

MOXONIDINE – AGREED CORE SAFETY PROFILE – 6 MARCH 2013

4.3 Contraindications

Moxonidine is contraindicated in patients with:

- hypersensitivity to the active substance or to any of the excipients
- sick sinus syndrome
- bradycardia (resting HR <50 beats/minute)
- AV-block 2nd and 3rd degree
- Cardiac insufficiency

4.4 Special warnings and precautions for use

Cases of varying degrees of AV block have been reported in the post-marketing setting in patients undergoing moxonidine treatment. Based on these case reports, the causative role of moxonidine in delaying atrioventricular conduction cannot be completely ruled out. Therefore, caution is recommended when treating patients with a possible predisposition to developing an AV block.

When moxonidine is used in patients with 1st degree AV block, special care should be exercised to avoid bradycardia. Moxonidine must not be used in higher degree AV blocks (see section 4.3).

When moxonidine is used in patients with severe coronary artery disease or unstable angina pectoris, special care should be exercised due to the fact that there is limited experience in this patient population.

Caution is advised in the administration of moxonidine to patients with renal impairment as moxonidine is excreted primarily via the kidney. In these patients careful titration of the dose is recommended, especially at the start of therapy.

Dosing should be initiated with 0.2 mg daily and can be increased to a maximum of 0.4 mg daily for patients with moderate renal impairment (GFR > 30 ml/min but < 60 ml/min) and to a maximum of 0.3 mg daily for patients with severe renal impairment (GFR < 30 ml/min), if clinically indicated and well tolerated.

If moxonidine is used in combination with a β -blocker and both treatments have to be discontinued, the β -blocker should be discontinued first, and then moxonidine after a few days.

So far, no rebound-effect has been observed on the blood pressure after discontinuing the treatment with moxonidine. However, an abrupt discontinuance of the moxonidine treatment is not advisable; instead the dose should be reduced gradually over a period of two weeks.

The elderly population may be more susceptible to the CV effects of blood pressure lowering drugs. Therefore therapy should be started with the lowest dose and dose increments should be introduced with caution to prevent the serious consequences these reactions may lead to.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration moxonidine and other antihypertensive agents result in an additive effect.

Since tricyclic antidepressants may reduce the effectiveness of centrally acting antihypertensive agents, it is not recommended that tricyclic antidepressants be co-administered with moxonidine.

Moxonidine can potentiate the sedative effect of tricyclic anti-depressants (avoid co-prescribing), tranquillisers, alcohol, sedatives and hypnotics.

Moxonidine moderately augmented the impaired performance in cognitive functions in subjects receiving lorazepam. Moxonidine may enhance the sedative effect of benzodiazepines when administered concomitantly.

Moxonidine is excreted through tubular excretion. Interaction with other agents that are excreted through tubular excretion cannot be excluded.

4.6 Pregnancy and lactation

Pregnancy:

There are no adequate data from use of moxonidine in pregnant woman. Studies in animals have shown embryo-toxicological effects (see section 5.3). The potential risk for humans is unknown.

Moxonidine should not be used during pregnancy unless clearly necessary.

Lactation:

Moxonidine is secreted in breast milk and should therefore not be used during breast feeding. If therapy with moxonidine is considered absolutely necessary, the breast feeding shall be stopped.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Somnolence and dizziness have been reported. This should be borne in mind when performing these tasks.

4.8 Undesirable effects

Most frequent side effects reported by those taking moxonidine include dry mouth, dizziness, asthenia and somnolence. These symptoms often decrease after the first few weeks of treatment.

Undesirable Effects by System Organ Class: *(observed during placebo-controlled clinical trials with n=886 patients exposed to moxonidine resulted in frequencies below):*

*there was no increase in frequency compared to placebo

MedDRA System Organ Class	Very common > 1/10	Common ≥ 1/100, < 1/10	Uncommon ≥ 1/1,000, < 1/100
Cardiac disorders			Bradycardia
Ear and labyrinth disorders			Tinnitus
Nervous system disorders		Headache*, Dizziness, vertigo, Somnolence	Syncope*
Vascular disorders			Hypotension, (including orthostatic)
Gastrointestinal disorders	Dry mouth	Diarrhoea, Nausea, vomiting, dyspepsia	
Skin and subcutaneous		Rash, pruritus	Angioedema

tissue disorders			
General disorders and administration site conditions		Asthenia	Oedema
Musculoskeletal and connective tissue disorders		Back pain	Neck pain
Psychiatric disorders		Insomnia	Nervousness

4.9 Overdose

Symptoms of overdose

In the few cases of overdose that have been reported, a dose of 19.6 mg was ingested acutely without fatality. Signs and symptoms reported included: headache, sedation, somnolence, hypotension, dizziness, asthenia, bradycardia, dry mouth, vomiting, fatigue and upper abdominal pain. In case of a severe overdose close monitoring of especially consciousness disturbances and respiratory depression is recommended.

In addition, based on a few high dose studies in animals, transient hypertension, tachycardia, and hyperglycaemia may also occur.

Treatment of overdose

No specific antidote is known. In case of hypotension, circulatory support such as fluids and dopamine administration may be considered. Bradycardia may be treated with atropine. Alpha-receptor antagonists may diminish or abolish the paradoxical hypertensive effects of a moxonidine overdose.