AUSTRALIAN PRODUCT INFORMATION – DBL™ GLYCERYL TRINITRATE CONCENTRATE INJECTION (GLYCERYL TRINITRATE)

1. NAME OF THE MEDICINE

Glyceryl trinitrate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of DBL Glyceryl Trinitrate Concentrate Injection contains 5 milligrams of glyceryl trinitrate, absolute ethanol and propylene glycol in Water for Injections.

Excipient with known effect

Ethanol absolute

For the full list of excipients, see **Section 6.1 List of excipients**.

3. PHARMACEUTICAL FORM

Glyceryl trinitrate is a white to pale yellow, thick, flammable, explosive liquid. It is slightly soluble in water, and soluble in acetone, alcohol, carbon disulphide, chloroform, dichloromethane, ether, ethyl acetate, glacial acetic acid and methanol.

DBL Glyceryl Trinitrate Concentrate Injection is a sterile, clear, practically colourless solution for intravenous infusion after dilution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

DBL Glyceryl Trinitrate Concentrate Injection is indicated for:

- Control of blood pressure in perioperative hypertension, ie hypertension associated with surgical procedures, especially cardiovascular procedures, such as the hypertension seen during intratracheal intubation, anaesthesia, skin incision, sternotomy, cardiac bypass and in the immediate post-surgical period.
- Congestive heart failure associated with acute myocardial infarction.
- Treatment of angina pectoris in patients who have not responded to recommended doses of organic nitrates and/or a beta blocker.
- Production of controlled hypotension during neurosurgical and orthopaedic surgical procedures.

4.2 Dose and Method of Administration

Dosage

The initial dosage of glyceryl trinitrate when non-absorbing tubing is used should be 5 micrograms/min, delivered through an infusion pump capable of exact and constant delivery of the drug. Subsequent titration must be adjusted to the clinical situation, with dose increments becoming more cautious as partial response is seen. Initial titration should be in 5 micrograms/min increments, with increases every 3 to 5 minutes until some response is noted. If no response is seen at 20 micrograms/min, increments of 10 and later 20 micrograms/min can be used. Once a partial blood pressure response is observed, the dose increase should be reduced and the interval between dosage increments should be lengthened.

There is no fixed optimum dose of glyceryl trinitrate. Due to variations in the responsiveness of individual patients to the drug, each patient must be titrated to the desired level of haemodynamic function. Therefore, continuous monitoring of physiologic parameters (eg blood pressure, heart rate, and pulmonary capillary wedge pressure) MUST BE PERFORMED to achieve the correct dose. Adequate systemic blood pressure and coronary perfusion pressure must be maintained.

Method of Administration

NOT FOR DIRECT INTRAVENOUS INJECTION.

DBL GLYCERYL TRINITRATE CONCENTRATE INJECTION IS A CONCENTRATED POTENT DRUG WHICH MUST BE DILUTED IN 5% GLUCOSE OR 0.9% SODIUM CHLORIDE PRIOR TO ITS INFUSION.

DBL GLYCERYL TRINITRATE CONCENTRATE INJECTION SHOULD NOT BE ADMIXED WITH OTHER DRUGS.

Glyceryl Trinitrate for injection must be mixed under aseptic conditions immediately after opening.

Due to the problem of glyceryl trinitrate absorption by polyvinyl chloride (PVC) tubing, Glyceryl Trinitrate Concentrate Infusion should be used with the least absorptive infusion tubing (i.e. non-PVC tubing) available. Administration sets which incorporate polyethylene are recommended.

Initial dilution: To obtain a final concentration of 100 micrograms/mL glyceryl trinitrate, aseptically transfer the contents of one DBL Glyceryl Trinitrate Concentrate Injection 50 mg/10 mL ampoule into a glass infusion bottle containing 490 mL of either 5% glucose or 0.9% sodium chloride. Invert the glass parenteral bottle several times following admixture to ensure uniform dilution of glyceryl trinitrate.

Maintenance dilution: It is important to consider the fluid requirements of the patient as well as the expected duration of infusion in selecting the appropriate dilution of DBL Glyceryl Trinitrate Concentrate Injection.

After the initial dosage titration, the concentration of the admixture solution may be increased, if necessary, to limit fluids given to the patient. The glyceryl trinitrate concentration should not exceed 400 micrograms/mL.

