SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Moxonidine 200 microgram Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 200 micrograms moxonidine.

Excipient with known effect:

Each film-coated tablet contains 88.92 mg of lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

Pale pink coloured (approx. 6 mm) round biconvex film coated tablets debossed with MX2 on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Mild to moderate essential or primary hypertension.

4.2 Posology and method of administration

Adults (including the elderly):

Treatment should be started with 200 micrograms of moxonidine in the morning. The dose may be titrated after three weeks to 400 micrograms, given as one dose or as divided doses (morning and evening) until a satisfactory response has been achieved. If the response is still unsatisfactory after a further three weeks' treatment, the dosage can be increased up to a maximum of 600 micrograms in divided doses (morning and evening).

A single dose of 400 micrograms of moxonidine and a daily dose of 600 micrograms in divided doses (morning and evening) should not be exceeded.

In patients with moderate renal dysfunction (GFR above 30 ml/min, but below 60 ml/min), the single dose should not exceed 200 micrograms and the daily dose should not exceed 200 micrograms of moxonidine.

The tablets should be taken with sufficient liquid. As the intake of food has no influence on the pharmacokinetic properties of moxonidine, the tablets may be taken before, during or after the meal.

Paediatric population

Moxonidine is not recommended for use in children and adolescents below 18 years due to lack of data on safety and efficacy.

4.3 Contraindications

Moxonidine should not be used in cases of:

- hypersensitivity to the active substance or to any of the excipients listed insection 6.1.
- sick sinus syndrome or sino-atrial block
- 2nd or 3rd degree atrioventricular block
- bradycardia (below 50 beats/minute at rest)
- severe heart failure (see Section 4.4)
- severe renal dysfunction (GFR <30 ml/min, serum creatinine concentration >160 µmol/l).

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 kidneys. In these patients' careful titration of the dose is recommended, especially at the start oftherapy. Dosing should be initiated with 200 micrograms daily and can be increased to a maximum of 400 micrograms daily for patients with moderate renal impairment (GFR above 30 ml/min, but below 60 ml/min), if clinically indicated and well tolerated.

If moxonidine is used in combination with a beta-blocker and both treatments have to be discontinued, the beta-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.

Due to a lack of clinical data supporting the safety in patients with co-existing moderate heart failure, moxonidine must be used with caution in such patients.

The elderly population may be more susceptible to the cardiovascular 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.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Due to a lack of data on safety and efficacy, moxonidine should not be used in children and adolescents below 18 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent administration of other antihypertensive agents enhances the hypotensive effect of moxonidine.

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 Fertility, 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.

Breast-feeding:

Moxonidine is secreted in breast milk and should therefore not be used during breast-feeding.

If therapy with moxonidine is considered absolutely necessary, breast-feeding should 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):*

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 tissue disorders		Rash/ Pruritus	Angioedema
General disorders and administration site reactions		Asthenia	Oedema
Musculoskeletaland connective tissue disorders		Back pain	Neck pain
Psychiatricdisorders		Insomnia	Nervousness

* there was no increase in frequency compared to placebo

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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. α-Receptor antagonists may diminish or abolish the paradoxal hypertensive effects of a moxonidine overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Imidazoline receptor agonists, moxonidine, ATC code: C02AC05.

In different animal models, moxonidine has been shown to be a potent antihypertensive agent. Available experimental data convincingly suggest that the site of the antihypertensive action of moxonidine is the central nervous system (CNS). Within the brainstem, moxonidine has been shown to selectively interact with I1-imidazoline receptors. These imidazoline-sensitive receptors are concentrated in the rostral ventrolateral medulla, an area critical to the central control of the peripheral sympathetic nervous system. The net effect of this interaction with the I1-imidazoline receptor appears to result in a reduced activity of sympathetic nerves (demonstrated for cardiac, splanchnic and renal sympathetic nerves).

Moxonidine differs from other available centrally acting antihypertensives by exhibiting only low affinity to central α_2-adrenoceptors as compared to I1-imidazoline receptors; α_2-adrenoceptors are considered the molecular target via which sedation and dry mouth, the most common undesired side effects of centrally acting antihypertensives, are mediated.

