

# NEW ZEALAND DATA SHEET

## 1. PRODUCT NAME

DBL™ Glyceryl Trinitrate, Solution for injection, 50 mg/10 mL

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of DBL™ Glyceryl Trinitrate for Injection contains 5 milligrams of glyceryl trinitrate, absolute ethanol and propylene glycol in Water for Injections. DBL™ Glyceryl Trinitrate for Injection is available in ampoules in 50 mg glyceryl trinitrate/10 mL.

### Excipient(s) with known effect

- Ethanol
- Propylene glycol

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection for intravenous infusion.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

DBL™ Glyceryl Trinitrate for Injection for intravenous infusion, are indicated as follows:

1. Acute myocardial infarction with or without left ventricular failure.
2. Left heart failure associated with subacute and acute pulmonary oedema.
3. To reduce ventricular ectopic activity following myocardial infarction.
4. To reverse symptomatic coronary artery spasm following provocative testing in the diagnosis of variant angina.
5. Control of hypertension during surgical cardiovascular procedures and in the production of controlled hypotension during such procedures.
6. Treatment of angina pectoris in patients who have not responded to recommended doses of organic nitrates and/or a beta blocker.

### 4.2 Dose and method of administration

Dosage is affected by the type of infusion set used (see below). Dosage recommendations represented as mcg glyceryl trinitrate per minute can only be offered as a starting infusion rate. The correct dose for individual patients will be determined by the response to therapy. All patients should be on continuous cardiovascular monitoring during infusion therapy.

The dosage for DBL™ Glyceryl Trinitrate for Injection infusion solution should be initially 5 mcg/minute delivered through an infusion pump capable of exact and constant medicine delivery. Increments should be cautious and adjusted to the clinical situation. Initially titration should be in 5 mcg/minute increments with increases each 3-5 minutes until some response is noted.

If there is no response at 20 mcg/minute, larger increments may be used, but once a blood pressure response is observed the increment should be reduced in magnitude and with longer intervals.

There is no fixed dose of DBL™ Glyceryl Trinitrate for Injection. Each patient must be titrated to his/her individual needs. Continuous monitoring of physiological parameters must be performed to achieve the correct dose. Maintenance of adequate systemic B.P. and coronary perfusion is essential.

The maximum dose is 8 (-10) mg per hour of glyceryl trinitrate.

**DBL™ Glyceryl Trinitrate for Injection must be diluted.**

DBL™ Glyceryl Trinitrate for Injection is compatible with the following infusion solutions:

- 0.9% NaCl solution
- 5% Dextrose.

### **4.3 Contraindications**

Glyceryl trinitrate may not be used if there is:

- 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 a soluble guanylate cyclase (GC) stimulator, such as riociguat due to potentiation of hypotensive effects.

For acute myocardial infarction with low filling pressures, glyceryl trinitrate should only be used with caution. Administration of glyceryl trinitrate for acute myocardial infarction should only be performed under a doctor's supervision. A drop in systolic pressure below 90 mmHg should be avoided.

Concomitant administration of sildenafil (Viagra) and DBL™ Glyceryl Trinitrate for Injection is contraindicated due to an increase in the hypotensive effect of DBL™ Glyceryl Trinitrate for Injection. This may result in severe side effects such as syncope or myocardial infarction.

## 4.4 Special warnings and precautions for use

### Warning: Intravenous Giving Sets

- Glyceryl trinitrate is readily absorbed onto certain plastics. The dilution and storage of glyceryl trinitrate for i.v. infusion should only be in glass. Plastic parenteral solution containers should not be used.
- Some filters absorb glyceryl trinitrate. Filters in the i.v. giving set should be avoided.

Adsorption is substantially less (5% or less) where polyethylene or polypropylene sets are utilised. Highest adsorption rates occur when the flow rates are low, glyceryl trinitrate concentrations are high, and the tubing is long.

However, because the amount of vascular binding varies inter-individually there is no correlation between plasma level and the effect. Higher plasma levels can be measured in arterial than in venous blood. In patients showing a greater response to nitrates, lower plasma levels indicate a high vascular binding. Therefore, the dose is always chosen individually according to the prevailing haemodynamic parameters.

It is recommended that:

- That low adsorptive giving sets are utilised where possible.
- That dosage is individually titrated to patient needs by careful attention to dosage rates and response as documented by physiological monitoring.

In summary, the ideal giving set should be as short as possible, not include a blood filter or burette chamber and, if possible, be of different material than PVC.

### Diabetes

Special care is required when treating diabetic patients since the medicine contains 5% w/v glucose.

