## Milrinone

**Alert**
May cause hypotension. Caution advised when using loading dose. Reduce infusion rate in infants with renal impairment and prematurity.

**Indication**
Inotrope and vasodilator for:
- Treatment of low cardiac output states and as an adjunct to inhaled nitric oxide in neonates with persistent pulmonary hypertension of the neonate.
- Prevention of low cardiac output syndrome (LCOS) post cardiac surgery.
- Treatment of myocardial dysfunction in neonates and children with shock particularly in context of enteroviral infection.

**Action**
Selective inhibitor of type 3 cAMP phosphodiesterase in cardiac and vascular muscle.

**Drug Type**
Inotrope and vasodilator.

**Trade Name**
Primacor, Milrinone GH.

**Presentation**
1 mg/mL (1000 microgram/mL) vial.

**Dosage/Interval**

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Term infants</strong></td>
<td>Continuous IV infusion: 0.5 microgram/kg/minute (Range 0.33 - 0.75 microgram/kg/minute). OPTIONAL: Loading dose: 75 microgram/kg over 60 minutes (Caution - risk of hypotension with loading dose).</td>
</tr>
<tr>
<td><strong>Pre-term infants</strong></td>
<td>Continuous IV infusion: 0.2 microgram/kg/minute. OPTIONAL: Loading dose: 135 microgram/kg over 3 hours (Caution - risk of hypotension with loading dose).</td>
</tr>
<tr>
<td><strong>Renal Impairment (including hypoplastic left heart syndrome undergoing surgery)</strong></td>
<td>Continuous IV infusion: 0.2 - 0.33 microgram/kg/minute.</td>
</tr>
</tbody>
</table>

**Route**
Continuous IV infusion.

**Maximum Daily Dose**
Maximum IV Infusion rate: 1 microgram/kg/minute – caution as risk of drug accumulation over time.

**Preparation/Dilution**

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Term infants</strong></td>
<td>Draw up 1.5 mL/kg (1500 microgram/kg of milrinone) and make up to a final volume of 50 mL with sodium chloride 0.9%. <strong>Infusing at a rate of 1 ml/hour = 0.5 microgram/kg/minute</strong> OPTIONAL- Give a loading dose of 2.5 mL (75 microgram/kg) over 1 hour (Note: risk of hypotension with loading dose).</td>
</tr>
<tr>
<td><strong>Pre-term infants</strong></td>
<td>Draw up 1.5 mL/kg (1500 microgram/kg of milrinone) and make up to a final volume of 50 mL with sodium chloride 0.9%. <strong>Infusing at a rate of 0.4 ml/hour = 0.2 microgram/kg/minute</strong> OPTIONAL - Give a loading dose of 4.5 mL (135 microgram/kg) over 3 hours (Note: risk of hypotension with loading dose).</td>
</tr>
</tbody>
</table>

**Administration**
Continuous IV infusion preferably via a central line. Adjust infusion rate based on haemodynamic and clinical response. For term infants – if loading is not given, higher maintenance infusion may be required to reach the steady state – range 0.5-0.75 microgram/kg/minute. For preterm infants – if loading dose is not given, titrate the maximal infusion rate to 0.5 microgram/kg/minute if required. Avoid prolonged infusion > 0.2 microgram/kg/min in very preterm infants.

---

This RHW document is a modification of Neomed version. Dosage schedules remain the same. However, information on the commercial preparations not used at RHW is deleted. The risk rating is modified as per the local health district policy.
Monitoring
Continuous heart rate, ECG and blood pressure monitoring preferable.
Assess urine output and peripheral perfusion frequently.
Monitor fluid and electrolytes.

Contraindications
Severe obstructive aortic or pulmonary valvular disease or hypertrophic subaortic stenosis.
Hypersensitivity to milrinone, other 3,4'-bipyridines (inamrinone) or any other ingredient of the formulation.

Precautions
Ensure adequate circulating blood volume prior to commencement.

