

Moxonidine (Physiotens) for hypertension

(mox-ON-i-deen)

Summary

- Moxonidine is a centrally acting antihypertensive similar to clonidine.
- Moxonidine may be used as add-on therapy to further lower blood pressure if combination therapy with first- and second-line agents is insufficient or unsuitable.
- The effect of moxonidine on cardiovascular morbidity and mortality has not been tested in clinical trials.
- Moxonidine is less likely to cause rebound hypertension than clonidine. Dry mouth and tiredness are the most common adverse effects of moxonidine.
- Do not prescribe moxonidine for people with heart failure of any grade, as it has been associated with increased mortality and adverse events.
- Reduce the dose for people with renal impairment.

PBS listing

Restricted benefit

Moxonidine is listed on the Pharmaceutical Benefits Scheme for hypertension when used in combination with other antihypertensive agents.¹

Reason for PBS listing

Moxonidine was listed on a cost-minimisation basis compared with clonidine as an add-on therapy for hypertension. The Pharmaceutical Benefits Advisory Committee considered moxonidine to be no worse than clonidine in efficacy and that it appears to be less toxic.

Place in therapy

Moxonidine is similar to clonidine, but with reduced adverse effects. As with other centrally acting antihypertensives it will be useful for a small proportion of patients who are resistant or intolerant to first- and second-line drugs. While moxonidine lowers blood pressure effectively, there have been no large-scale trials to determine its effect on cardiovascular outcomes. In the UK, moxonidine has been available since 1996 but is not widely used.²

Moxonidine may be used as an add-on therapy if first- and second-line agents are insufficient or unsuitable

Moxonidine is a centrally acting antihypertensive that decreases activation of the sympathetic nervous system.³ It is similar to clonidine but is selective for imidazoline I₁ receptors over alpha₂-adrenergic receptors.⁴ This selectivity may explain why rebound hypertension appears less common with moxonidine than with clonidine.⁴

Centrally active agents are only recommended if first- and second-line agents fail to control blood pressure or are contraindicated or not tolerated.⁵⁻⁷ Moxonidine is an alternative to clonidine under these circumstances. A thiazide diuretic is recommended as first-line therapy, except for people with comorbidities that are compelling indications for using another drug class.^{5,7} Second-line choices include an ACE inhibitor, a beta blocker or a calcium-channel blocker.⁵⁻⁷ Combination therapy with up to three agents may be needed to reduce blood pressure sufficiently in some patients.

Moxonidine has been combined with all classes of first- and second-line antihypertensives. Be aware that combining moxonidine with a beta blocker may increase the likelihood of rebound hypertension on withdrawal of moxonidine (see Moxonidine is less likely to cause rebound hypertension than clonidine, opposite).

The effect of moxonidine on cardiovascular morbidity and mortality has not been tested in clinical trials

Clinical trials of moxonidine have been small scale, of up to 6-months' duration and have not analysed the effect of blood-pressure lowering with moxonidine on cardiovascular morbidity and mortality; in these trials, moxonidine lowered blood pressure as effectively as clonidine and first- and second-line agents.^{8–13} The lack of large-scale trials means that UK National Institute for Health and Clinical Excellence (NICE) guidelines do not recommend moxonidine for initial treatment of raised blood pressure.⁵

Safety issues

Moxonidine causes fewer adverse events than clonidine and in small trials was as well tolerated as first- and second-line antihypertensives. Moxonidine is contraindicated for patients with bradycardia (heart rate < 50 beats/minute), severe bradyarrhythmia, malignant arrhythmia, heart failure or severe renal impairment (see Dosing issues). Moxonidine can potentiate the action of benzodiazepines.

Report suspected adverse reactions to the Adverse Drug Reactions Advisory Committee (ADRAC) online (see www.tgasime.health.gov.au) or by using the 'Blue Card' distributed with *Australian Prescriber*. For information about reporting adverse drug reactions, see the Therapeutic Goods Administration website (www.tga.gov.au).

Moxonidine is less likely to cause rebound hypertension than clonidine

No blood pressure rebound effect after sudden discontinuation of moxonidine has been observed in clinical use or in animal models.^{3,14,15} Nevertheless, moxonidine should be withdrawn over a period of days rather than stopped abruptly.³

The prescribing information states that the likelihood of rebound hypertension when stopping moxonidine may be

increased with patients who are also taking a beta blocker. The beta blocker should be stopped first, then moxonidine withdrawn (as above) a few days later, with blood pressure monitored regularly.³ The manufacturer has not provided clinical data to support this recommendation.

Dry mouth and tiredness occur in some patients

Incidence of adverse effects is low, with dry mouth, headache, dizziness and tiredness most common.³ In 2 small trials the overall incidence of adverse events was less with moxonidine than with clonidine, while blood pressure control was similar.^{8,9}

Do not use moxonidine in people with heart failure of any grade

Moxonidine is contraindicated for people with heart failure, as it appears to worsen outcomes.³ The MOXCON trial in patients with heart failure was stopped early because of a greater number of deaths among participants who took moxonidine rather than placebo.¹⁶ Hospitalisation for heart failure, and acute myocardial infarction and adverse events were also more frequent in the moxonidine group.¹⁶

Dosing issues

Initiate moxonidine at 0.2 mg once daily (in the morning). If blood pressure needs further lowering after 2 weeks, increase to 0.4 mg/day (either as a single morning dose or as 2 divided doses, morning and evening). The dose may be increased to a maximum of 0.6 mg/day after a further 2 weeks, if required. Any single dose should not exceed 0.4 mg.³

Reduce the dose in people with renal impairment

If the estimated creatinine clearance is 30–60 mL/min, each single dose should be no more than 0.2 mg and the daily dose no more than 0.4 mg. Moxonidine is contraindicated if the estimated creatinine clearance is < 30 mL/min.³

Information for patients

Advise patients that moxonidine:

- has dry mouth as its most common side effect
- may cause tiredness or dizziness, and that they should avoid driving or operating machinery if they are affected
- may increase the effects of alcohol or any benzodiazepine-type medicines
- must not be stopped without medical supervision.

For more detailed information about moxonidine, suggest or provide the Physiotens consumer medicine information (CMI).

References

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.