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

VASOVIN XL

1. Generic Name

Timed Release Capsules of Nitroglycerin 2.5 mg and 6.5 mg

2. Qualitative and quantitative

Composition: VASOVIN XL 2.5 mg

Each timed-release capsule contains:

Diluted nitroglycerin I.P.

Equivalent to nitroglycerin

2.5mg Excipients q.s.

Empty hard gelatin capsule contains approved colors.

The excipients used are ready to use Nitroglycerin SR pellets.

VASOVIN XL 6.5 mg

Each timed-release capsule contains:

Diluted nitroglycerin I.P.

Equivalent to nitroglycerin

6.5mg Excipients q.s.

Empty hard gelatin capsule contains approved colors.

The excipients used are ready to use Nitroglycerin SR pellets.

3. Dosage form and

strength Dosage

form: Capsule

Strength: Nitroglycerin Capsules 2.5 and 6.5mg

4. Clinical particulars

4.1 Therapeutic indication

Nitroglycerin Extended-Release Capsules are indicated for the prevention of angina pectoris due to coronary artery disease. The onset of action of oral nitroglycerin is not sufficiently rapid for this product to be useful in aborting an acute anginal episode.

4.2 Posology and method of administration

Posology

Treatment of acute attacks of Angina Pectoris

When angina starts, 500micrograms glyceryl trinitrate (one tablet) should be taken and if symptoms do not resolve, may be repeated at five-minute intervals for a total of three doses. If symptoms have not resolved after a total of three doses, the patient should seek prompt

medical attention.

The patient should preferably rest in the sitting position because of the risk of symptomatic postural hypotension.

Prophylaxis of Angina Pectoris

Glyceryl trinitrate, 500micrograms (one tablet), may be used prior to activity which is likely to precipitate angina pectoris.

Paediatric population

No reported data are available on the use of glyceryl trinitrate in children.

Elderly

Hypotension and syncope can be a particular problem with use of nitrates in the elderly. Patients should be advised to sit down whenever possible when taking sublingual glyceryl trinitrate.

Method of administration:

Nitroglycerin have shown that maintenance of continuous 24-hour plasma levels of nitroglycerin results in tolerance (i.e., loss of clinical response). Every dosing regimen for Nitroglycerin Extended-Release Capsules should provide a daily nitrate-free interval to avoid the development of this tolerance. The minimum necessary length of such an interval has not been defined, but studies with other nitroglycerin formulations have shown that 10 to 12 hours is sufficient. Large, controlled studies with other formulations of nitroglycerin show that no dosing regimen with Nitroglycerin Extended-Release Capsules should be expected to provide more than about 12 hours of continuous antianginal efficacy per day.

The pharmacokinetics of Nitroglycerin capsules, and the clinical effects of multiple-dose regimens, has not been well studied. The initial regimen of Nitroglycerin has been 2.5 to 6.5 mg three to four times a day, with subsequent upward dose adjustment guided by symptoms and side effects.

4.3 Contraindications

- Hypersensitivity to the active substance, to other nitro compounds, or to any of the excipients listed in section 6.1.
- Patients taking phosphodiesterase type 5 inhibitors (e.g. sildenafil, vardenafil, tadalafil)
- Angina caused by hypertrophic obstructive cardiomyopathy as it may exaggerate outflow obstruction.
- Patients with possible increased intracranial pressure (e.g. cerebral haemorrhage or head trauma).
- Marked anaemia
- Closed angle glaucoma.

4.4 Special warnings and precautions for use

Glyceryl trinitrate should be used with caution in patients in whom adequate preload is important for maintaining cardiac output (e.g. acute circulatory shock including hypovolemic shock or cardiogenic shock with inadequate diastolic filling pressures, severe mitral stenosis, pericardial tamponade, constrictive pericarditis, orthostatic dysfunction) because administration of a vasodilator in these patients may worsen clinical status.

Glyceryl trinitrate should be used with caution in patients with severe hypotension (systolic blood pressure below 90 mm Hg) and patients with cardiogenic shock, unless a sufficiently high left ventricular end diastolic pressure is assured by intra-aortal counterpulsation or positive inotropic drugs.Glyceryl trinitrate should be used with caution in patients with cerebrovascular disease since symptoms may be precipitated by hypotension.

