VASOCOR

Tablets

Composition
Each tablet contains Isosorbide-5-mononitrate 20 or 40 mg

Action
Like other nitrates, isosorbide-5-mononitrate is suitable for the chronic treatment of coronary heart disease and heart failure. In angina pectoris its fundamental mechanism of action is primarily based on an increase in venous capacitance (venous pooling) leading to a decreased return of blood to the heart. Owing to this phenomenon, left-ventricular end-diastolic pressure (preload) and hence filling volume diminishes, resulting in a decreased myocardial oxygen requirement at rest and especially during exercise, an improvement in exercise capacity in patients with angina pectoris. In the coronary arterial circulation, isosorbide-5-mononitrate dilates both extramural conductance and small resistance vessels. The drug appears to cause a redistribution of coronary blood flow to the ischemic subendocardium by selectively dilating large epicardial vessels. It also produces relaxation of vasospasm, whether spontaneous or induced by ergometrine.

In addition, isosorbide-5-mononitrate exerts a dose-dependent dilating effect on the arteriolar vascular bed, because of which systemic vascular resistance (after load) and left-ventricular systolic wall tension decrease, leading to a reduction in myocardial oxygen consumption.

In chronic heart failure, the dilating action exerted by isosorbide-5-mononitrate on the veins lowers the elevated left-ventricular filling pressure, while at the same time cardiac output either remains unchanged or increases slightly.

Isosorbide-5-mononitrate proves especially effective in patients with severe heart failure showing prominent signs and symptoms of venous pulmonary congestion due to a pronounced increase in left-ventricular filling pressure. If an increase in cardiac output desired, combined treatment with an arterial vasodilator recommended.

The duration of action of isosorbide-5-mononitrate is longer than that of its parent compound. A therapeutic efficacy similar to that of isosorbide dinitrate may be achieved with approximately half the dose.

Pharmacokinetics
Isosorbide-5-mononitrate is rapidly and completely absorbed from the conventional dosage forms. Unlike isosorbide dinitrate, isosorbide-5-mononitrate is free from first-pass metabolism in the liver, and its bioavailability therefore shows lower interindividual variability.

AUC values assessed by reference to the plasma levels increase linearly with the dose. Mean half-lives of isosorbide-5-mononitrate calculated after administration range between 4.0 and 4.8 hours.

No accumulation of isosorbide-5-mononitrate seen after repeated once-daily administration in normal volunteers or in patients. The results of pharmacokinetic studies suggest that no alterations of the dosage should be necessary in patients with coronary heart disease, renal failure, or liver cirrhosis. Ingestion of food reported to have only a negligible effect on the absorption of isosorbide-5-mononitrate.

Indications
- Long-term treatment of coronary heart disease (CHD)
- Prophylaxis of angina pectoris
- Adjunctive therapy in chronic congestive heart failure which is concomitantly being treated with glycosides, diuretics, ACE inhibitors or arterial vasodilating medicines
- Treatment of pulmonary hypertension

Contraindications

- Marked hypotension (BP ≤ 90 mm Hg systolic)
- Circulatory collapse, shock
- Cardiogenic shock unless sufficient end-diastolic pressure is maintained e.g. by the use of positive inotropic medicines or intra-aortic balloon counter pulsation
- Myocardial infarction with low ventricular filling pressure
- Hypersensitivity to organic nitrates
- Concomitant administration of Isosorbide 5-mono nitrate and phosphodiesterase 5 inhibitors is contraindicated.

Warnings

The benefits of this drug during the early days following an acute myocardial infarction not been established. If organic nitrates used in early infarction, hemodynamic monitoring and frequent clinical assessment should be conducted, because of the potential deleterious effects of hypotension.

Pregnancy

Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers

It is unknown whether this drug is excreted in human milk. However, because many drugs are excreted in human milk, caution should be exercised when this drug is administered to nursing mothers.

Adverse Reactions

Cutaneous vasodilatation with flushing may occur. Headache is common and may be severe and persistent during initial therapy.

Transient episodes of dizziness, palpitations, vertigo and weakness, as well as other signs of cerebral ischemia associated with postural hypotension, may develop occasionally.

An occasional individual may exhibit a marked sensitivity to the hypotensive effects of nitrates, and severe responses (nausea, vomiting, weakness, restlessness, pallor, perspiration and collapse) may occur, even with the usual therapeutic dose.

Paradoxical bradycardia and increased angina pectoris may accompany nitrate-induced hypotension. Drug rash and/or exfoliative dermatitis may sometimes occur.

Precautions

Nitrate therapy may aggravate the angina caused by hypertrophic cardiomyopathy.
Marked symptomatic orthostatic hypotension has been reported when calcium channel blockers and organic nitrates have been used in combination. Dose adjustment of either class of agents may be necessary.

Tolerance to the vascular and antianginal effects of organic nitrates has been demonstrated in clinical trials. Tolerance to this drug and cross-tolerance to other nitrates and nitrites may occur.
Headache, which may occur during initial therapy with this drug, is usually relieved by the use of standard remedies, or by lowering the dose. It tends to disappear after the first or second week of medication.

In clinical trials involving patients with angina, there have been reports of attacks being more easily provoked and of rebound in hemodynamic effects, soon after nitrate withdrawal. Therefore, it would appear prudent to withdraw the drug gradually, rather than stop the treatment abruptly.

Although nitrate therapy permits more normal activity, patients should be warned not to misinterpret freedom from anginal attack as a signal to drop all restrictions.

Drug Interactions

Alcohol
Alcohol may enhance any marked sensitivity to the hypotensive effect of nitrates.

Calcium antagonists, ACE inhibitors, β-blockers, diuretics, antihypertensives, tricyclic antidepressants, or major tranquilizers- Concomitant administration may may potentiate the blood-pressure-lowering effect of Isosorbide.

Phosphodiesterase 5 inhibitors
Increases the blood pressure-lowering effect of acutely and chronically administered nitrates and other nitric oxide (NO) donors. Use of phosphodiesterase 5 inhibitors is therefore contraindicated.

Diagnostic Interference
Nitrates may interfere with the Zlatkis-Zak color reaction, causing a false report of decreased serum cholesterol.

Dosage and Administration

The usual dose is 20 mg, 2-3 times daily if necessary; the total daily dosage may be increased up to a maximum of 120 mg in order to protect patients from attacks of angina.

Over Dosage

Manifestations
High doses of isosorbide-5-mononitrate may lead to more pronounced systemic side effects, e.g. to a marked fall in blood pressure or to collapse. Excessive dosage of all nitrates may rarely provoke methemoglobinemia.

Treatment
Overdosage should be treated symptomatically. The main symptom is likely to be hypotension, which may be treated by elevation of the legs and passive exercise of the extremities to promote venous return. Gastric lavage may also be useful.

Presentation

Vasocor 20 mg Tablets
Box of 40 tablets.

Vasocor 40 mg Tablets
Box of 40 tablets