STADA

Isosorbide-5-mononitrate Angistad

Formulation:
1 tablet contains:
Active compound: Isosorbide-5-mononitrate 20 mg.
Isosorbide-5-mononitrate 40 mg.

Indications:
- long-term treatment of circulatory disorders affecting the coronary arteries (ischaemic heart disease)
- prevention of attacks of angina (heart pain)
- follow-up treatment of heart attack when symptoms of angina persist
- high blood pressure in the lung circulation (pulmonary hypertension)
- treatment of severe weakness of heart muscle (chronic cardiac failure), in combination with cardiac glycosides and/or diuretics.

Contraindications:
ISMN must not be used in patients with:
- hypersensitivity to nitrate compounds
- acute myocardial infarction with low filling pressures
- impaired function of the left ventricle (left heart failure) with low filling pressures
- shock
- very low blood pressure
- diseases of the heart muscle with narrowing of the cavity of the heart (hypertrophic obstructive cardiomyopathy)
- constrictive pericarditis
- pericardial tamponade
- aortic stenosis
- mitral stenosis
- marked anaemias
- head trauma
- cerebral haemorrhage
- closed-angle glaucoma
- hyperthyroidism
- concomitant therapy with sildenafil citrate

Note:
Administration of ISMN, particularly to patients with high blood pressure of unknown cause in the lung circulation (primary pulmonary hypertension) may give rise to transient reduction in the oxygen content of the arterial blood (hypoxaemia), due to the passage of a relative excess of blood to under-ventilated segments of the lung (hyperperfusion) of hypoventilated alveolar territory).
This applies particularly to patients with circulatory disorders of the coronary arteries (ischaemic heart disease). Particularly careful medical supervision is required in:
- aortic and/or mitral stenosis
- tendency to circulatory disorders associated with low blood pressure (orthostatic circulatory disorders)
- diseases associated with increased pressure inside the skull (intracranial hypertension) (further increases in pressure have so far only been observed in association with intravenous administration of glyceryl trinitrate)
- patients with severe disorders of kidney function

ISMN is not suitable for the treatment of acute attacks of angina.

Mode of Action:
Isosorbide-5-mononitrate has a direct relaxant effect on vascular smooth muscle, and leads to vasodilation. Isosorbide-5-mononitrate causes dilatation particularly of venous vessels. The blood supply to the heart is reduced and the preload causes a fall in the raised filling pressures of both ventricles, with a consequent reduction in ventricular size and wall tension. This results in reduced myocardial oxygen consumption. Arterial dilatation also occurs, leading to a reduction in afterload and a fall in blood pressure.
Finally, there is also a coronary vasodilator effect.

Pharmacokinetics Data:
Isosorbide is rapidly and completely absorbed following oral administration. The systemic availability is 90-100%. Isosorbide-5-mononitrate is almost completely metabolised in the liver. The metabolites formed are inactive. The plasma half-life is 4-5 hours. Isosorbide-5-mononitrate is almost entirely excreted by the kidneys in the form of its metabolites. Only approximately 2% is eliminated by the kidneys in unchanged form. In the presence of impaired renal function, the plasma half-life may be prolonged.

Side Effects:
It is common for headaches to occur at the beginning of treatment (”nitrate headache”); experience has generally shown that this disappears after a few days when treatment is continued.
A fall in blood pressure frequently occurs, particularly on first use of the drug but also when the dose is increased. This may be associated with a reflex rise in the pulse rate, and with dizziness and weakness.
Nausea, vomiting, transient skin disorders (flushing) and allergic skin reactions may sometimes occur. In rare cases, in

association with a marked fall in blood pressure, there may be aggravation of the symptoms of angina (paradoxical nitrate effect), and/or marked paradoxical bradycardia (slowing of the pulse rate).

Special Note:
Even when appropriately used, this drug may alter the patient's reaction times to such an extent as to impair the capacity to drive or operate machinery. This applies particularly in combination with alcohol.

Interaction with other drugs:
Simultaneous ingestion of blood pressure lowering agents (antihypertensive agents), beta blockers, calcium antagonists, other blood vessel dilating agents (vasodilators), neuroleptics or tricyclic anti-depressants and alcohol may potentiate the blood pressure lowering effect of ISMN.
The blood pressure raising effect of dihydroergotamine may be increased by simultaneous ingestion of ISMN. Weakening of the effect of ISMN by the ingestion of non-steroidal antirheumatic drugs cannot be ruled out. Concomitant therapy with NO-donators e.g. the active substance of ISMN and sildenafil citrate a marked increase of blood lowering effect may occur.

Precautionary statement:
Development of tolerance may occur with all forms of nitrate therapy particularly with the long acting preparations that maintain continuously high plasma nitrate concentration.

Symptoms and Treatment for Overdosage and Antidote(s):
a) Depending on the degree of intoxication, the clinical picture includes the following principal symptoms: Hypotension with reflex tachycardia, weakness, dizziness, confusion, headache, asthmatic symptoms, flushing, nausea, vomiting, diarrhea. With severe intoxication, cyanosis, dyspnea, confusion, slowing of breathing and heart rate, and paralysis may develop.
Very high doses may lead to a rise in intracranial pressure with cerebral symptoms. With chronic overdosage, methaemoglobinaemia may occur.

b) Treatment of Overdosage
In addition to general measures such as gastric lavage, and supine posture with elevation of the legs, patients must be given intensive care with monitoring and if necessary correction of vital parameters. In the presence of severe hypotension and/or shock, volume replacement should be given. In addition, noradrenaline and/or dopamine may be infused to assist the circulation.
Administration of adrenaline and related substances is contraindicated.
In Methaemoglobinaemia, exchange transfusion is given. In milder cases, 10-20ml of methylene blue solution (1%) is given intravenously.

Dosage:
Unless otherwise prescribed, 40 mg once daily, or 20 mg twice daily. In exceptional cases, the dose may be increased to 40 mg twice daily. In order to obtain the full effect of the drug, when a daily dose of 40 mg twice daily is taken, the second tablet should not be taken not more than 8 hours after the first.

Route and duration of use:
Tablets should be swallowed whole with a little fluid after meals.
Treatment with ISMN should not be abruptly discontinued, but tailed off gradually, since withdrawal phenomena (a "rebound effect") cannot be ruled out.

Storage:
Store at temperatures not exceeding 30°C. Keep dry and protect from light.

Keep drugs out of reach of children.

Caution:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription (List B')

Availability:

Blister pack x 10's (Box of 100's)

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