra-uterine growth retardation. Hypoadrenalism may occur in the neonate. Patients with pre-eclampsia or fluid retention require close monitoring.

Breast-feeding

Corticosteroids are found in breast milk.

Infants born of mothers who have received substantial doses of corticosteroids during pregnancy or during breast feeding should be carefully observed for signs of hypoadrenalism. Maternal treatment should be carefully documented in the infant's medical records to assist in follow up.

Drug interactions:

For a full list of interactions, please refer to SPC for complete and up to date list of drug interactions.

Oral Anticoagulants	Corticosteroids may potentiate or decrease anticoagulant action
anticholinesterases	Effects of anticholinesterases may be antagonised
Antidiabetics	Corticosteroids may increase blood glucose; diabetic control should be monitored, especially when corticosteroids are initiated, discontinued, or changed in dosage.
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, is expected to 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 possibility 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 Acetate. Patients should be carefully observed for possible diminished effect of steroid, and the dosage should be adjusted 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

Midodrine

Areas of responsibility

Specialist responsibilities	
1.	Initiate Midodrine in patients with postural hypotension in line with recommended criteria
2.	Complete pre-treatment and initial monitoring: • Baseline urea and electrolytes, liver function tests and heart rate. • Baseline LSBP then check again one week after initiation with a check of peripheral circulation. (It is not necessity to repeat LSBP after first week unless this is needed for dose titration) Once no further dose titration is needed can be transferred to primary care
3.	Discuss treatment with midodrine with the patient including; • Counselling points; to include but not limited to: • Advise on dosage and frequency. • Advise on common side effects with the patient/ carer and symptoms the patient may experience. • Ongoing requirement for monitoring/review • Patients or their carers should be advised to seek help if side effects are suspected. • Advise people who want and are able to monitor their blood pressure to use home blood pressure monitoring. Please see NHS pressure@home scheme and advise on blood pressure monitors using the British Heart Foundation Guide.
4.	Ensure that patient/carer is informed and made aware of their responsibilities (see 'Patient/carer responsibilities').
5.	Prescribe and titrate midodrine prior to transferring prescribing to primary care. (see 'Criteria for prescribing in primary care')
6.	At the point of requesting the transfer to primary care, to provide advice to prescribers which includes but is not limited to the following: - Clear diagnosis and information that has been discussed with patient and carer - Dosing regime - Additional monitoring requirements (if different to standard ongoing monitoring detailed in primary care prescriber responsibilities below) - Stopping/escalation (re-referral) criteria Specialist team contact details for GPs to obtain advice and support

GP/primary care responsibilities	
1.	Review the request from the specialist and consider if sufficient information has been provided to take on the responsibility for prescribing midodrine in adult patients, patient is on a stabilised dose and indication is according to the agreed licensed indications for use.
2.	Prescribe midodrine at the dose advised by the specialist team.
3.	Complete ongoing monitoring: • Urea and electrolytes and Liver function tests 6 monthly. 6 monthly check of resting BP to ensure systolic hypertension is not problematic. Monitor for signs or symptoms of bradycardia at review and on an ad hoc basis (LSBP to be repeated if patient has persistent symptoms).

	• Monitor for symptoms of supine hypertension such as chest pain, palpitations, shortness of breath, headache, and blurred vision, and advise patients to self-monitor and report immediately. • Review need for treatment at 6 monthly intervals .
4.	Advise people who want and are able to monitor their blood pressure to use home blood pressure monitoring. Please see NHS pressure@home scheme and advise on blood pressure monitors using the British Heart Foundation Guide.
5.	Check for possible drug interactions when newly prescribing or stopping concurrent medication.
6.	Seek advice from the specialist team when required regarding any concerns, for example: side-effects or lack of efficacy.
7.	To deal with general health issues of the patient.
8.	To report any adverse events to MHRA