If the glyceryl trinitrate concentration is adjusted, it is imperative to flush or replace the infusion set before a new concentration is utilised. Depending on the infusion set used and the flow rate, it could take from 1 to 2 minutes to 3 hours for the new concentration to reach the patients if the infusion set is not flushed or replaced.

When stored in glass containers, the diluted solution is physically and chemically stable for up to 40 hours when stored below 25°C and up to seven days under refrigeration.

However, to avoid microbial contamination hazards, infusion should be commenced as soon as practicable after preparation of the solution. Infusion should be completed within 24 hours and any residue discarded.

Dosage is affected by the type of containers and administration sets used (see **Section 4.4 Special warnings and precautions for use**).

Although the usual starting adult dose range reported in clinical studies was 25 micrograms/min or more, these studies used PVC ADMINISTRATION SETS. DOSES NEED TO BE REDUCED IF NON-ABSORBING TUBING IS USED.

Dosage Adjustments

Some patients with normal or low left ventricular filling pressures or pulmonary capillary wedge pressure (eg angina patients without other complications) may be hypersensitive to the effects of glyceryl trinitrate and may respond fully to doses as small as 5 micrograms/min. These patients require especially careful titration and monitoring.

The posology of intravenous glyceryl trinitrate should be adjusted to achieve the desired clinical response. Additional dose adjustments in patients with severe hepatic insufficiency or severe renal failure may be necessary and require additional monitoring.

***Paediatric Population**:*

Not recommended for use in children.

Elderly Population:

See **Section 4.4 Special warnings and precautions for use**.

4.3 Contraindications

DBL Glyceryl Trinitrate Concentrate Injection is contraindicated in the following cases:

- Hypersensitivity to glyceryl trinitrate or a known idiosyncratic reaction to organic nitrates.
- Hypersensitivity to any other component of this product.
- Hypotension or uncorrected hypovolaemia, as the use of DBL Glyceryl Trinitrate Concentrate Injection, in such states, could produce severe hypotension or shock.
- Increased intracranial pressure (e.g. head trauma or cerebral haemorrhage).
- Constrictive pericarditis and pericardial tamponade.
- Severe anaemia, angina caused hypertrophic obstructive cardiomyopathy or arterial hypoxaemia.
- Acute circulatory failure (shock, circulatory collapse).
- Pronounced hypotension (systolic blood pressure < 90 mmHg).

- Cardiogenic shock, in so far as sufficiently high left ventricular end-diastolic pressure is not ensured by intra-aortal counterpulsation or positive inotropic medicines.
- Concomitant administration of glyceryl trinitrate with phosphodiesterase inhibitors used for the treatment of erectile dysfunction or pulmonary arterial hypertension, such as sildenafil which has been shown to potentiate the vasodilatory effects of glyceryl trinitrate, resulting in severe hypotension.
- As a supplementary medication for obstructive cardiomyopathy, especially if it is associated with aortic or mitral stenosis or constrictive pericarditis; as it has been shown that nitrate therapy may aggravate the angina caused by hypertrophic cardiomyopathy.
- Concomitant administration of a soluble guanylate cyclase (GC) stimulator, such as riociguat due to potentiation of hypotensive effects.

4.4 Special Warnings and Precautions for Use

NOT FOR DIRECT INTRAVENOUS INJECTION.

DBL GLYCERYL TRINITRATE CONCENTRATE INJECTION MUST BE DILUTED IN 5% GLUCOSE OR 0.9% SODIUM CHLORIDE PRIOR TO INFUSION (See Section 4.2 Dosage and method of administration). THE ADMINISTRATION SET USED WILL AFFECT THE AMOUNT OF GLYCERYL TRINITRATE DELIVERED TO THE PATIENT (see below and Section 4.2 Dosage and method of administration).

Glyceryl trinitrate readily migrates into many plastics. To avoid absorption of glyceryl trinitrate into plastic parenteral solution containers, DBL Glyceryl Trinitrate Concentrate Injection should only be diluted and stored in glass parenteral solution bottles.

Filters should be avoided as some absorb glyceryl trinitrate.

