Ballarat Health Services

DRUG GUIDELINE

GLYCERYL TRINITRATE (Intravenous)

SCOPE (Area): **FOR USE IN:** Intensive Care Unit, Coronary Care Unit, ED, CVS, Theatre, 4N
EXCLUSIONS: Paediatrics (seek Paediatrician advice) and other General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

BRAND NAMES
DBL or Hospira Glyceryl Trinitrate Concentrate Injection®.

PHARMACOLOGY AND PHARMOCOKINETICS
Glyceryl trinitrate relaxes arterial and venous smooth muscle leading to vasodilatation, which results in reduced afterload and preload. This results in a reduction of myocardial oxygen demand, some coronary artery dilation and a reduction in blood pressure. Glyceryl trinitrate has a rapid onset of action (1-2 minutes), a short half-life (1-4 minutes) and is predominantly hepatically cleared.

INDICATIONS
- Unstable Angina.
- Heart failure associated with acute myocardial infarction.
- Hypertensive emergency.
- Acute pulmonary oedema.
- Production of controlled hypotension during some surgical procedures.
- Short term adjunct in pulmonary hypertension.

This guideline does not cover specialised use in Cardiovascular Suite.

CONTRAINDICATIONS
- **Hypotension or uncorrected hypovolaemia** – can result in severe hypotension or shock.
- **Phosphodiesterase 5 inhibitors** – see Drug Interactions.
- **Riociguat** – see Drug Interactions.
- **Ergot derivatives** – see Drug Interactions.
- **Raised intracranial pressure (e.g. head trauma or cerebral haemorrhage).**
- **Constrictive pericarditis and pericardial tamponade.**
- **Severe anaemia and arterial hypoxaemia.**
- **Hypertrophic obstructive cardiomyopathy** – glyceryl trinitrate may worsen angina especially when associated with aortic stenosis, mitral stenosis or constrictive pericarditis.
- **Aortic or mitral stenosis.**
- **Cor pulmonale.**
- **Hypersensitivity to nitrates, ethanol or propylene glycol**.

PRECAUTIONS

- **Not for administration undiluted** – see Dosage and Administration.
- **Post myocardial infarction** – a sudden blood pressure drop may extend cardiac ischaemia.
- **Pulmonary disease –** may worsen hypoxaemia.
- **Elderly** – may be particularly sensitive to the effect of glyceryl trinitrate.
- **Severe renal or hepatic disease, malnutrition, hypothermia, hypothyroidism or hyperthyroidism** – use with caution.

PREGNANCY AND BREASTFEEDING

Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- **Phosphodiesterase 5 inhibitors (sildenafil, tadalafil and vardenafil) -** contraindicated. An exaggerated hypotensive result or myocardial infarction may occur if glyceryl trinitrate is administered in the 24 hours post-dose sildenafil or vardenafil, or 48 hours post-dose tadalafil. A longer gap before administration of glyceryl trinitrate may be required in the elderly, or if a drug interaction prolongs the effect of the relevant phosphodiesterase 5 inhibitor.
- **Riociguat** – contraindicated. Nitrates potentiate the hypotensive effect of riociguat.
- **Ergot derivatives** – contraindicated. May diminish vasodilatory effect of glyceryl trinitrate, is of greatest concern in patients being treated for angina.
- **Rosiglitazone –** increased risk of coronary ischaemia if used with glyceryl trinitrate. Avoid combination where possible.
- **Heparin** – glyceryl trinitrate may reduce the anticoagulant effect of heparin. If using heparin and glyceryl trinitrate infusions at the same time, monitor APTT more frequently.
- **Drugs that lower blood pressure** – additive hypotensive effects when used with glyceryl trinitrate.
- **Nitric oxide, dapsone (topical) -** increases the risk of methaemoglobinaemia with glyceryl trinitrate.
- **Alteplase** – glyceryl trinitrate may increase hepatic blood flow, leading to increased clearance of alteplase. This may reduce the thrombolytic efficacy of alteplase – monitor for adequate reperfusion and possible reocclusion. Avoid glyceryl trinitrate if alteplase is required. This does not occur with other thrombolytics.

DOSAGE AND ADMINISTRATION

Requires continuous ECG monitoring.
For administration only

- **in Intensive Care Unit, Coronary Care Unit, ED, CVS or Theatre**
- **by MET or Code Blue**
- **in 4N (with telemetry, only lower doses as described below)**

Administer via CVC or a large peripheral vein. Glyceryl trinitrate ampoules contain 30% propylene glycol and 30% ethanol which are very irritant to veins, always dilute prior to use. Where administered peripherally a second peripheral line is required to ensure continuity of the infusion. Avoid administration on lines where other infusions may be bolused or flushed.

Note: Some references still recommend administering glyceryl trinitrate in glass bottles and polyethylene administration sets. More recent studies have shown that clinical response is adequate using standard PVC bags and giving sets as dose is titrated to effect.

General Ward IV infusion (via CVC or large peripheral vein):
Requires telemetry, restricted to 4N
Use glyceryl trinitrate 50 mg/10 mL ampoules to prepare infusion.
Withdraw 6 mL from a 100 mL sodium chloride 0.9% minibag.
Glyceryl trinitrate 30 mg (6 mL from ampoule) added to remaining 94 mL sodium chloride 0.9% in the minibag.
Total Volume: 100 mL.
Final concentration: 300 microgram/mL.
Starting rate: 5 microgram/min (1 mL/hr). The Prescriber must specify the blood pressure target.
Rate increase: 5 microgram/min (1 mL/hr) increase every 15 minutes until desired clinical response is achieved. The Prescriber must specify incremental increases when writing the order.
Usual rate: 5-40 microgram/min (1-8 mL/hr).
Maximum rate: 40 microgram/min (8 mL/hr). For patients requiring doses above this maximum, contact the Registrar or Consulting Physician for advice regarding further management.
Ceasing infusion: do not cease infusion abruptly (unless hypotension occurs) as rebound symptoms can occur. Wean by 5 microg/min every 15 minutes. Monitor closely for return of symptoms (e.g. angina, hypertension).