Patient/Carer responsibilities	
1.	Report to GP if there is not a clear understanding of their treatment and discuss any concerns in relation to treatment.
2.	Report any adverse effects to their GP and/or specialist whilst using their treatment (Refer to adverse effects section).
3.	Patients should be told to report promptly any indication of urinary retention (e.g. hesitancy or frequency of micturition).
4.	Monitor blood pressure at home if able to as per GP/specialist recommendations at frequencies advised. Ensure an approved blood pressure monitor is used as per the British Heart Foundation Guide.
5.	Report any changes in disease symptoms to GP and/or specialist whilst taking midodrine.
6.	Patients who experience dizziness or light-headedness should refrain from driving or operating machinery.
7.	Alert GP and/or specialist of any changes of circumstance which could affect management of disease
8.	Inform GP or specialist of any other medicines being taken including over-the-counter products such as decongestants
9.	Attend appointments for regular reviews and monitoring tests at the request of specialist/primary care
9.	The last daily dose should be taken at least 4 hours before bedtime to prevent supine hypertension.

Further information

For full details, please refer to the current individual drug Summary of Product Characteristics (SPC) and BNF. Further information also available on the NICE evidence summary (2015)

Treatment for orthostatic hypotension:

Midodrine is available in 2.5mg, 5mg and 10mg tablets. Ideally midodrine is given first thing in the morning (before getting out of bed), mid-morning and mid-afternoon with enough fluid.

A careful evaluation of the clinical response to treatment and of the overall balance of the expected benefits and risks needs to be undertaken before any dose increase and advice to continue therapy for long periods.

Depending on the results of supine and standing blood pressure recordings, this dose may be increased weekly up to a dose of 10mg three times a day. This is the usual maintenance dosage.

Effects can be seen from as little as half to 1 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** to prevent supine hypertension.

Contra-indications and cautions:

Contra-indicated with:

- Hypersensitivity to the active substance or to any of the excipients.
- Severe organic heart disease (e.g. bradycardia, myocardial infarction, congestive heart failure, cardiac conduction disturbances or aortic aneurysm).
- Hypertension.
- Serious obliterative blood vessel disease, cerebrovascular occlusions and vessel spasms.
- Vasovagal hypotension
- Acute nephritis
- Severe renal impairment (creatinine clearance of less than 30 ml/min).
- Hypertrophy of the prostate gland
- Urinary retention
- Proliferative diabetic retinopathy
- Pheochromocytoma
- Hyperthyroidism
- Narrow angle glaucoma.

Cautions:

Please refer to BNF for complete and up to date list of cautions

- Severe orthostatic hypotension with supine hypertension: Regular monitoring of resting blood pressure is necessary due to the risk of hypertension in the supine position.
- Severe disturbances of the autonomic nervous system: In patients suffering from a severe disturbance of the autonomic nervous system, administration of midodrine may lead to a further reduction of blood pressure when standing.
- Prostate disorders: Caution is advised in patients with prostate disorders. Use of the drug may cause urinary retention.
- Renal and hepatic function: It is recommended to evaluate the renal and hepatic parameters before starting treatment with midodrine and on a regular basis. Great caution should be

exercised in patients with mild to moderate renal insufficiency (creatinine clearance >30ml/min and <90ml/min).

- Heart rate: Slowing of the heart rate may occur after midodrine administration, due to vagal reflex. Caution is advised when midodrine is used concomitantly with cardiac glycosides (such as digitalis preparations) and other agents that directly or indirectly reduce heart rate. Patients should be monitored for signs or symptoms suggesting bradycardia.
- The use of midodrine in patients who have an increased risk of or suffering from glaucoma / increased intra-ocular pressure or who are treated with mineralocorticoids / fludrocortisone acetate (which may increase intra-ocular pressure) should be avoided or monitored very closely.
- Patients with diabetes mellitus who show high blood pressure levels in supine position due to underlying neurological disorders (diabetic autonomic neuropathy) may suffer from supine hypertension with midodrine. Hence, caution is recommended.
- Elderly: Manufacturer recommends cautious dose titration

Side effects:

Please refer to SPC for complete and up to date list of side effects.