Loading dose: Considered optional depending on clinical circumstances. May cause hypotension. Monitor BP and heart rate closely and ensure adequate volume replacement.

Prematurity: Long half-life reported (10 hours) in very preterm infants. Avoid prolonged higher rate infusion (≥0.2 microgram/kg/min).

Renal impairment: Significantly increases half-life of milrinone. A reduction in the infusion rate in patients with renal impairment to prevent drug accumulation is advised.

Patient recovery: Improvement in cardiac output with resultant diuresis may necessitate a reduction in the dose of diuretic. Potassium loss due to excessive diuresis may predispose digitalised patients to arrhythmias.

Drug Interactions
None known.

Adverse Reactions
Ventricular arrhythmias in cardiac patients.
Patent ductus arteriosus has been reported.
May cause hypotension.

Compatibility
Fluids: Glucose 5%, sodium chloride 0.9%.

Y-site: Amino acid solutions, adrenaline (epinephrine) hydrochloride, amiodarone, atracurium, bivalirudin, calcium gluconate monohydrate, caspofungin, dexametomidine, digoxin, dobutamine, dopamine, doripenem, fentanyl, glycercyl trinitrate, heparin sodium, insulin (short-acting), magnesium sulfate heptahydrate, metoprolol, midazolam, morphine sulfate penta hydrate, noradrenaline (norepinephrine), pancuronium, potassium chloride, ranitidine, rocuronium, sodium nitroprusside, vecuronium, verapamil.

Incompatibility
Fluids: Sodium bicarbonate.

Y-site: Bumetanide, esmolol, furosemide (frusemide), imipenem + cilastatin, ondansetron.

Stability
Diluted solution: Store below 30°C and use within 24 hours.

Storage
Vials: Store below 25°C. Protect from light. Discard remainder after use.

Special Comments
Discard admixtures exhibiting colour change.

Evidence summary
Efficacy:
Treatment of pulmonary hypertension in near term infants: Case series report improvements in pulmonary and systemic haemodynamics and oxygenation in infants with pulmonary hypertension treated with nitric oxide. 1, 6, 7 (LOE IV GOR C)
Treatment of very pre-term infants: An RCT found no difference in measures of systemic blood flow when used preventatively in extremely premature infants. 8 Case series reported improvement in oxygenation and a fall in blood pressure in pre-term infants with pulmonary hypertension treated with nitric oxide. 9 There are insufficient data to determine the efficacy and safety of milrinone in pre-term infants with pulmonary hypertension and/or myocardial dysfunction. 10 (LOE II 8, GOR C)
Neonates and infants undergoing cardiac surgery: A single RCT found high dose milrinone reduced the risk of LCOS post cardiac surgery. 2, 3 (LOE II, GOR B) An historical control study reported use of milrinone post ductal ligation improved ventilation and reduced inotrope use 11 (LOE IV, GOR C).
Infants and children with shock associated with myocardial dysfunction: An RCT found milrinone 0.5 microgram/kg/min reduced mortality in children with enterovirus 71-induced pulmonary
Milrinone

2016


6. James AT, Corcoran JD, McNamara PJ, Franklin O, El-Khuffash AF. The effect of milrinone on right and left ventricular function when used as a rescue therapy for term infants with pulmonary hypertension. Cardiology in the young. 2015:1-10.


15. MIMS accessed via CIAP on 4th November 2015
18. Micromedex 2.0 accessed via CIAP on 4th November 2015

<table>
<thead>
<tr>
<th>Original version Date: 5/12/2015</th>
<th>Author: NeoMed Consensus Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Version number: 2</td>
<td>Version Date: 16/02/2016</td>
</tr>
<tr>
<td>Risk Rating: High</td>
<td>Due for Review: 16/02/2018</td>
</tr>
<tr>
<td>Approval by: As per Local policy</td>
<td>Approval Date:</td>
</tr>
</tbody>
</table>