# Specialist Initiated Drugs

# Prescribing Information Sheet

**April 2016**

## Midodrine

Midodrine is a post-synaptic alpha adrenergic receptor stimulant with little effect on the beta-adrenergic receptors in the heart. Its actions are essentially identical with those of other alpha-adrenergic stimulants, such as phenylephrine or methoxamine. The most prominent effects of midodrine consist of a rise in systolic and diastolic blood pressures accompanied by a marked reflex bradycardia. The increase in blood pressure is due almost entirely to an increase in peripheral resistance. This means supine hypertension should be guarded against and safest use is when patient BP during titration is monitored by a carer.

It is presently the only licensed medication for severe orthostatic hypotension. Although newly licensed it has been the most commonly prescribed unlicensed medication in adults for some time.

**Formulary Status**

Midodrine for the treatment of severe orthostatic hypotension due to autonomic dysfunction should be initiated by a specialist who will prescribe the initial supply.

It also has recognised use out of license in baroreceptive disorders that cause symptomatic hypotension.

The specialist will:
1. Define criteria for success for midodrine treatment for that individual and communicate these to the GP and patient

2. Assess renal function and carry out FBC and LFTs (if not recently done)

3. Ensure patient has BP monitored after first dose. Blood pressure monitoring during titration must be done both supine and erect.

4. Will prescribe and titrate the dose until the patient is stable. This usually takes 1 -2 months but will vary per patient.

**Approved by:** East Kent Prescribing Group *(Representing Ashford CCG, Canterbury and Coastal CCG, South Kent Coast CCG and Thanet CCG)*
**Date: April 2016**
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On-going prescribing can be continued by a GP.

The responsibility for increasing/decreasing the dose or stopping treatment due to lack of effect or side effects remains with the specialist, (although mutual communication will be sufficient in most cases)

**Full prescribing guidance – Summary of Product Characteristics**
**http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1446187110673.pdf**

## Indication and Dosage

**Indication**- for the treatment of severe orthostatic hypotension in adults, due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate.

**Presentation**- 2.5mg and 5mg tablets

**Dosage and Administration** – Initial dose: 2.5 mg three times a day. 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. It can be expected that 50% of elderly patients will get sufficient benefit at 2.5mg three times a day.

The last daily dose should be taken at least 4 hours before bedtime in order to prevent supine hypertension. The risk of supine hypertension occurring during the night can be reduced by elevating the head.

**Renal impairment**
Midodrine is contraindicated in patients with acute renal impairment and severe renal impairment.

**Hepatic impairment**
No experience of use.

**Issues during titration phase**

If the patient contacts their GP because of difficulty contacting the specialist, the advice in the sections below covers most likely issues. However be aware that in very advanced autonomic dysfunction midrodrine can worsen the orthostatic hypotension paradoxically.

**Monitoring**
Supine and standing BP every three months, (by GP after titration phase), or if patient complains of new headaches.
Midodrine will need to be reduced (or stopped) if supine blood pressure exceeds 200 systolic or standing is above 160 systolic. Seek advice from initiating consultant.

The other main monitoring function of the GP will be to prevent the introduction of common medications such as alpha blockers (eg for prostatism), high dose tricyclic antidepressants and antihistamines.

**Stopping treatment**

Should the patient develop symptoms consistent with cerebrovascular or ischaemic heart disease withdraw midodrine therapy.

Ask for advice from the initiating consultant before discontinuing medication in the supine BP range 160 to 200 systolic.

## Contra indications

Hypersensitivity to the active substance or to any of the excipients.

Patients with severe organic heart disease, high blood pressure, arrhythmias, acute renal disease, prostatic hyperplasia, urinary retention, phaeochromocytoma, thyrotoxicosis, glaucoma.

Pregnancy

There is no data from the use of midodrine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). 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.

Breastfeeding

It is not known whether the drug is excreted in breast milk; this drug should not be given to nursing mothers.

## Adverse effects, special warnings and precautions for use (consult SPC for full list)

Patients should be told to report symptoms of supine hypertension immediately such as chest pain, palpitations, shortness of breath, headache and blurred vision, and should be monitored for these side effects by the treating physician. Supine hypertension may often be controlled by an adjustment to the dose. If supine hypertension occurs, which is not overcome by reducing the dose, treatment with midodrine must be stopped.

The most frequent and very common adverse reactions related to midodrine therapy are piloerection, pruritus of the scalp and dysuria.

## Drug Interactions (consult SPC for full list)

Potentially significantly increased hypertensive effect with tricyclic antidepressants. antihistamines, thyroid hormones(not usually an issue if used at replacement dose) and MAOIs. Avoid concomitant use.

Effect antagonised by alpha antagonists e.g prazosin.

Avoid concomitant use with drugs that reduce heart rate e.g digoxin

Midodrine may potentiate or enhance the hypertensive effects of 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.

In general it is recommended that midodrine be first tried alone rather than in combination with flucortisone and the blood pressure monitoring takes into account that steroids take several weeks to have maximal onset and to have their effects disappear.

**Pre Surgery**
If a patient is to receive a general anaesthetic then it is essential that the surgical team are aware that a patient is taking midodrine.

Limited studies have taken place with other drugs used out of license or completely unlicensed to treat orthostatic hypotension. These other drugs include NSAIDs, fludrocortisone, domperidone, pyridostigmine and droxidopa (L-DOPS). Droxidopa has been recently licensed in the USA and it is particularly important on theoretical grounds that patients do not take both it and midodrine. Some of the unlicensed alternatives, such as fludrocortisone are cheaper at standard dosage and continue at this time to have a place in therapy for the common indications midodrine is used for. However the only drugs that can be regarded as of 2016 to have a reasonable randomised trial evidence base are midrodrine and droxidopa. The trial populations for the other drugs are much smaller.

**Contact details of Specialist Team**

Contact initiating consultant as per hospital letter.