Glyceryl trinitrate may worsen hypoxaemia in patients with lung disease or cor pulmonale. Arterial hypotension with bradycardia may occur in patients with myocardial infarction; this is thought to be reflexly mediated.

The use of glyceryl trinitrate could theoretically compromise myocardial blood supply in patients with left ventricular hypertrophy associated with aortic stenosis because of the detrimental effects of tachycardia and decreased aortic diastolic pressure.

Detailed haemodynamic studies in a small number of patients with valvular aortic stenosis with and without concomitant significant coronary artery disease studied in the supine position have not shown adverse effects with sublingual glyceryl trinitrate. However, it seems prudent to be cautious in treating ambulant patients with the combination of angina and moderate to severe valvular aortic stenosis.

Caution is necessary in patients with severe hepatic or renal impairment, hypothyroidism, hypoxaemia, hypothermia or a recent history of myocardial infaraction and malnutrition.

Sublingual tablets

If angina symptoms have not resolved after a total of three doses, the patient should be instructed to seek prompt medical attention.

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

4.5 Drugs interactions

Consistent with its known effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway, phosphodiesterase type 5 inhibitors (e.g. sildenafil, vardenafil and tadalafil) have been shown to potentiate the hypotensive effects of nitrates, and coadministration with glyceryl trinitrate is therefore contraindicated.

Treatment with other agents with hypotensive effects (e.g. vasodilators, antihypertensives, beta-blockers, calcium channel blockers and neuroleptics, tricyclic antidepressants and sapropterin) may potentiate the hypotensive effect of glyceryl trinitrate. In addition to these agents, the risk of hypotension and syncope with use of glyceryl trinitrate may be enhanced by alcohol.

N-acetylcysteine may potentiate the vasodilator effects of glyceryl trinitrate.

The possibility of tolerance to the effects of glyceryl trinitrate should be considered when used in conjunction with long-acting nitrate preparations.

There is evidence that systemic nitrates may interfere with the anticoagulant effects of heparin. Early and frequent monitoring of anticoagulation is recommended when systemic nitrates and heparin are used in combination.

There is a potential for drugs that cause dry mouth (eg anticholinergic, antimuscarinics, tricyclic antidepressants) to reduce the effectiveness of sublingual nitrates.

An enhanced hypotensive effect with sublingual apomorphine may occur as a result of concomitant administration with glyceryl trinitrate.

Ergot alkaloids may oppose the coronary vasodilatation of nitrates. Ergot alkaloids can precipitate

angina and glyceryl trinitrate can reduce the first pass hepatic metabolism of dihydroergotamine.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Reported Animal studies did not indicate harmful effects with respect to pregnancy, embryofoetal development, parturition or postnatal development. However, the relevance of these animal findings to man is unknown. The administration of glyceryl trinitrate during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

Breast-feeding

It is unknown if glyceryl trinitrate or its metabolites are excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue/abstain from breast-feeding or to discontinue/abstain from glyceryl trinitrate therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

Animal studies did not indicate harmful effects with respect to fertility. However, the relevance of these animal findings to man is unknown.

4.7 Effects on ability to drive and use machines.

As Glyceryl trinitrate can cause dizziness patients should make sure they are not affected before driving or operating machinery. This effect appears to be accentuated by alcohol.

4.8 Undesirable effects

System Organ Class	**Very Common (≥ 1/10)**	**Common (≥ 1/100 < 1/10)**	**Uncommon (≥ 1/1,000 < 1/100)**	**Rare (≥ 1/10,000 < 1/1,000)**	**Very Rare (< 1/10,000)**	**Frequency not known (cannot be estimated from the available data)**
Blood and lymphatic system disorders					Methaemoglobinaemia	
Psychiatric disorder					Restlessness	
Nervous system disorders	Throbbing headache**	Vertigo**, Dizziness**, Drowsiness	Syncope		Cerebral ischaemia	

Eye disorders						Increased ocular pressure
Cardiac disorders		Tachycardia		Enhanced angina, Pectoris symptoms, Bradycardia, Cyanosis		Hypoxaemia, palpitations
Vascular disorders		Orthostatic hypertension*,	Facial flushing, Circulatory collapse			
Gastrointestinal disorders			Nausea, Vomiting		Heartburn, Halitosis	
Respiratory, thorasic and mediastinal disorders					Impairment of respiration	
Skin and subcutaneous tissue disorders				Allergic skin reactions	Exfoliative dermatitis, Drug rash	
General disorders and administration site complications		Asthenia	Localised burning sensation, tongue blisters			Weakness
Investigations		Blood pressure decreased *				

* Particularly upon initiation of therapy and following an increase in dose.

