Milrinone - Standard Concentration

Newborn use only

2025

Alert	May cause hypotension. Caution advised when using loading dose. Reduce infusion rate for infants with renal impairment and prematurity.
Indication	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]
Action	Selective inhibitor of type 3 cAMP phosphodiesterase in cardiac and vascular muscle.
Drug type	Inotrope and vasodilator.
Trade name	Primacor, Milrinone GH, Milrinone-Baxter
Presentation	10mg/10mL (1000 microgram/mL) vial.
Dose	**STANDARD Regimen – with NO loading dose**

	Term infant	**Preterm infant**
Maintenance NO loading dose	0.33 − 0.75 microgram/kg/minute	0.2 microgram/kg/minute

OPTIONAL Regimen – with loading dose
Caution: Risk of hypotension with loading dose!

	Term infant	**Preterm infant**
OPTIONAL Loading dose	Loading: 75 microgram/kg over 1 hour	Loading: 45 microgram/kg over 1 hour
Followed by maintenance dose	0.33 − 0.75 microgram/kg/minute	0.2 microgram/kg/minute

Dose adjustment	**Renal impairment (including hypoplastic left heart syndrome undergoing surgery)** 0.2 −0.33 microgram/kg/minute IV infusion
Maximum dose	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.
Total cumulative dose	
Route	IV infusion.
Preparation	**Note: Refer to Appendix for tables to assist with concentration selection.** **Weight suggestions for infusion concentrations below are a guide only. Clinicians may choose infusion concentration different to the suggested based on expected dose and the corresponding 24-hour fluid volumes.**

Infant weight	<2 kg	≥2 kg
Suggested milrinone concentration	**50 microgram/mL**	**200 microgram/mL**
0.2 microgram/kg/minute	0.24 mL/kg/hour	0.06 mL/kg/hour

20mL Syringe

Draw up milrinone and add compatible fluid* as per table below to make a final volume of 20 mL

Milrinone concentration	**50 microgram/mL**	**200 microgram/mL**
Volume of milrinone (1 mg/mL)	1 mL (=1000 micrograms)	4 mL (=4000 micrograms)
Volume of compatible fluid*	19 mL	16 mL
Total volume	20 mL	20 mL

*Compatible fluid: glucose 5% or sodium chloride 0.9%

	50mL Syringe Draw up milrinone and add compatible fluid* as per table below to make a final volume of 50 mL **Milrinone concentration** | **50 microgram/mL** | **200 microgram/mL** **Volume of milrinone (1 mg/mL)** | 2.5 mL (=2500 micrograms) | 10 mL (10,000 micrograms) **Volume of compatible fluid*** | 47.5 mL | 40 mL **Total volume** | 50 mL | 50 mL *Compatible fluid: glucose 5% or sodium chloride 0.9% 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.
Administration	Continuous IV infusion preferably via central line. Change solution every 24 hours. Adjust infusion rate based on haemodynamic and clinical response. 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%. **PN at Y site:** compatible with 2 in 1 solution (Amino acid-glucose-trace element mixture), SMOF lipid **Y-site:** Aciclovir, adrenaline (epinephrine) hydrochloride, amikacin, amiodarone, amphotericin B liposome, ampicillin, anidulafungin, atenolol, atracurium, azithromycin, aztreonam, bivalirudin, caffeine citrate, calcium chloride, calcium gluconate, caspofungin, cefazolin, cefepime, cefiderocol, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, ciprofloxacin, cisatracurium, clindamycin phosphate, cloxacillin, dexamethasone sodium phosphate, dexmedetomidine, digoxin, dobutamine, dopamine, doripenem, doxycycline, enalaprilat, epinephrine, erythromycin lactobionate, fentanyl, fluconazole, ganciclovir, gentamicin sulfate, glyceryl trinitrate, glycopyrrolate, heparin, hydralazine, hydrocortisone sodium succinate, insulin (short-acting), ketamine, labetalol, linezolid, lorazepam, magnesium sulfate, meropenem, methadone, methylprednisolone sodium succinate, metoprolol, metronidazole, midazolam, morphine sulfate, naloxone, nicardipine, nitroglycerin, noradrenaline (norepinephrine), octreotide, pamidronate, pancuronium, pentobarbital, phenobarbital, piperacillin/tazobactam, potassium acetate, potassium chloride, propofol, propranolol, ranitidine, remifentanil, rocuronium, sildenafil, sodium acetate, sodium bicarbonate, sodium nitroprusside, succinylcholine, sulfamethoxazole/trimethoprim, tacrolimus, ticarcillin, ticarcillin/clavulanate, tobramycin, vancomycin, vasopressin, vecuronium, verapamil, voriconazole, zidovudine.
Incompatibility	**Fluids:** No information. **Y-site:** Alprostadil, Amphotericin B, Amphotericin B lipid complex, esmolol, furosemide (frusemide), lidocaine, ondansetron, pantoprazole, phenytoin

