xxxxxxxx-8883

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

NIKORAN

(Nicorandil Tablets, 5 mg and 10 mg)

COMPOSITION

NIKORAN-5 : Each uncoated tablet contains Nicorandil..... 5 mg
NIKORAN-10 : Each uncoated tablet contains Nicorandil.....10mg

DESCRIPTION

Nicorandil is a medication that belongs to a novel class of agents for the management of Coronary Heart Disease. It has a dual mode of action being a selective ATP dependent potassium channel opener and nitric oxide donor.

CLINICAL PHARMACOLOGY

Nicorandil is a new antianginal drug having potent vasodilator and antispasmodic properties which are relatively selective to the coronary arteries. Nicorandil is a potassium channel opener that also contains a nitrate moiety. Potassium channel opening hyperpolarizes vascular cell membranes, causing voltage operated calcium (Ca^{++}) ion channels to close with a consequent reduction in free intracellular Ca^{++} concentration that results in a reduction in vasomotor tone, particularly in the coronary resistance vessels. Nicorandil also induces vascular smooth muscle relaxation by releasing NO which in turn increases intracellular cyclic guanosine monophosphate (cGMP) levels. Nicorandil markedly increases coronary blood flow in a dose dependent manner and has little effect on cardiac output, arterial pressure and pulse pressure. Nicorandil thus dilates the large coronary arteries to the same extent as nitroglycerine through NO release and reduces the vasomotor tone of the resistant coronary vessels through its potassium channel opener action. In non-ischemic myocardium, Nicorandil at therapeutic doses has neither negative inotropic effect nor any effect on atrioventricular conduction. The overall action improves blood flow to post-stenotic regions and the oxygen balance in the myocardium. Furthermore, increasing experimental evidence suggests that potassium channel activation may also exert a direct cytoprotective effect by augmenting normal physiological processes which protect the heart against ischemic events mimicing the action of Adenosine.

Nicorandil is well absorbed with absolute bioavailability of 75± 23% indicating that no significant hepatic first-pass effect exists. Maximum plasma concentrations are achieved within 30 to 60 minutes and are dose related. Metabolism is mainly by denitration of the molecule into the nicotinamide pathway with approximately 20% of an administered dose being excreted in the urine mainly as metabolites. Although Nicorandil is rapidly eliminated from the plasma with a half-life of about 50 minutes the duration of action persists for almost 12 hours thus enabling a twice daily dosage. Nicorandil is only slightly bound to plasma proteins. No clinically relevant modification in the pharmacokinetic profile have been seen in the elderly or in patients with liver disease or chronic renal failure.

INDICATIONS

Nicorandil tablets are indicated for the long-term management of coronary heart disease.

CONTRAINDICATIONS

Nicorandil is contraindicated in patients with cardiogenic shock, left ventricular failure with low filling pressure and in hypotension. It is also contraindicated in patients who have demonstrated an idiosyncratic response or hypersensitivity to nicorandil.

WARNING

The use of Nicorandil should be avoided in patients with depleted blood volume, low systolic blood pressure, acute pulmonary oedema or acute myocardial infarction with acute left ventricular failure and low filling pressures.

PRECAUTIONS

Patients on vasodilator therapy should be warned not to drive or operate machinery until it is established that their performance is unimpaired. This may apply to Nicorandil.

USE IN PREGNANCY, LACTATION & CHILDREN

Animal studies have not revealed any harmful effect of nicorandil on the foetus although there is no experience in humans. It should not be used in pregnant patients unless there is no safer alternative.

As it is not known whether nicorandil is excreted in human milk, breast feeding should be avoided by nursing mothers who require therapy. A paediatric dosage has not been established and use of nicorandil is not recommended in children.

ADVERSE REACTIONS

The most frequent effect to be anticipated is transitory headache, especially when treatment is initiated. The headache resolves with continued therapy. The incidence and the severity of the headache can be reduced by initiating the therapy at lower doses. Cutaneous vasodilation with flushing is less frequent. Nausea, vomiting, dizziness and a feeling of weakness have occasionally been reported. At high dosage a reduction in blood pressure and/or an increase in heart rate may occur.

DRUG INTERACTIONS

No pharmacological or pharmacokinetic interactions have been observed in humans or animals with beta-blockers, digoxin, rifampicin, cimetidine, nicoumalone, calcium antagonist or a combination of digoxin and frusemide. Nevertheless, there is the possibility that nicorandil may potentiate the blood pressure lowering effect of other vasodilators, tricyclic antidepressants or alcohol.

DOSAGE & ADMINISTRATION

Adults : The recommended starting dose is 10mg nicorandil twice daily although 5mg twice daily may be employed in patients particularly susceptible to headache. Subsequently the dosage should be titrated upward depending on the clinical response. The usual therapeutic dosage is in the range 10 to 20 mg nicorandil twice daily, although dose of up to 40mg twice daily has been reported.

Elderly : There is no special requirement for dosage adjustment in elderly patients. As with all medicines the lowest effective dosage should be used.

Children: Paediatric dosage has not been established and use of nicorandil is not recommended.

OVERDOSAGE

Acute overdosage is likely to be associated with peripheral vasodilation, decreased blood pressure and reflex tachycardia. Cardiac function should be monitored and general supportive measures employed. If necessary, circulating plasma volume should be increased by infusion of suitable fluid. In life-threatening situations administration of vasopressors should be considered. There is no experience of massive overdosage in humans although the LD50 in dogs is in the range 65.5 to 125 mg/kg and in rodents it is in the order of 1200 mg/kg.

STORAGE CONDITION

Nicorandil is sensitive to moisture and heat. Nicorandil tablets should be stored at 2^{O} to 8^{O}C (in a refrigerator). Replace desiccant and cap after use. Once opened it is desirable to use the contents of the bottle pack within 1 month.

KEEP OUT OF REACH OF CHILDREN

PRESENTATION

NIKORAN-5: It is available as white, flat, heart shaped, uncoated tablets debossed with “5” on one side, in bottle pack of 20 tablets and also in bottle pack of 6 tablets.

NIKORAN-10: It is available as white, flat, heart shaped, uncoated tablets debossed with “10” on one side, in bottle pack of 20 tablets and also in bottle pack of 6 tablets.

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Manufactured by :
TORRENT PHARMACEUTICALS LTD.
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