Headache and dizziness, persisting after relief of angina may be minimised by removing the glyceryl

trinitrate tablet before it has completely dissolved. Glyceryl trinitrate-induced hypotension may cause cerebral ischaemia.

Large dose of glyceryl trinitrate may cause vomiting, cyanosis, restlessness, methaemoglobinaemia and impairment of respiration.

During treatment with glyceryl trinitrate, temporary hypoxemia may occur due to a relative redistribution of the blood flow in hypoventilated alveolar areas.

Reporting of suspected adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://torrentpharma.com/index.php/site/info/adverse_event_reporting
By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

Symptoms and Signs

Signs and symptoms encountered with overdose are generally similar to those events reported during treatment use although the magnitude and/or severity of the reactions may be more pronounced (See section 4.8). At very high doses an increase in intracranial pressure with cerebral symptoms may occur. Additional gastrointestinal effects such as colicky pain and diarrhoea have also been reported.

Treatment

In the case of overdose, the patient's clinical status including vital signs and mental status should be assessed and supportive treatment of the cardiovascular and respiratory systems provided as clinically indicated or as recommended by the national poisons centre, where available.

In the event of mild hypotension, passive elevation of the patient's legs and/or lowering of the head may be effective.

Arterial blood gas estimation should be performed and if there is acidosis or the patient is clinically cyanosed, then severe methaemoglobinaemia must be assumed. Oxygen therapy should be given with 1 to 2 mg/kg bodyweight of i.v. Methylene Blue over five min unless the patient is known to have G-6-PD deficiency.

5 Pharmacological properties

5.1 Mechanism of Action

5.2 Pharmacodynamic properties

Glyceryl trinitrate is a vasodilator and is used for angina of effort. Vasodilation is achieved by the releasing of free redical nitric oxide which activates guanylate cyclase and increases synthesis of guanosine 3′ and 5′-monophosphate with resultant effects on the phosphorylation of proteins in smooth muscle. If taken in excess, its vasodilatory effect can cause headache.

5.3 Pharmacokinetic properties

Glyceryl trinitrate is readily absorbed from the oral mucosa, but rapidly metabolised so that it only has a fleeting duration of action.

Glyceryl trinitrate is also readily absorbed from the gastrointestinal tract, but owing to extensive first-pass metabolism in the liver its bioavailability is reduced (short plasma half-life).

Glyceryl trinitrate is metabolised by hydrolysis to dinitrates and the mononitrate, which is the main urinary metabolite.

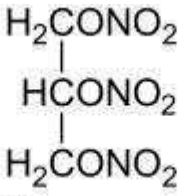
6 Nonclinical properties

6.1 Animal toxicology or Pharmacology

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

7 Description

Nitroglycerin is a solution of Propane-1,2,3-triol trinitrate in Ethanol(95 percent) having molecular formula of $C_3H_5N_3O_9$.



Molecular Formula: $C_3H_5N_3O_9$ Molecular Weight: 227.09

Product Description:

Hard gelatin, size '4', capsules with red cap and white body printed with 'VASOVIN XL 2.5' & Torrent logo (square emblem only) on the shell of capsules filled with white to off white pellets.

8 Pharmaceutical particulars

8.1 Incompatibilities

Not Applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

VASOVIN-XL 2.5 is packed in HDPE Bottle of 25 Capsules

Vasovin XL 6.5 is available as 25 capsules in HDPE container.

8.4 Storage and handing instructions.

KEEP THE CONTAINER WELL CLOSED, IN A COOL DRY PLACE, PROTECTED FROM LIGHT.

Keep out of reach of children.

9 Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10 Details of manufacturer

Torrent Pharmaceuticals Ltd Vill.
Bhud & Makhnu Majra,
Baddi- 173 205, Dist, Solan(H.P.),INDIA.

11 Details of permission or license number with date

Mfg Lic No. MNB/05/183 issued on 31.03.2014.

12 Date of revision

FEB- 2022

MARKETED BY

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