Administration in Intensive Care Unit, Coronary Care Unit, ED, CVS and Theatre:

Standard IV infusion (via CVC or large peripheral vein):
Restricted to Intensive Care Unit, Coronary Care Unit, ED, Theatre, CVS, Code Blue or MET
Use glyceryl trinitrate 50 mg/10 mL ampoules to prepare infusion.
Withdraw 6 mL from a 100 mL sodium chloride 0.9% minibag.
Glyceryl trinitrate 30 mg (6 mL from ampoule) added to remaining 94 mL sodium chloride 0.9% in the minibag.
Total Volume: 100 mL.
Final concentration: 300 microgram/mL.
Starting rate: 5-10 microgram/min (1-2 mL/hr). The Prescriber must specify the BP target.
Rate increase: 5 microgram/min (1 mL/hr) increase every 3-5 minutes until desired response.
Coronary Care Unit dose range: 5-25 microgram/min (1-5 mL/hr).
Coronary Care Unit maximum rate: 50 microgram/min (10 mL/hr).
ICU, ED, Theatre and CVS usual rate: 5-200 microgram/min (1-40 mL/hr). Usual dose range in heart failure is 20-80 microgram/min (4-16 mL/hr).
ICU, ED, Theatre and CVS maximum rate: 400 microgram/min (80 mL/hr) may be required in extreme cases (e.g. refractory hypertension).
Ceasing infusion: do not cease infusion abruptly (unless hypotension occurs) as rebound symptoms can occur. Low doses (up to 50 microg/min) wean by 5 microg/min every 15 minutes. Higher doses (above 50 microg/min) wean by 5-20 microg/min every 15 minutes. Monitor closely for return of symptoms (e.g. angina, hypertension).

Larger volume IV infusion (via CVC or large peripheral vein):
Restricted to Intensive Care unit, ED, CVS and Theatre only
For high rate infusions a larger volume of the same concentration can be prepared.
Use glyceryl trinitrate 50 mg/10 mL ampoules to prepare infusion.
Withdraw 30 mL from a 500 mL sodium chloride 0.9% IV bag.
Glyceryl trinitrate 150 mg (30 mL from THREE ampoules) added to remaining 470 mL sodium chloride 0.9% in the IV bag.
Total Volume: 500 mL.
Final concentration: 300 microgram/mL.
Rate: As for standard IV infusion above.

Syringe Unit/Pump IV infusion (via CVC or large peripheral vein):
Restricted to Intensive Care unit, Coronary Care Unit, ED, CVS and Theatre only
Use glyceryl trinitrate 50 mg/10 mL ampoules to prepare infusion.
Glyceryl trinitrate 15 mg (3 mL from ampoule) diluted to 50 mL with sodium chloride 0.9% in a luer lock syringe.
Total Volume: 50 mL.
Final concentration: 300 microgram/mL.
Rate: As for standard IV infusion above.

General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly after adding glyceryl trinitrate to avoid inadvertently giving a more concentrated dose.
  Sodium chloride 0.9% can be substituted for different compatible IV fluid as requested by the Medical Officer.
  Discard any remaining solution after 24 hours.
- **Infusion pump:** Alaris LVP or syringe unit with Guardrails® or ED syringe pump.
- **Routes of administration:**
  IV injection: No
  IV intermittent infusion (15-60 minutes): No
  IV continuous infusion: Yes
  IM injection: No
  Subcut injection: No
- **Compatible/incompatible IV drugs/fluids:**
  Consult the Australian Injectable Drugs Handbook ('Yellow book') in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**

MONITORING (INCLUDING BLOOD TESTS)

- Avoid excessive hypotension (systolic blood pressure less than 90-95 mmHg).
- Dose range and clinical goals should be documented by the Medical Officer.
- Patients can develop tolerance to the effect of glyceryl trinitrate (within 24 hours) requiring an increase in the rate of infusion.

NURSING PRACTICE POINTS

- Continuous ECG monitoring during infusion.
- Wear gloves during preparation of infusion as glyceryl trinitrate is readily absorbed through the skin.
- Baseline12 lead ECG, and for angina patients repeat when patient is pain free**.**
- With unstable patients, or when altering the infusion monitor heart rate, rhythm, blood pressure (and angina if indicated) every 2-5 minutes, or continuously via arterial line.
- When blood pressure (and angina if indicated) are stable, monitor vital signs half to one hourly, or continuously via arterial line.
- All injections, infusions and lines are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

ADVERSE EFFECTS

Most adverse reactions are due to vasodilator effects

- **Common** – headache, flushing, palpitations, orthostatic hypotension, reflex tachycardia, dizziness, fainting, nausea, vomiting, apprehension, muscle twitching, restlessness, retrosternal discomfort, abdominal pain, decreased PaO2, peripheral oedema.
- **Infrequent** – rebound angina.
- **Rare** – methaemoglobinaemia, paradoxical bradycardia, ethanol intoxication with high doses.

DRUG PRESENTATIONS AND STORAGE

Glyceryl trinitrate 50 mg/10 mL ampoules.

Store below 25°C. Do not freeze. Protect ampoules from light.