## 4.5 Interaction with other medicines and other forms of interaction

Concurrent administration of other vasodilators, antihypertensive agents, calcium antagonists, tricyclic antidepressants and alcohol may enhance the antihypertensive effect of glyceryl trinitrate. When used concurrently with dihydroergotamine, glyceryl trinitrate may cause an increase in the DHE level and thus enhance its effect. Simultaneous administration of heparin and glyceryl trinitrate diminishes the effect of heparin.

Concomitant use of DBL™ Glyceryl Trinitrate for Injection and sildenafil (Viagra) enhances the hypotensive effect. Therefore, the concomitant administration of DBL™ Glyceryl Trinitrate for Injection and Viagra is contraindicated. If a patient treated with sildenafil (Viagra) needs a rapidly effective nitrate (e.g. in the case of an acute angina pectoris attack) he/she must be hospitalised immediately.

## **4.6 Fertility, pregnancy and lactation**

### **Fertility**

No data available.

### **Pregnancy and Lactation**

Pregnancy Category: B2.

Animal experiments have provided no evidence of damage to the foetus by glyceryl trinitrate. However, glyceryl trinitrate should only be administered under a doctor's supervision during pregnancy and lactation.

## **4.7 Effects on ability to drive and use machines**

No data available.

## **4.8 Undesirable effects**

Headaches caused by vasodilation occur frequently, especially at the onset of therapy. Flushing, drowsiness, orthostatic hypotension and reflex tachycardia are reported occasionally. Less often states of collapse occur, sometimes accompanied by bradyarrhythmias. In rare cases where there is a large drop in blood pressure, symptoms of angina pectoris may be enhanced.

### **Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

## **4.9 Overdose**

Glyceryl trinitrate is well tolerated and has a very wide safety margin. In the event of overdose a higher incidence of the known undesirable effects may occur, such as headaches, drop in blood pressure with orthostatic regulatory disorders and reflex tachycardia. At higher doses (> 20mcg/kg body weight) anticipate formation of methaemoglobin, cyanosis and tachypnoea resulting from nitrate ions formed during metabolism (degradation).

### **Emergency Procedure**

Direct all therapeutic counter-measures towards raising the blood pressure. In less serious cases placing the patient in the supine position with the legs higher than the head will cause the symptoms to disappear.

In cases of severe overdose apply general guidelines for treating overdose and/or shock therapy. For pronounced hypotension, volume substitution can be performed.

In exceptional cases, use sympathomimetic agents.

Depending on the degree of severity, the following antidotes may be used:

1. Vitamin C: 1 g p.o. or as sodium salt i.v.
2. Methylene blue: up to 5 mL of a 1% methylene blue solution i.v.
3. Toluidine blue: initially 2-4 mL/kg body weight strictly intravenously.
4. Oxygen therapy, haemodialysis, exchange transfusion.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

#### **Mechanism of action**

Glyceryl trinitrate relaxes smooth muscle, including vascular muscle and reduces blood pressure. Its anti-anginal effect is exerted by reducing myocardial oxygen demand through peripheral vasodilation. This causes decreased venous tone resulting in a reduction in preload and decreased arterial resistance resulting in a reduction in afterload.

### **5.2 Pharmacokinetic properties**

Glyceryl trinitrate is rapidly metabolised after injection so that a constant infusion is required to maintain levels. Metabolism occurs by hydrolysis to dinitrates and the mononitrate. Extrahepatic clearance is high. A relationship between clinical effect and plasma concentration of glyceryl trinitrate has not been determined.

### **5.3 Preclinical safety data**

#### **Genotoxicity**

No data available.

#### **Carcinogenicity**

No data available.

#### **Reproductive and developmental toxicity**

No data available.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

- Ethanol

- Propylene glycol
- Water for injection

## **6.2 Incompatibilities**

No data available.

## **6.3 Shelf life**

36 months.

## **6.4 Special precautions for storage**

Store below 25°C. Protect from light.

## **6.5 Nature and contents of container**

DBL™ Glyceryl Trinitrate for Injection 10 mL glass ampoules are supplied in boxes each containing 5 x 10 mL ampoules.

## **6.6 Special precautions for disposal**

Any unused medicine or waste material should be disposed of in accordance with local requirements.

## **7. MEDICINE SCHEDULE**

Prescription Medicine.

## **8. SPONSOR**

Pfizer New Zealand Limited  
P O Box 3998  
Auckland, New Zealand, 1140  
Toll Free Number: 0800 736 363

## **9. DATE OF FIRST APPROVAL**

12 September 1985

## **10. DATE OF REVISION OF THE TEXT**

20 February 2019

### Summary table of changes

Section changed	Summary of new information
All	New Data Sheet format in accordance with Medsafe guidance