Forty to eighty percent of the total amount of glyceryl trinitrate in the final diluted solution for infusion is absorbed by the polyvinyl chloride (PVC) tubing of the intravenous administration sets currently in general use. The higher rates of absorption occur when flow rates are low, glyceryl trinitrate concentrations are high, and the administration set is long.

Although the rate of loss is highest during the early phase of infusion (when flow rates are lowest), the loss is neither constant nor self limiting; consequently no simple calculation or correction can be performed to convert the theoretical infusion rate (based on the concentration of the infusion solution) to the actual delivery rate.

Due to the problem of glyceryl trinitrate absorption by polyvinyl chloride (PVC) tubing, Glyceryl Trinitrate Concentrate Infusion should be used with the least absorptive infusion tubing (i.e. non-PVC tubing) available. Administration sets which incorporate polyethylene are recommended.

Use with caution in the following circumstances

Severe hypotension may occur with even small doses of glyceryl trinitrate.

Glyceryl trinitrate should only be used in acute myocardial infarction for treating definite left ventricular failure. Careful haemodynamic monitoring must be observed during infusion of glyceryl trinitrate in patients with acute myocardial infarction to avoid a sudden fall in arterial blood pressure and reflex tachycardia, which might reduce coronary perfusion and increase myocardial oxygen demand, thereby extending the area of ischaemic tissue injury.

Dosage must be carefully titrated to avoid the significant risk of a precipitous fall in blood pressure, particularly in patients with severe coronary or cerebral arteriosclerosis. Profound hypotension and bradycardia have been reported with sublingual, topical and intravenous glyceryl trinitrate.

Excessive hypotension, especially for prolonged periods of time, must be avoided because of the possible deleterious effects on the brain, heart, liver and kidney from impaired perfusion and the attendant risk of ischaemia, thrombosis and altered functions of these organs. Paradoxical bradycardia and increased angina pectoris may accompany glyceryl trinitrate induced hypotension. Patients with low pulmonary wedge pressure are especially sensitive to the hypotensive effects of glyceryl trinitrate. As a fall in pulmonary capillary wedge pressure precedes the onset of arterial hypotension, the pulmonary capillary wedge pressure is a useful guide to safe titration of glyceryl trinitrate dosage.

Glyceryl trinitrate should be used with caution in patients predisposed to closed angle glaucoma.

Administration of vasodilators to hypertensive patients has been suspected of causing acute blindness.Long term or repeated administration of organic nitrates may induce tolerance or cross-tolerance to glyceryl trinitrate or other organic nitrates. Larger doses of glyceryl trinitrate may be required with chronic sublingual administration or when a patient is receiving oral nitrate vasodilators. Although clinical tolerance has not been observed during intravenous infusion of glyceryl trinitrate, the possibility of this occurring should be kept in mind.

Nitrate dependence is a potentially serious problem. Death, myocardial infarction, coronary spasm and chest pain syndromes have been documented in industrial workers who leave the work environment for several days after exposure to glyceryl trinitrate and nitroglycol. There is some clinical evidence of nitrate dependence in patients with both angina and congestive heart failure.

Although withdrawal syndromes have not been reported to occur following intravenous infusion of glyceryl trinitrate for up to 9 days, it may be necessary to carefully taper therapy in patients with proven coronary arteriosclerosis who have received prolonged high dose infusions of the drug.

Arterial oxygen tension decreases after administration of glyceryl trinitrate in normal subjects and in patients with coronary artery disease. Hypoxaemia occurs as a result of increased pulmonary ventilation-perfusion mismatch, but the clinical significance of this effect is dependent on the severity of the underlying pulmonary disease and pre-existing hypoxaemia. Caution should be observed in patients with severe ischaemic heart disease, as a decrease in available oxygen may oppose the antianginal effect of glyceryl trinitrate. Glyceryl trinitrate may worsen hypoxaemia in patients with pulmonary disease or cor pulmonale.

Methaemoglobinaemia has been reported in association with glyceryl trinitrate therapy. Methaemoglobinaemia may be clinically significant, especially in the presence of methaemoglobin reductase deficiencies or in congenital M haemoglobulin variants.

Glyceryl trinitrate should be used with caution in patients with malnutrition, hypothermia, hypothyroidism or hyperthyroidism.

Glyceryl trinitrate concentrate contains propylene glycol which can lead to hyperosmolality, haemolysis and lactic acidosis.

