Mexonidine Tablets 0.2 mg / 0.3 mg

Ifimox® 0.2 - Ifimox® 0.3

COMPOSITION

Infimox® 0.2

Each film coated tablet contains :

Moxonidine BP.....0.2 mg

Colour: Titanium Dioxide IP

Infimox® 0.3

Each film coated tablet contains :

Moxonidine BP.....0.3 mg

Colour: Titanium Dioxide IP

PHARMACEUTICAL FORM

Film Coated Tablet

THERAPEUTIC INDICATION

It is indicated for the treatment of hypertension.

POSOLOGY AND METHOD OF ADMINISTRATION

Posology

Adults

Treatment should be started with 1 tablet (0.2mg) of Moxonidine in the morning. The dose may be titrated after three weeks to 0.4mg, 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 0.6 mg in divided doses (morning and evening).

A single dose of 0.4 mg Moxonidine and a daily dose of 0.6 mg Moxonidine in divided doses (morning and evening) should not be exceeded.

Treatment must be instituted with the lowest dose of Moxonidine.

Paediatric population

Moxonidine should not be given to children and adolescents under 16 years of age as insufficient therapeutic data are available for this.

Elderly

Provided that renal function is not impaired, dosage recommendation is the same as for adults.

Renal impairment

In patients with moderately impaired renal function (GFR > 30 ml/min but < 60 ml/min), the single dose should be not more than 0.2 mg and the daily dose not more than 0.4 mg moxonidine.

Hepatic impairment

No studies are available in patients with impaired hepatic function. However, as moxonidine lacks extensive hepatic metabolism no major influence on the pharmacokinetics may be expected and dosage recommendation is the same for patients with mild to moderate hepatic impairment as for adults.

The treatment should not be stopped abruptly, but withdrawn over a period of two weeks.

Method of administration: For oral use only.

As concomitant ingestion of food does not affect the pharmacokinetics of moxonidine, moxonidine can be taken before, during or after meals. The tablets should be taken with sufficient fluid.

CONTRAINDICATIONS

Moxonidine is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients.

Moxonidine should not be used in cases of:

- Sick sinus syndrome or sino-atrial block
- 2nd or 3rd degree atrioventricular block
- Bradycardia (below 50 beats/minute at rest)
- Severe heart failure
- Severe renal dysfunction (GFR <30 ml/min, serum creatinine concentration >160 µmol/l).

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.

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 of therapy. 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, the rare Lapp 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.

DRUG INTERACTION

Concomitant administration of moxonidine and other antihypertensive medicinal products result in an additive effect.

Since tricyclic antidepressants may reduce the effectiveness of centrally acting antihypertensive medicinal products, 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), tranquillizers, 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 medicinal products that are excreted through tubular excretion cannot be excluded.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no adequate data from use of moxonidine in pregnant women. Studies in animals have shown embryo-toxicological effects. 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, the breast feeding shall be stopped.

Paediatric use

Moxonidine should not be given to children below the age of 16 years as insufficient therapeutic experience exists in this group.

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.

UNDESIRABLE EFFECTS

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

MedDRA system organ class	Very Common ≥ 1/10	Common ≥ 1/100, <1/10	Uncommon ≥ 1/1000, <1/100
Cardiac disorders			Bradycardia
Ear and labyrinth disorders			Tinnitus
Nervous system disorders			Syncope*
Vascular disorders			Hypotension* (including orthostatic)
Gastrointestinal disorders	Dry mouth	Diarrhea, Nausea / Vomiting / Dyspepsia	
Skin and subcutaneous tissue disorders		Rash / Pruritus	Angioedema
General disorders and administration site reactions		Asthenia	Oedema
Musculoskeletal and connective tissue disorders		Back pain	Neck pain
Psychiatric disorders		Insomnia	Nervousness

*there was no increase in frequency compared to placebo

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Kindly report any suspected adverse reactions to pharmavigil@jbcpl.com

OVERDOSE

Symptoms

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

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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: anti-hypertensives, antiadrenergic agents, centrally acting, imidazoline receptor agonists.

In various animal models moxonidine has been shown to be a potent antihypertensive. Available experimental data indicate that the site of action of the antihypertensive effect of moxonidine is the central nervous system (CNS).

Moxonidine has been shown to bind selectively to the I1-imidazoline receptors in the brain stem. These imidazoline-sensitive receptors are concentrated in the rostral ventrolateral medulla, an area which is of crucial importance for central control of the peripheral sympathetic nervous system. The result of this effect on the I1-imidazoline receptors has been apparent in reduced activity in the sympathetic nerves. (demonstrated for cardiac, splanchnic and renal sympathetic nerves).

Moxonidine differs from other available centrally acting antihypertensives by having only a weak affinity for central alpha-2-adrenoceptors compared to I1-imidazoline receptors alpha-2 adrenoceptors are considered to be the molecular target though which most common adverse reactions of centrally acting antihypertensives such as drowsiness and dry mouth - are mediated. In humans, moxonidine results in a reduction of systemic vascular resistance and consequently of arterial blood pressure.

The effects of moxonidine on mortality and cardiovascular morbidity are currently unknown.

PHARMACOKINETIC PROPERTIES

Absorption

In humans, about 90% of an oral dose of moxonidine is absorbed; there is no first-pass effect and the bioavailability is 88%. Food intake does not affect moxonidine.

Distribution

The peak plasma concentration of moxonidine is reached in the course of 30-180 minutes after administration of a film-coated tablet.

Only about 7% of moxonidine is plasma protein bound (VDss = 1.8 ± 0.4 l/kg).

Biotransformation

10-20% of moxonidine is metabolised, principally to 4,5-dehydromoxonidine and a guanidine derivative on opening of the imidazoline ring. The hypotensive effect of 4,5-dehydromoxonidine is only 1/10 that of moxonidine and for the guanidine derivative it is less than 1/100.

Elimination

Moxonidine and its metabolites are excreted almost exclusively via the kidneys. More than 90% of the dose is eliminated via the kidneys in the course of the first 24 hours after administration, but only about 1% is eliminated in the faeces. The cumulative elimination of unchanged moxonidine via the kidneys is about 50–75%. The mean plasma elimination half-life is 2.2–2.3 hours and the renal elimination half-life is 2.6–2.8 hours.

Pharmacokinetics in the elderly

Small variations in the pharmacokinetic properties of moxonidine in healthy elderly patients and young adults have not proved to be clinically significant. As there is no accumulation of moxonidine, a dose adjustment is not necessary, provided that renal function is normal.

Pharmacokinetics in children

No pharmacokinetic studies in children have been performed.

Pharmacokinetics in impaired renal function

In patients with moderately impaired renal function (GFR 30-60 ml/min), the AUC is increased by 85 % and the clearance reduced by 52 %. In these patients, the hypotensive effect of moxonidine should be monitored carefully, particularly at the beginning of treatment. In addition, the individual dose should not exceed 0.2 mg and the daily dose 0.4 mg.

INCOMPATIBILITY

None stated.

PACKAGING INFORMATION

Blister of 10 tablets & 4 tablets

STORAGE INSTRUCTIONS

Store protected from light & moisture, at a temperature not exceeding 30°C.

Keep all medicines out of reach of children.

Marketed by & ® Regd. Trade Mark of :
J. B. CHEMICALS & PHARMACEUTICALS LTD.
Neelam Centre, 'B' Wing, Hind Cycle Road,
Worli, Mumbai - 400 030. India.

DATE OF REVISION
October 2021

Note: This prescribing information is applicable for India Market only.