Drug Guideline Title: Milrinone (Primacor)

Summary:
Milrinone is a positive inotrope and vasodilator that relaxes the muscles in blood vessels to help them dilate. This lowers blood pressure and allows blood to flow more easily through veins and arteries. Milrinone is used as a short-term treatment for treat life-threatening heart failure.

Approved by: ICU Director, ICU - NUM

Publication (Issue) Date: March 2015

Next Review Date: March 2018

Replaces Existing Drug Guideline: milrinone_2014 (Primacor)

Previous Review Dates: 2005, 2014

Background Information:
Milrinone is a positive inotrope and vasodilator used in the intensive care setting. Unlike catecholamines, milrinone is a phosphodiesterase inhibitor (PDI) that does not affect the adrenergic receptors. The inhibition of phosphodiesterase leads to the inhibition of the breakdown of cyclic adenosine monophosphate. This results in increase in myocardial contractility (increase CI) and venous and arterial dilation (decrease preload and SVR). The resulting vasodilation may lead to a slight increase in heart rate.

1. Introduction contains:
The risk addressed by this policy:

Milrinone will be administered safely and without any adverse side effects

The Aims / Expected Outcome of this policy:

The use of milrinone is administered safely to patients by accredited nursing staff who complies with hospital and ICU guidelines and policies

Related Standards or Legislation

NSQHS Standard 1 Governance
National Standard 4 Medication Safety

Related Policies

LH_PD2013_C03.01 Drug Administration
LH_PD2013_C03.03 Drug Calculation Formulas
LH_PD2013_C03.00 Drug Prescribing
LH_PD2013_C03.12 Administration of Intravenous (IV) Medications
2. **Policy Statement:**

- All care provided within Liverpool Hospital will be in accordance with infection control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer/authorised nurse practitioner (NP) unless required during an emergency.
- All drugs administered during an emergency (under the direction of a medical officer/authorised nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
- Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require ‘same time’ administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritised) and are to be signed by the administering nurse.
- Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The “rights of drug administration” must be followed: right: patient, drug, dose, route, administration, and time, reason for the drug, documentation, education and evaluation/outcome.
- Adverse drug reactions are to be documented and reported to a medical officer.
- Medication errors are to be reported using the hospital electronic reporting system: IIMS.
- Guidelines are for adult patients unless otherwise stated
- Milrinone infusions may be titrated or weaned by accredited RNs.
- Medical Officers must ensure that titration and/or weaning parameters are specified on the management plan, and have been discussed with the nurse assigned to that patient.
- Milrinone must always be administered via a dedicated lumen, and never “piggybacked” with other drugs or fluids. Where multiple infusions are required, it may be acceptable to administer milrinone with other inotropes, via a three-way tap.
- Milrinone infusions must be administered by syringe pump or infusion pump.
- Milrinone infusions must not be administered via the drug infusion port on a haemodialysis circuit.

For the purposes of this Policy, an accredited RN is: a Registered Nurse (RN) who has completed the required self directed learning packages and has been accredited by an Educator/Clinical Nurse Consultant, to administer/titrate inotropic drugs when caring for an Intensive Care Unit (ICU) Patient. The Educator/Clinical Nurse Consultant may deem the nurse competent if the nurse has previous documented experience/qualifications.

3. **Principles / Guidelines**

**Actions**

- Milrinone is a positive inotrope and vasodilator.
- Improves diastolic function as evidenced by improvements in left ventricular diastolic relaxation.
- It inhibits phosphodiesterase leading to an increase of intracellular cyclic AMP in cardiac and vascular smooth muscle. This promotes calcium entry, producing a positive inotropic effect. There is potent dilatation of the systemic and pulmonary arterial and venous circulation.
- It has a half-life of 2-3 hours.

**Indications**

- Severe congestive cardiac failure unresponsive to other therapies.
- Low output states after cardiac surgery.