Common side effects (≥ 1/100 to < 1/10): Chills, Flushing, Gastrointestinal discomfort, Headache, Nausea, Paraesthesia, Piloerection, Scalp Pruritus, Skin reactions, Stomatitis, Supine hypertension (dose dependent), Urinary disorders
Uncommon side effects (≥ 1/1000 to < 1/100): reflex bradycardia, sleep disorders, restlessness, excitability, irritability
Rare side effects (≥ 1/10000 to < 1/1000): tachycardia, palpitations, hepatic dysfunction; also reported abdominal pain, vomiting, diarrhoea, anxiety, confusion, dizziness

Hepatic and Renal Impairment

Typically, midodrine is contraindicated in patients with acute renal impairment and severe renal impairment.
It is advisable to monitor the renal function and blood pressure in patients undergoing long-term treatment with midodrine.

Sufficient data is not available for patients with hepatic impairment. Therefore, it is recommended to monitor the liver function before and during treatment with midodrine.

Action and Advice

Review and discontinuation of medication

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 and < 180mmHg)	Usually, dose related so check if last dose taken at least 4 hours before bedtime. Consider dose reduction or withhold and discuss with specialist team. If persistent symptoms despite dose reductions, consider

	discontinuing treatment in consultation 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
Signs or symptoms suggestive of bradycardia (pulse slowing, increased dizziness, syncope, cardiac awareness)	Discontinue treatment
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
Urinary Retention	Withhold until discussed with specialist
Change in mobility e.g. bedbound or prognosis that means midodrine is no longer needed. E.g. end of life	Discontinue treatment
AST, ALT > twice upper limit of reference range	Withhold until discussed with specialist team
Intolerable side effects	Withhold until discussed with specialist team

Pregnancy and Lactation

There are no data from the use of midodrine in pregnant women. Animal studies have shown reproductive toxicity.

Midodrine is **not recommended during pregnancy** and in women of childbearing potential not using contraception. Any woman becoming pregnant during treatment should be withdrawn from the treatment immediately upon established pregnancy.

It is unknown whether midodrine/metabolites are excreted in breast milk. A risk to the newborns/infants cannot be excluded. Midodrine should not be used during breast-feeding.

Drug interactions:

For a full list of interactions, please refer to SPC for complete and up to date list of side effects.

Medications	**Drug interaction information**
Sympathomimetic medicines and other vasopressor agents e.g. decongestants, tricylic antidepressants	Avoid the concomitant use of midodrine with vasoconstrictor, sympathomimetic pressor agents should be avoided as this may cause excessive hypertension.
Alpha-adrenergic antagonists e.g. doxazosin, tamsulosin	The effects of Midodrine may be antagonised by alpha receptor blockers so avoid.
Heart rate reducing medicines e.g. beta blockers	The cardiac frequency reducing effect of beta blockers can be potentiated by midodrine. The concomitant use of beta- receptor blocking agents (which reduce the heart rate) and midodrine requires careful monitoring.
Cardiac glycosides	Great caution should be taken when administering midodrine to patients experiencing bradycardia produced by digitalis (or other glycosides) or psychopharmaceutical drugs since midodrine may potentiate reflex bradycardia and other kinds of conduction disorders or arrhythmias.
Ergot alkaloid	Deterioration of peripheral blood circulation. The patient may experience an increase in blood pressure and reduced blood flow to organs and hands/feet. Avoid concomitant use of drugs that increase blood pressure. If concomitant use cannot be avoided, the blood pressure is to be monitored closely.
Corticosteroid preparations	Patients being treated with midodrine in combination with, mineralocorticoids or glucocorticoids (e.g. fludrocortisone) may be at increased risk of glaucoma/increased intraocular pressure, and should be carefully monitored. Midodrine may enhance or potentiate the possible hypertensive effect of corticosteroid preparations.
Drugs metabolised by CYP2D6.	Midodrine is an inhibitor of CYP2D6 and may affect the metabolism of drugs that are mainly metabolised by CYP2D6 e.g. selective serotonin inhibitors (SSRI), antiarrhythmics etc

Version	1. 0 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include: • Rebadging with HWE ICB and removal of WECCG header • Review date removed and replaced with standard statement.
Developed by	HWEICS PMOT team
Approved by	WEMOPB
Date approved/updated	WEMOPB September 2017 updated APC September 2024
Review date:	The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available.
Superseded version	Original V.01

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