Use in hepatic/renal impairment

Glyceryl trinitrate should be used with caution in patients with severe liver or renal disease.

Use in the elderly

Elderly patients may be particularly sensitive to the side effects of glyceryl trinitrate. If side effects occur, the dose should be reduced.

Paediatric use

The use of glyceryl trinitrate in children is not recommended, as its safety and effectiveness in children have not been established.

Effects on laboratory tests

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

Serum triglyceride assays that rely on glycerol oxidase may give falsely elevated serum triglyceride concentrations, as a result of the propylene glycol content of this product.

4.5 Interactions with Other Medicines and Other Forms of Interactions

Concomitant use with alcohol and levodopa may cause hypotension due to an enhanced vasodilatory effect of glyceryl trinitrate. The risk of syncope may also be enhanced.

Information on potential interaction with other medicines is poorly documented. Caution should be observed if other medicines are given concomitantly during infusion of glyceryl trinitrate as an interaction may adversely affect the haemodynamic response to the drug. Careful haemodynamic monitoring is essential.

Infusion of glyceryl trinitrate increases the duration of pancuronium induced neuromuscular blockade. This clinical observation has been supported by studies in the cat, however, glyceryl trinitrate did not prolong neuromuscular blockade induced by succinylcholine and d-tubocurarine. The mechanism of the interaction between glyceryl trinitrate and pancuronium is unknown.

Caution should be observed when morphine and glyceryl trinitrate are administered concurrently. One patient who received four 3 milligram doses of intravenous morphine sulphate during a 24 hour period with intravenous glyceryl trinitrate, became unarousable, eventually responding to nalorphine. The possibility that intravenous glyceryl trinitrate slows morphine metabolism in this patient has been suggested.

As ergot alkaloids may precipitate angina, patients being treated with glyceryl trinitrate for angina should avoid ergot alkaloids if at all possible.

Tricyclic antidepressants, anticholinergic agents, vasodilators such as hydralazine, minoxidil, prozosin and antihypertensive agents (including calcium antagonists, beta-blockers, diuretics and ACE inhibitors), major tranquillisers and opioid analgesics may potentiate the hypotensive effect of glyceryl trinitrate. Caution should therefore be observed when any of these medicines

are given concomitantly with glyceryl trinitrate. Dosage adjustment may be required in these circumstances.

Glyceryl trinitrate may potentiate the action of other hypotensive drugs, and the hypotensive and anticholinergic effects of tricyclic anti-depressants.

Concomitant use of phosphodiesterase inhibitors used for the treatment of erectile dysfunction or pulmonary arterial hypertension, such as sildenafil with glyceryl trinitrate is contraindicated. A severe and possibly dangerous fall in blood pressure may occur. This can result in collapse, unconsciousness and may be fatal. If a patient treated with these drugs for erectile dysfunction or pulmonary arterial hypertension needs a rapidly effective nitrate, he/she should be closely monitored (see **Section 4.3 Contraindications**).

Concomitant use of a soluble guanylate cyclase (GC) stimulator, such as riociguat with glyceryl trinitrate is contraindicated due to potentiation of hypotensive effect (see **Section 4.3 Contraindications**)

Aspirin and other non-steroidal anti-inflammatory drugs may diminish the therapeutic response to glyceryl trinitrate.

The effects of noradrenaline may be decreased when it is used concurrently with glyceryl trinitrate.

Concurrent use of sympathomimetics may reduce the antianginal effects of nitrates. Nitrates may counteract the pressor effects of sympathomimetics, possibly resulting in hypotension.

The anticoagulant effect of heparin may be decreased in patients receiving intravenous glyceryl trinitrate. The solvent, propylene glycol, may be responsible for this effect. Patients should therefore be monitored to avoid inadequate anticoagulation. If intravenous glyceryl trinitrate therapy is discontinued in patients receiving heparin, a reduction in heparin dosage may be necessary.

4.6 Fertility, Pregnancy and Lactation

Effects on fertility

Lower doses of glyceryl trinitrate did not affect fertility in rats, but doses up to 230 milligrams/kg/day caused moderate to severe testicular degeneration and/or atrophy, with severe to complete aspermatogenesis.

Use in pregnancy – Category B2

Category B2: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.

