Midodrine
Proprietary Names: Gutron, Midon, ProAmatine
(Unlicensed medicine information for GPs)

Summary of Information

Description: Midodrine is a pro-drug, which is metabolised to desglymidodrine, a direct-acting sympathomimetic agent with $\alpha_1$-selective activity on the $\alpha$-adrenergic receptors of the arterial and venous vasculature. Total peripheral resistance is increased, resulting in increased systolic and diastolic blood pressure. Midodrine has virtually no stimulant effect on $\beta$-adrenergic receptors, including those of the heart, and because it only poorly crosses the blood-brain barrier, causes very little CNS stimulation [1-3].

Usage: Midodrine is used in the treatment of hypotensive states and in particular for orthostatic (or postural) hypotension. It should be used after non-drug therapies and fluid expansion has failed. Alpha agonist drugs such as midodrine have also been used in the management of urinary incontinence. Midodrine is licensed in a number of countries including France, Germany, USA and Ireland but not in the UK [1-4].

Dosage: The usual initial dosage of midodrine for postural hypotension is 2.5mg twice daily orally, adjusted gradually according to patient response; up to 10mg three times daily may be required. [1-3] In renal impairment the recommended starting dose is 2.5mg per day [3]. In urinary incontinence the usual suggested dose is 2.5mg to 5mg orally two to three times daily [1, 3]. To reduce the risk of supine hypertension midodrine should not be taken after the evening meal or less than 4 hours before bed time; however food is not thought to affect its absorption [1].

Adverse reactions: Supine hypertension is the most serious and common side effect; other effects are paraesthesias, dysuria, pilomotor reactions (piloerection or goose flesh), pruritis and rashes. Administration should only be continued in patients who experience significant symptomatic relief within the first 1 to 2 weeks because of the risk of supine hypertension [1-3].

Interactions: Concomitant use with a vasoconstrictive agent may cause additive hypertension; caution should be exercised with patients who have received a monoamine oxidase (MAO) inhibitor within the previous 14 days [1-5]. The use of linezolid is contraindicated with sympathomimetics due to its weak MAO-inhibitory properties, unless facilities for close observation and blood pressure monitoring are available [6]. Decongestants such as pseudoephedrine and phenylpropranolamine and appetite suppressants containing sympathomimetics should be avoided. Midodrine plus salt retaining steroids such as fludrocortisone may also increase the risk of supine hypertension. The effects of midodrine may be enhanced by tricyclic antidepressants and may also potentiate the bradycardia caused by drugs such as digoxin and beta blockers. A combination of midodrine with some psychotropics can increase the risk of akathisia and dystonia [1-5].

Updated February 2013 (Katie Smith, East Anglia Medicines Information Service on behalf of Ipswich & East Suffolk CCG, West Suffolk CCG, Ipswich Hospital and West Suffolk Hospital)
Summary of Clinical Evidence
A review of midodrine published by the UK Medicines Information network in 2011, concluded that there are only a few studies of a suitable quality which have investigated the value of midodrine in the treatment of orthostatic hypotension. However, the evidence base for other drugs used to treat orthostatic hypotension is no better and probably worse than that for midodrine [2].

The efficacy of midodrine has been assessed mainly on the surrogate outcome of raising systolic blood pressure on standing compared to placebo. There is little evidence that midodrine improves patients’ abilities to carry out activities of daily living, which is the principal aim of treatment. The two largest studies, which between them enrolled 268 patients (but had high drop-out rates), suggest that midodrine may reduce symptoms associated with OH, such as light-headedness, and make patients ‘feel better’ [2, 7, 8].

Jankovic et al reported on a 4-week, double-blind, placebo-controlled study in 97 patients with orthostatic hypotension [7]. Patients were randomised to either placebo, 2.5mg, 5mg or 10mg three times a day for three weeks after a 1 week run in phase. Only midodrine 10mg three times daily significantly increased the systolic blood pressure. Overall side effects were reported by 22% of the placebo treated patients compared with 27% of the midodrine treated group. Scalp pruritis/tingling, was the most frequent side effect.

Low et al randomised a total of 171 patients for a 3 week double blind period to either midodrine 10mg three times daily or placebo. Midodrine treatment resulted in a mean rise in systolic blood pressure of 21.8 mmHg and an improvement in light-headedness and global symptom relief score. The most common side effects were piloerection (13%) and scalp pruritis (10%), and midodrine was deemed to be efficacious and safe in the treatment of neurogenic orthostatic hypotension [8].

No double blind studies have extended beyond four week’s treatment and comparative data are lacking. Results from two small cross-over studies suggest that midodrine may be more effective than ephedrine and fludrocortisone in increasing standing blood pressure [2, 9, 10].