In humans, moxonidine leads to a reduction of systemic vascular resistance and consequently in arterial blood pressure.

5.2 Pharmacokinetic properties

Oral moxonidine treatment of rats and dogs resulted in rapid and almost complete absorption and peak plasma levels within <0.5 hours. Average plasma concentrations were comparable in both species after p.o. and i.v. administration. The elimination half-lives of radioactivity and unchanged compound were estimated to be 1-3 hours. Moxonidine and its two main metabolites (4,5-dehydromoxonidine and a guanidine derivative) was predominantly excreted in the urine. No indication of moxonidine cumulation was observed in either species during chronic toxicity studies after 52 weeks.

In humans, about 90% of an oral dose of moxonidine is absorbed; it is not subject to first-pass metabolism and its bioavailability is 88%. Food intake does not interfere with moxonidine pharmacokinetics. Moxonidine is 10-20% metabolised, mainly to 4,5-dehydromoxonidine and to a guanidine derivative by opening of the imidazoline ring. The hypotensive effect of 4,5-dehydromoxonidine is only 1/10, and that of the guanidine derivative is less than 1/100 of that of moxonidine. The maximum plasma levels of moxonidine are reached 30-180 minutes after the intake of a film-coated tablet.

Only about 7% of moxonidine is bound to plasma protein (Vd_{SS} = 1.8 □ 0.4 1/kg). Moxonidine and its metabolites are eliminated almost entirely via the kidneys. More than 90% of the dose is eliminated via the kidneys in the first

24 hours after administration, while only about 1% is eliminated via the faeces. The cumulative renal excretion of unchanged moxonidine is about 50-75%.

The mean plasma elimination half-life of moxonidine is 2.2-2.3 hours, and the renal elimination half-life is 2.6-2.8 hours.

Pharmacokinetics in the elderly

Small differences between the pharmacokinetic properties of moxonidine in the healthy elderly and younger adults are unlikely to be clinically significant. As there is no accumulation of moxonidine, dosage adjustment is unnecessary provided renal function is normal.

Pharmacokinetics in children

No pharmacokinetic studies have been performed in children.

Pharmacokinetics in renal impairment

In moderately impaired renal function (GFR 30-60 ml/min), AUC increased by 85% and clearance decreased to 52%. In such patients the hypotensive effect of moxonidine should be closely monitored, especially at the start of treatment; additionally, single doses should not exceed 200 micrograms and the daily dose should not exceed 200 micrograms.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

Chronic oral treatment for 52 weeks of rats (with dosages of 0.12-4 mg/kg) and dogs (with dosages of 0.04-0.4 mg/kg) revealed significant effects of moxonidine only at the highest doses.

Slight disturbances of electrolyte balance (decrease of blood sodium and increase of potassium, urea and creatinine) were found in the high dose rats and emesis and salivation only for the high dose dogs. In addition, slight increases of liver weight were obvious for both high dose species.

Reproductive toxicity studies showed no effect on fertility and no teratogenic potential. Embryo-fetal toxicity was seen at doses associated with maternal toxicity.

Increased embryo-fetal loss and delayed fetal development were seen in rats with doses above 2 mg/kg/day and in rabbits with doses above 0.7 mg/kg/day.

In a peri- and post-natal study in rats reduced pup weight, viability and delayed development was noted with doses above 1 mg/kg/day.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet:

Lactose monohydrate

crospovidone

povidone

magnesium stearate

Film-coating agent:

- hypromellose
- titanium dioxide
- macrogol
- talc
- ferric oxide red

Purified water

6.2 Incompatibilities

No incompatibilities are known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The tablets are packed in blister strips made of clear PVC/PVdC film with Aluminium lidding foil, within cartons. Each carton contains 14, 28 or 84 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Relonchem Limited,

Cheshire House,

Gorsey Lane,

Widnes,

Cheshire,

WA8 0RP,

United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 20395/0399

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/09/2025

10 DATE OF REVISION OF THE TEXT

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