Animal reproduction studies have not been conducted with glyceryl trinitrate. It is also not known whether glyceryl trinitrate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Glyceryl trinitrate should be given to a pregnant woman only if clearly needed.

Use in lactation

It is not known whether glyceryl trinitrate or its metabolites are excreted into breast milk. Caution should be exercised if there is a need to administer glyceryl trinitrate to a breast-feeding woman.

4.7 Effects on Ability to Drive and Use Machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration. Patients should refrain from driving or using machines until they know that the medicinal product does not negatively affect these abilities.

4.8 Adverse Effects (Undesirable Effects)

Adverse reactions to glyceryl trinitrate are generally dose-related; almost all the reported reactions are the result of its vasodilatory activity.

The most frequent adverse reaction in patients treated with glyceryl trinitrate is headache, which occurs in approximately 2% of patients, and is dose dependent. Other adverse reactions, occurring in less than 1% of patients, are the following: tachycardia, nausea, vomiting, apprehension, restlessness, muscle twitching, retrosternal discomfort, palpitations, dizziness and abdominal pain. Hypotension and bradycardia (see **Section 4.4 Special warnings and precautions for use**) have been reported with intravenous glyceryl trinitrate. Decreased arterial oxygen tension has also been reported.

Severe arterial hypotension with bradycardia has been reported in patients who received intravenous glyceryl trinitrate within the first 24 hours after myocardial infarction; these effects were reversed by discontinuing the drug and elevating the lower extremities.

Adverse reactions to the solvents in DBL Glyceryl Trinitrate Concentrate Injection may occur. Alcohol intoxication has been reported in patients receiving high dose intravenous infusions. The propylene glycol content may lead to hyperosmolarity.

The following additional adverse reactions have been reported with the oral and/or topical use of glyceryl trinitrate: cutaneous flushing, weakness, and occasionally drug rash or exfoliative dermatitis, hypertension, methaemoglobinaemia, postural hypotension and syncope on assuming upright posture, withdrawal syndrome, e.g. increased frequency of angina attack, blurred vision, cyanosis (rarely), fainting/lightheadedness and anaphylaxis.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

Symptoms

Overdosage of glyceryl trinitrate may result in severe hypotension, transient headache and reflex tachycardia.

Methaemoglobinaemia has been reported in accidental overdosage (see **Section 4.4 Special warnings and precautions for use**).

Treatment

Patients should be treated by elevating the legs and decreasing or temporarily terminating the infusion until the patient's condition stabilises. Since the duration of the haemodynamic effects following glyceryl trinitrate administration is quite short, additional corrective measures are usually not required. However, if further therapy is indicated, administration of an intravenous alpha adrenergic agonist (eg dopamine, methoxamine or phenylephrine) should be considered.

Methaemoglobinaemia may be treated with intravenous methylene blue at a dose of 1 to 2 milligrams/kg. Oxygen and assisted respiration may be required.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia). In New Zealand call 0800 764 766.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Glyceryl trinitrate, an organic nitrate, is a vasodilator. Its principal pharmacological action is the relaxation of vascular smooth muscle. Glyceryl trinitrate produces a dose related dilation of both arterial and venous beds. Venous dilation predominates over dilation of the arterioles. Dilation of the post-capillary vessels, including large veins, promotes peripheral pooling of blood and decreases venous return to the heart, reducing left ventricular end-diastolic pressure and pulmonary capillary wedge pressure (pre-load). Arteriolar relaxation reduces systemic vascular resistance and arterial pressure (after-load). Glyceryl trinitrate also dilates the coronary arteries, although this effect is short lived.

Myocardial oxygen consumption or demand (as measured by the pressure-rate product, tension time index and stroke work index) is decreased by both the arterial and venous effects of glyceryl trinitrate, and a more favourable supply demand ratio can be achieved.

Therapeutic doses of intravenous glyceryl trinitrate reduce systolic, diastolic and mean arterial blood pressure. Effective coronary perfusion pressure is usually maintained, but can be compromised if blood pressure falls excessively or an increased heart rate decreases diastolic filling time.

Glyceryl trinitrate reduces elevated central venous and pulmonary capillary wedge pressures, pulmonary vascular resistance and systemic vascular resistance. Heart rate is usually slightly increased, presumably a reflex response to the fall in blood pressure.