References

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Midrodrine
Proprietary Names: Gutron, Midon, ProAmatine
(Unlicensed medicine information for patients)

This leaflet tells you about the midodrine tablets that you have been given by the hospital.

What is midodrine for? - Midodrine is used in the treatment of low blood pressure (also known as hypotension) which your doctor may think that you are suffering from. Low blood pressure may be causing you to feel dizzy, feel faint or fall particularly when you first stand up. This is known as orthostatic or postural hypotension.

Most medicines used in the UK have a licence so that they are used and monitored in a controlled way. Some drugs that are only used in small numbers of patients do not have a licence, but this does not mean that they are unsafe. Midodrine is a drug that does not have a licence in the UK. It does however have a licence in Ireland and the USA.

How is it usually taken? – Your doctor will usually start you on midodrine at a low dose (for example 2.5mg or 5mg twice daily) and increase it if necessary up to 10mg three times daily. You should try and space the doses throughout the day but should not take the last dose after your evening meal or less than 4 hours before bedtime. If you take midodrine just before going to bed it may give you a headache, blurred vision or pounding in your ears.

What should I do if I miss a dose? – If you miss a dose of midodrine, take it as soon as possible. However, if it is almost time for your next dose, forget the missed dose and start taking your tablets again as normal. Do not take a missed dose less than 4 hours before bedtime and do not take a double dose.

What are the side effects of midodrine? – Most medicines can cause some side effects although you may not suffer from any.
Check with your doctor if any of the following side effects occur:
More commonly – blurred vision, headache, pounding in the ears.
Rarely – fainting, worsening dizziness, slow pulse.

Other side effects may occur which you do not need to inform your doctor of, unless you find them troublesome:
More commonly – prickling or itching of the scalp, goose bumps and feeling that your hairs are standing on end, chills and feeling that you need to pass water more often.
Rarely – rashes, dry mouth, confusion, dizziness or cramps.

Can I take any other medicines with midodrine? – You should check with your doctor or pharmacist before taking any other medicines including those you buy, with midodrine.

If you need any more information please ask you doctor or pharmacist.
Midrodrine

Proprietary Names: Gutron, Midon, ProAmatine

(Unlicensed medicine information for Community Pharmacists and Dispensers)

Prescribing Information – Midodrine is an unlicensed medicine in the UK used for the treatment of orthostatic hypotension. Midodrine is a direct acting sympathomimetic agent with activity on the α-adrenergic receptors of the arterial and venous vasculature. Total peripheral resistance is increased, resulting in increased systolic and diastolic blood pressure.

The initial dosage is 2.5mg twice daily increasing slowly according to response and tolerance to 10mg three times daily. In renal impairment the recommended starting dose is 2.5mg once daily. To reduce the risk of supine hypertension, midodrine should not be taken after the evening meal or less than 4 hours before bedtime, however food is not thought to affect its absorption.

Adverse reactions: Supine hypertension is the most serious and common side effect; other effects are paraesthesias, dysuria, pilomotor reactions (piloerection or goose flesh), pruritis and rashes. Because of the risk of supine hypertension, administration should only be continued in patients who experience significant symptomatic relief within the first 1 to 2 weeks.

Interactions: Concomitant use with a vasoconstrictive agent may cause additive hypertension; caution should therefore be exercised with patients who have received a monoamine oxidase inhibitor within the previous 14 days. Because of its weak MAO-inhibitory properties, the manufacturers of linezolid contraindicate its use with sympathomimetics unless facilities for close observation and blood pressure monitoring are available.

Decongestants such as pseudoephedrine and phenylpropanolamine and appetite suppressants containing sympathomimetics should be avoided. Midodrine plus salt retaining steroids such as fludrocortisone may also increase the risk of supine hypertension. The effects of midodrine may be enhanced by tricyclic antidepressants and may also potentiate the bradycardia caused by drugs such as digoxin and beta blockers. A combination of midodrine with some psychotropics can increase the risk of akathisia and dystonia.

Suppliers of midodrine:
2.5mg and 5mg tablets are available on a named patient basis from a number of suppliers of unlicensed medicines including:

- Idis World Medicines, Idis House, Churchfield Road, Weybridge, Surrey, KT13 8DB.
  Tel: 01932 824100, email: idis@idispharma.com
- Mawdsley Unlicensed Medicines, Unit 4, Crompton Road Business Park, Crompton Road, Doncaster, DN2 4PW.
  Tel: 01302 553000, email: http://www.mawdsleys.co.uk/enquiryum.asp