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	**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 oedema and/or shock. A loading dose was not used.[4] (LOE II, GOR B) **Safety** Reports of arrhythmias, tachycardia, hypotension and hypokalaemia, bronchospasm, headaches, thrombocytopenia, anaemia and elevated serum liver enzymes. In neonates treated with milrinone, hypotension and intraventricular haemorrhage have been observed.[2, 6] (LOE IV) **Pharmacokinetics** Extremely pre-term infants for prevention of low systemic blood flow: $T_{½}$ averaged 10 hours. Milrinone loading infusion 0.75 microgram/kg/min for 3 hours followed by maintenance infusion 0.2 microgram/kg/min achieved target concentrations of 180–300 nanogram/mL.[5] (LOE IV GOR C) Term infants with pulmonary hypertension: Half-life ($t_{½}$) averaged 4 hours. Loading dose 50 microgram/kg resulted in sub-therapeutic concentrations. Maintenance infusion 0.33–0.99 microgram/kg/min resulted in concentrations above target range (180–300 nanogram/mL).[1] (LOE IV GOR C) Term newborns with hypoplastic left heart undergoing surgery: Neonates received an initial dose of either a 100 or 250 microgram/kg of milrinone into the cardiopulmonary bypass circuit. A constant infusion of 0.5 microgram/kg/min resulted in drug accumulation during the initial 12 h of drug administration. Postoperatively, milrinone clearance was significantly impaired. Initial loading dose of 100 microgram/kg on cardiopulmonary bypass resulted in plasma concentrations similar to those observed in other therapeutic settings. In the postoperative setting of markedly impaired renal function, an infusion rate of 0.2 microgram/kg/min should be considered.[12] Paediatric patients with septic shock: $T_{½}$ averaged 1.47 hours (range, 0.62 to 10.85 hours). Loading dose 75 microgram/kg and starting infusion rates 0.75–1.0 microgram/kg/min for patients with normal renal function recommended.[13] Prevention of low cardiac output syndrome post cardiac surgery in infants: Loading dose 50 microgram/kg then infusion 3 microgram/kg/min for 30 minutes and then a maintenance infusion 0.5 microgram/kg/min, with adjustment for age.[14] (LOE IV GOR C).
Practice points	
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Appendix

Infusion tables to assist with concentration selection

Table 1: Infusion rates when using milrinone concentration **50 microgram/mL**
(suggested for weight <2kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate microgram/kg/minute**									
0.5	0.17	0.33	0.5	0.67	0.83	1	1.17	1.33	1.5	1.67
1	0.08	0.17	0.25	0.33	0.42	0.5	0.58	0.67	0.75	0.83
1.5	0.06	0.11	0.17	0.22	0.28	0.33	0.39	0.44	0.5	0.56
2	0.04	0.08	0.13	0.17	0.21	0.25	0.29	0.33	0.38	0.42
2.5	0.03	0.07	0.10	0.13	0.17	0.2	0.23	0.27	0.3	0.33

3	0.03	0.06	0.08	0.11	0.14	0.17	0.19	0.22	0.25	0.28
3.5	0.02	0.05	0.07	0.1	0.12	0.14	0.17	0.19	0.21	0.24
4	0.02	0.04	0.06	0.08	0.1	0.13	0.15	0.17	0.19	0.21
4.5	0.02	0.04	0.06	0.07	0.09	0.11	0.13	0.15	0.17	0.19
5	0.02	0.03	0.05	0.07	0.08	0.10	0.12	0.13	0.15	0.17

Table 2: Infusion rates when using milrinone concentration **200 microgram/mL**
(suggested for weight ≥2 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate microgram/kg/minute**									
0.5	0.67	1.33	2	2.67	3.33	4	4.67	5.33	6	6.67
1	0.33	0.67	1	1.33	1.67	2	2.33	2.67	3	3.33
1.5	0.22	0.44	0.67	0.89	1.11	1.33	1.56	1.78	2	2.22
2	0.17	0.33	0.5	0.67	0.83	1	1.17	1.33	1.5	1.67
2.5	0.13	0.27	0.4	0.53	0.67	0.8	0.93	1.07	1.2	1.33
3	0.11	0.22	0.33	0.44	0.56	0.67	0.78	0.89	1	1.11
3.5	0.1	0.19	0.29	0.38	0.48	0.57	0.67	0.76	0.86	0.95
4	0.08	0.17	0.25	0.33	0.42	0.5	0.58	0.67	0.75	0.83
4.5	0.07	0.15	0.22	0.3	0.37	0.44	0.52	0.59	0.67	0.74
5	0.07	0.13	0.2	0.27	0.33	0.4	0.47	0.53	0.60	0.67

$$\text{Dose (microgram/kg/min)} = \frac{\text{Rate (mL/hr)} \times \text{Concentration (microgram/mL)}}{\text{Weight (kg)} \times 60}$$

$$\text{Rate (mL/hr)} = \frac{60 \times \text{Dose (microgram/kg/min)} \times \text{Weight (kg)}}{\text{Concentration (microgram/mL)}}$$

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