Milrinone
Newborn use only

2020

<table>
<tr><td>Alert</td><td>May cause hypotension. Caution advised when using loading dose.
Reduce infusion rate for infants with renal impairment and prematurity.</td></tr>
<tr><td>Indication</td><td>Inotrope and vasodilator for:
1. Treatment of low cardiac output and as an adjunct to inhaled nitric oxide in neonates with persistent pulmonary hypertension of the neonate [1].
2. Prevention of low cardiac output syndrome (LCOS) post cardiac surgery[2, 3].
3. Treatment of myocardial dysfunction in neonates and children with shock particularly in context of enteroviral 71 infection [4].</td></tr>
<tr><td>Action</td><td>Selective inhibitor of type 3 cAMP phosphodiesterase in cardiac and vascular muscle.</td></tr>
<tr><td>Drug type</td><td>Inotrope and vasodilator.</td></tr>
<tr><td>Trade name</td><td>Primacor, Milrinone GH, Milrinone-Baxter</td></tr>
<tr><td>Presentation</td><td>10mg/10mL (1000 microgram/mL) vial.</td></tr>
<tr><td>Dose</td><td>
<table>
<tr><th></th><th>Term infant</th><th>Preterm infant</th></tr>
<tr><td>Maintenance NO loading dose</td><td>0.33 − 0.75 microgram/kg/minute</td><td>0.2 microgram/kg/minute</td></tr>
<tr><td rowspan="2">OPTIONAL Loading dose Followed by maintenance dose</td><td>Loading: 75 microgram/kg over 1 hour</td><td>Loading: 45 microgram/kg over 1 hour</td></tr>
<tr><td>0.33 − 0.75 microgram/kg/minute</td><td>0.2 microgram/kg/minute</td></tr>
</table>
Caution: Risk of hypotension with loading dose!</td></tr>
<tr><td>Dose adjustment</td><td>Renal impairment (including hypoplastic left heart syndrome undergoing surgery)
0.2 −0.33 microgram/kg/minute IV infusion</td></tr>
<tr><td>Maximum dose</td><td>Maximum IV Infusion rate for the maintenance dose is 1 microgram/kg/minute and 0.5 microgram/kg/minute for term and preterm infants respectively – caution as risk of drug accumulation over time.</td></tr>
<tr><td>Total cumulative dose</td><td></td></tr>
<tr><td>Route</td><td>IV infusion.</td></tr>
<tr><td>Preparation</td><td><u>Term infants</u>

<table>
<tr><th><u>Infusion strength</u></th><th><u>Prescribed amount</u></th></tr>
<tr><td>1 mL/hour = 0.33 microgram/kg/minute</td><td>1 mL/kg milrinone and make up to 50mL</td></tr>
</table>

Draw up 1mL/kg (1000 microgram/kg of milrinone) and add sodium chloride 0.9% or glucose 5% to make a final volume of 50mL. Infusing at a rate of 1mL/hour = 0.33 microgram/kg/minute

OPTIONAL- Give a loading dose of 3.75 mL (75 microgram/kg) over 1 hour (Note: risk of hypotension with loading dose).
For term infants – if loading is not given, higher maintenance infusion may be required to reach the steady drug range of 0.5−0.75 microgram/kg/minute.

<u>Pre-term infants and renal impairment</u>

<table>
<tr><th><u>Infusion strength</u></th><th><u>Prescribed amount</u></th></tr>
<tr><td>1 mL/hour = 0.2 microgram/kg/minute</td><td>0.6 mL/kg milrinone and make up to 50mL</td></tr>
</table>

Draw up 0.6mL/kg (600 microgram/kg of milrinone) and add sodium chloride 0.9% or glucose 5% to make a final volume of 50mL. Infusing 1mL/hour = 0.2microgram/kg/minute.

OPTIONAL - Give a loading dose of 3.75 mL (45 microgram/kg) over 1 hour (Note: risk of hypotension with loading dose).
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/minute in very preterm infants.</td></tr>
<tr><td>Administration</td><td>Continuous IV infusion preferably via central line. Change solution every 24 hours.
Adjust infusion rate based on haemodynamic and clinical response.</td></tr>
</table>

	For Loading dose: IV infusion over ONE hour
Monitoring	Heart rate, ECG and blood pressure Urine output and peripheral perfusion frequently. Fluid and electrolytes. Liver function. Platelets
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.[5] Avoid prolonged higher rate infusion ≥0.2 microgram/kg/minute. **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. May cause hypotension.
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9%. Y-site: Amino acid solutions, aciclovir, adrenaline (epinephrine) hydrochloride, amikacin, amiodarone, atracurium, bivalirudin, calcium chloride, calcium gluconate, caspofungin, cefazolin, cefepime, cefotaxime, dexmedetomidine, digoxin, dobutamine, dopamine, doripenem, fentanyl, glyceryl trinitrate, heparin sodium, insulin (short-acting), magnesium sulfate heptahydrate, meropenem, metoprolol, midazolam, morphine sulfate pentahydrate, noradrenaline (norepinephrine), pancuronium, potassium chloride, ranitidine, rocuronium, sodium nitroprusside, vancomycin, vecuronium, verapamil.
Incompatibility	Fluids: Sodium bicarbonate. Y-site: Bumetanide, esmolol, furosemide (frusemide), imipenem + cilastatin, ondansetron.
Stability	Primacore: If storage is necessary, diluted solution may be stored below 30°C and use within 24 hours. Milrinone GH: If storage is necessary, diluted solution may be stored at 2-8°C and use within 24 hours. Milrinone-Baxter: Diluted solution should be used immediately or as soon as practical to reduce microbiological hazard.
Storage	Primacor and Milrinone Baxter: Store below 30°C. Do not freeze. Milrinone GH: Store below 25°C. Do not freeze. Protect from light.
Excipients	Primacore, Milrinone GH, Milrinone-Baxter: Glucose (monohydrate or anhydrous), lactic acid or sodium hydroxide (for pH adjustment), and water for injections.
Special comments	Discard mixtures exhibiting colour change.
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

VERSION/NUMBER	**DATE**
Original	**5/12/2015**
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