Cardiac index may be increased, decreased or unchanged. Patients with elevated left ventricular filling pressure and systemic vascular resistance values in conjunction with a depressed cardiac index are likely to experience an improvement in cardiac index. Alternatively, when filling pressures and cardiac index are normal, cardiac index may be slightly reduced by intravenous glyceryl trinitrate.

5.2 Pharmacokinetic Properties

Distribution

Glyceryl trinitrate is widely distributed in the body, with an apparent volume of distribution of 200 litres in adult male subjects. In smooth muscle cells the nitrate group is cleaved to inorganic

nitrite and then to nitric oxide (thought to be responsible for glyceryl trinitrate's vasodilator effect).

Metabolism

Glyceryl trinitrate also undergoes hydrolysis in plasma and is rapidly hydrolysed in the liver by glutathione-organic nitrate reductase to dinitrates and mononitrates. It is also metabolised by enzymes in the blood.

Glyceryl trinitrate has a short half-life, estimated at 1 to 4 minutes. This results in a low plasma concentration after intravenous infusion. A therapeutic effect is apparent within 1 to 2 minutes of intravenous administration, while the duration of action following a single intravenous dose of glyceryl trinitrate is about 3 to 5 minutes.

At plasma concentrations of between 50 and 500 nanograms/mL, glyceryl trinitrate is approximately 60% bound to plasma proteins, while its metabolites, 1,3-glyceryl dinitrate and 1,2-glyceryl dinitrate, are approximately 60% and 30% bound respectively. The activity and half-life of the dinitrate metabolites are not well characterised. However, in animal studies, the vasodilator effects of glyceryl trinitrate were 10 to 14 times greater than those of its dinitrate metabolites. Glyceryl mononitrate, the principal metabolite, is inactive. The dinitrates are metabolised further to inactive mononitrates, and are metabolised ultimately to glycerol and carbon dioxide.

5.3 Preclinical Safety Data

Genotoxicity

No genotoxicity studies were undertaken with glyceryl trinitrate.

Carcinogenicity

Glyceryl trinitrate, given in the diet to rats at doses up to 1% caused an increase in the incidence of hepatic cholangiofibrosis, hepatocellular carcinomas and/or neoplastic nodules and Leydig cell tumours in the testis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Ethanol absolute

Propylene glycol

Water for injections

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Store below 25°C. Protect from light.

6.5 Nature and Contents of Container

DBL Glyceryl Trinitrate Concentrate Injection is available in glass ampoules in the following strength:

50 mg glyceryl trinitrate/10 mL (cartons contain 5 ampoules)

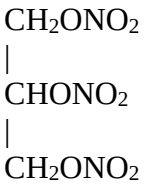
6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical Properties

Chemical structure

The chemical structure of glyceryl trinitrate is shown below:



Its chemical formula is $C_3H_5N_3O_9$, molecular weight is 227.1. The chemical name of glyceryl trinitrate is propane-1,2,3-triol trinitrate.

CAS number

CAS registry number is 55-63-0.

7. MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 (Prescription Only Medicine)

8. SPONSOR

Pfizer Australia Pty Ltd
Level 17, 151 Clarence Street
Sydney NSW 2000
Toll Free Number: 1800 675 229
www.pfizer.com.au

9. DATE OF FIRST APPROVAL

28 September 2000

10. DATE OF REVISION

25 January 2022

Summary Table of Changes

Section changed	Summary of new information
4.2	Add warning of dilution immediately after opening, and use in paediatric and elderly populations
4.3	Add contraindications, patients with angina, acute circulatory failure, pronounced hypotension or cardiogenic shock. Concomitant use with phosphodiesterase inhibitors.
4.4	Add warnings of severe hypotension, hyperosmolality, hemolysis or lactic acidosis. Use in patients with to closed angle glaucoma.
4.5	Glyceryl trinitrate potentiate the action of other hypotensive drugs, and the hypotensive and anticholinergic effects of tricyclic anti-depressants. Use with phosphodiesterase inhibitors.
4.7	General warning of patients should refrain from driving or using machines until they know that the medicinal product does not negatively affect these abilities.
4.9	Add treatment with methoxamine or phenylephrine, advice that oxygen and assisted respiration may be required.

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