

Midodrine

Approved indication: orthostatic hypotension

Vasodrine (Southern Cross Pharma)

2.5 mg and 5 mg tablets

In conditions affecting the autonomic nervous system, such as Parkinson's disease, patients may be unable to maintain their blood pressure when standing. The drop in blood pressure can result in light-headedness or syncope. Although education and non-drug therapy such as venous compression may help, some patients still have severe symptomatic orthostatic hypotension. One pharmacological approach to management is to use a sympathomimetic to raise venous tone.

Midodrine is a prodrug of desglymidodrine which stimulates alpha 1 adrenergic receptors. This results in venous vasoconstriction and consequently a rise in blood pressure, however the clinical effect is uncertain. Midodrine was given an accelerated approval in the USA in 1996, but in 2010 the drug was almost withdrawn from the market because its benefit had not been confirmed.¹

The conversion of midodrine to desglymidodrine is rapid with peak plasma concentrations within an hour of an oral dose. Desglymidodrine is metabolised and has a half-life of about three hours. It is mainly excreted with its metabolites in the urine. Midodrine is contraindicated if the creatinine clearance is below 30 mL/minute.

The main phase III study of midodrine was a six-week, placebo-controlled trial involving patients who had symptomatic neurogenic orthostatic hypotension with a drop of at least 15 mmHg in systolic blood pressure. A group of 82 patients took midodrine 10 mg three times a day. This regimen resulted in an average rise of 22 mmHg in standing systolic blood pressure. There was little change in the blood pressure of the 89 patients in the placebo group.²

The effect of midodrine on symptoms was assessed in a double-blind postmarketing study. This recruited 19 patients who had been taking the drug for at least three months to manage severe symptomatic orthostatic hypotension. The study had a crossover design with patients taking either midodrine or a placebo, then swapping over the next day. They were subjected to a tilt-table test, one hour after the dose, to see how quickly they felt faint. The mean time to the onset of symptoms was approximately 18 minutes with placebo and 27 minutes with midodrine.³

Although the phase III trial was relatively short, only 59 of the 82 patients taking midodrine completed the study.² Fifteen patients dropped out because of adverse effects such as hypertension and urinary frequency or

urgency. Other common adverse effects in that trial included pilomotor reactions, pruritus, paraesthesia and urinary retention. Midodrine should be used with caution in men with disorders of the prostate gland. Caution is also advised in patients with atherosclerotic disease and those at risk of QT prolongation.

Patients should begin midodrine at a low dose. This can be increased weekly according to the response. To reduce the risk of supine hypertension the evening dose of midodrine should be taken at least four hours before bedtime. Only eight patients need to be treated for one to develop supine hypertension. If this is not resolved by a dose reduction, midodrine should be stopped.

Orthostatic hypotension can be difficult to treat, but it is unclear how effective midodrine is. While the phase III trial showed a statistically significant advantage for midodrine in improving the symptom of light-headedness, the mean difference was less than one point on a 10-point visual analogue scale.² A systematic review found that midodrine improves standing systolic blood pressure, but the change in blood pressure when moving from a supine to standing position did not differ from control groups. The reviewers concluded that there was insufficient evidence to recommend midodrine for orthostatic hypotension.⁴ Its approval in Australia is limited to patients with severe symptomatic hypotension due to autonomic dysfunction after exacerbating factors have been addressed and other treatments have been inadequate.

TTT [manufacturer provided clinical evaluation](#)

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The Transparency Score is explained in [New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.](#)

At the time the comment was prepared, information about this drug was available on the website of the [Food and Drug Administration](#) in the USA.

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