Ballarat Health Services

DRUG GUIDELINE

MILRINONE

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

BRAND NAMES
Primacor® and generic brands.

PHARMACOLOGY AND PHARMACOKINETICS
Milrinone inhibits phosphodiesterase 3 in cardiac and smooth muscle tissues, thus increasing cyclic adenosine monophosphate levels and a resultant increase in intracellular ionised calcium. It is a positive inotrope and a systemic and pulmonary arterial vasodilator, with little positive chronotropic effect. Milrinone is predominantly renally cleared (around 85%), with a half-life in patients with normal renal function around 2.5 hours, but nearly doubled in renal failure. Haemodynamic improvements appear within 5-15 minutes of initiation of therapy after loading (not included in this guideline), or 30 minutes with maintenance infusion (when no load given).

INDICATIONS
- Cardiogenic shock secondary to acute decompensated systolic heart failure.
- Short term (less than 48 hours) treatment for severe cardiac failure in patients unresponsive to other therapy.

CONTRAINDICATIONS
- Severe obstructive aortic disease, pulmonary valvular disease or hypertrophic subaortic stenosis as milrinone may aggravate outflow tract obstruction.
- Hypersensitivity to milrinone (or other bipyridines) or any other ingredient of the formulation.

PRECAUTIONS
- **Hypovolaemia with hypotension** - correct before using milrinone.
- **Risk of systolic anterior motion of the mitral valve and/or dynamic left ventricular outflow tract obstruction.**
- **Myocardial infarction** - milrinone may increase myocardial oxygen consumption during the acute phase post myocardial infarction – use with caution.
- **Supraventricular and ventricular arrhythmias** – milrinone may cause or exacerbate.
- **Acute exacerbation of chronic heart failure** – milrinone may increase mortality.
- **Hypotension** – milrinone may worsen (especially higher doses).
- **Renal impairment (CrCL less than 50 mL/min)** – likely to require a reduced rate of infusion after initial starting rate, titrate to effect.

PREGNANCY AND BREASTFEEDING

Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- Monitor carefully with other drugs that also have vasodilatory and positive inotropic effects.
- Anagrelide, cilostazol – avoid giving with milrinone as also inhibit phosphodiesterase-3.
- Riociguat – milrinone may enhance the hypotensive effect of riociguat, use with caution.

DOSAGE AND ADMINISTRATION

Requires continuous ECG monitoring.
For administration only

- **in Intensive Care Unit, ED, CVS and Theatre**

Administer preferably via CVC, but may be given peripherally. Do not administer on lines where other infusions may be bolused or flushed.

Correct electrolyte abnormalities before commencing milrinone.

Concomitant use of a vasopressor (e.g. noradrenaline) is usually required to maintain mean arterial pressure during milrinone infusion.

Some references refer to a loading dose of 50 microg/kg over 20 minutes. This is not included in this guideline due to the increased risk of severe hypotension. Instead of a true load, a higher initial rate is used to provide a 'slow' load with the rate reviewed at 2 hours. The time to haemodynamic improvement, when starting an infusion without a load, is about 30 mins.

Milrinone must be diluted prior to use.

IV infusion preparation:

Use milrinone 10 mg/10 mL ampoules to prepare infusion.
Withdraw 20 mL from a 100 mL glucose 5% minibag.
Milrinone 20 mg (20 mL from TWO ampoules) added to remaining 80 mL glucose 5% in the minibag.
Total Volume: 100 mL.
Final concentration: 200 microgram/mL.

Note: for patients being retrieved, use Milrinone 10 mg (10 mL from ONE ampoule) diluted to 50 mL glucose 5% in a 50 mL luer lock syringe. Same concentration (200 microg/mL) and dosing.

IV infusion (vic CVC preferably)

Starting rate: Usually 0.5 microg/kg*/min (minimum 0.375 microg/kg*/min).

Note: review dose at 2 hours (or earlier if excessive response). Patients with renal impairment/failure are likely to require lower ongoing doses than those with normal renal function. Dose patients on CRRT as per normal renal function.

Rate increase/decrease/weaning: Adjust dose by 0.125 microg/kg*/min increments/decrements (as in table below) generally no more frequently than every 2-4 hours due to relatively long half-life. Titrate dose according to haemodynamic and clinical parameters set by Medical Staff. Do not stop abruptly. Manage decreases in blood pressure with noradrenaline infusion - see DRG0012 Noradrenaline (norepinephrine).

Usual rate range: 0.125 – 0.5 microg/kg*/min.

Maximum rate: 0.75 microg/kg*/min.

***Weight capped at 120 kg – use actual bodyweight. Note that the pump will allow doses up to 250 kg, ensure no weight greater than 120 kg is entered.**

Increment/decrements for milrinone infusion doses		
	0.125 microg/kg*/min	*Weight for dosing is actual body weight up to a maximum of 120 kg
	0.25 microg/kg*/min	
	0.375 microg/kg*/min	
Usual starting dose	0.5 microg/kg*/min	
	0.625 microg/kg*/min	
Maximum dose	0.75 microg/kg*/min	

Milrinone Infusion Rate Table

Rounded to one decimal as per Guardrails LVP calculations

(Note: syringe unit may round slightly differently as it allows for 2 decimals)

Actual Body Weight	0.125 microg/kg/min (mL/hr)	0.25 microg/kg/min (mL/hr)	0.375 microg/kg/min (mL/hr)	**Usual Starting Rate 0.5 microg/kg/min (mL/hr)**	0.625 microg/kg/min (mL/hr)	**Maximum dose** 0.75 microg/kg/min (mL/hr)
50 kg	1.9	3.8	5.6	**7.5**	9.4	11.3
60 kg	2.3	4.5	6.8	**9**	11.3	13.5
70 kg	2.6	5.3	7.9	**10.5**	13.1	15.8
80 kg	3	6	9	**12**	15	18
90 kg	3.4	6.8	10.1	**13.5**	16.9	20.3
100 kg	3.8	7.5	11.3	**15**	18.8	22.5
110 kg	4.1	8.3	12.4	**16.5**	20.6	24.8
120 kg (Max)	4.5	9	13.5	**18**	22.5	27

General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly after adding milrinone to avoid inadvertently giving a more concentrated dose.
  Glucose 5% can be substituted for different compatible IV fluid as requested by the Medical Officer.
  Infusion stable for 24 hours.
- **Infusion pump:** Alaris® LVP or syringe unit with Guardrails®.
- **Routes of administration:**
  IV injection: No
  IV intermittent infusion: No

IV continuous infusion: Yes
IM injection: No
Subcut injection: No

- **Compatible/incompatible IV drugs/fluids:**
  Of note milrinone is incompatible with frusemide. For other 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)

- Baseline and daily U&Es.
- Monitor lactate at baseline and as clinically indicated.
- Consider invasive cardiac output monitoring.

NURSING PRACTICE POINTS

- Continuous ECG monitoring.
- Monitor blood pressure continuously via arterial line.
- Baseline 12 lead ECG, and then daily.
- Monitor fluid balance (including urine output), heart rate and Cardiac Index.
- All injections and infusions are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

ADVERSE EFFECTS

- Common (greater than 1%) - supraventricular and ventricular arrhythmias, angina, hypotension, headache, nausea, tremor, somnolence.
- Infrequent (0.1–1%) - mild thrombocytopenia, hypokalaemia.
- Rare (less than 0.1%) - torsades de pointes, rash, abnormal liver function, bronchospasm, anaphylaxis.

DRUG PRESENTATIONS AND STORAGE

Milrinone 10 mg/10 mL ampoules.
Store below 30°C, do not freeze.