**Contraindications**

- Hypersensitivity to milrinone, inamrinone, or any component of the formulation; concurrent use of inamrinone
Precautions 1, 2, 3
- Acute phases of a myocardial infarction may lead to an undesirable increase in myocardial oxygen consumption (MVO2).
- Post-operative myocardial ischaemia
- Severe obstructive aortic or pulmonary valvular disease in lieu of surgical relief of the obstruction. Like other inotropic agents, it may aggravate outflow tract obstruction in hypertrophic subaortic stenosis.
- Dysrhythmias including ventricular tachycardia
- Milrinone produces a slight shortening of AV node conduction time, indicating a potential for an increased ventricular response rate in patients with atrial flutter/fibrillation which is not controlled with digitalis therapy.
- May induce hypotension as a consequence of its vasodilatory action.
- Renal failure may require dosage reduction.
- Monitor heart rate, rhythm, fluid balance, electrolytes, and renal function.
- There is no experience in controlled trials with infusions of Milrinone for periods exceeding 48 hours.

Significant Interactions 1, 2
- IV line precipitation with frusemide – infuse using a dedicated line.
- Incompatible with sodium bicarbonate

Adverse Effects 1
- Tachycardia.
- Dysrhythmias.
- Headache.
- Hypotension.
- Exacerbation of myocardial ischaemia
- Abnormal liver function tests
- Injection site reactions

Presentation
Milrinone 10mg in 10mL ampoule.

Administration Guidelines 1

- Milrinone is preferably administered via a central line.
- The loading dose is subjected to change as per clinical status of the patient

Loading dose: (optional, not recommended by ACCF/AHA 2013 heart failure guidelines) 1
- Dilute 10mg milrinone to 50mL sterile 0.9% sodium chloride to give a final concentration of 200micrograms/mL.

Give 50micrograms/kg milrinone as a slow IV bolus over 10 minutes
- Do not inject undiluted.
- Followed by a maintenance dose titrated according to hemodynamic and clinical response; Maintenance dose: IV infusion: 0.375-0.75 mcg/kg/minute

Infusion:
- Dilute 10mg milrinone to 50mL sterile 0.9% sodium chloride to give a final concentration of 200micrograms/mL.
- Titrate the infusion between 0.375 micrograms/kg/min and 0.75micrograms/kg/min, depending upon the desired cardiac output and PCWP response.
- IV fluid may be required to counteract hypotension.
- Infusions are regulated at either a low, medium or higher rate:
→ **Low** - 0.367 micrograms/kg/min or 8.5 mL/hr in an 80kg person
→ **Medium** - 0.5 micrograms/kg/min or 12.0 mL/hr in an 80kg person
→ **High** - 0.75 micrograms/kg/min or 18.0 mL/hr in an 80kg person.

The ACCF/AHA 2013 heart failure guidelines recommend a maintenance dose of 0.125-0.75 mcg/kg/minute

**Weaning:**
- Decrease by 1 mL/hr dependent upon haemodynamic status or as documented by the Medical Officer on the management plan.

### Milrinone 200 micrograms/mL infusion

(Doses calculated in **micrograms/kg/min**, corrected to 2 decimal places)

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Dosage Adjustment in Renally Impaired Patients$^{1,3}$

Data obtained from patients with severe renal impairment (creatinine clearance = 0 to 30mL/min) but without congestive heart failure have demonstrated that the presence of renal impairment significantly increases the terminal elimination half-life of milrinone. Reductions in the starting infusion rate may be necessary in patients with renal impairment. For patients with clinical evidence of renal impairment, the recommended infusion rate can be obtained from the following table:

<table>
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<tr>
<th>CREATININE CLEARANCE (mL/min/1.73m$^2$)</th>
<th>INFUSION RATE ($\mu$g/kg/min)</th>
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Clinical Considerations

- Monitor electrolytes (particularly potassium).
- Monitor fluid output.
- **Syringe Change** - When changing from a near completed infusion to a new syringe:
  - Observe MAP, when this begins to fall, you may safely cease the old infusion.
  - Closely monitor BP.
  - If BP falls below desired level, decrease infusion rate.

4. Performance Measures

All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. References / Links

3. Milrinone FDA Prescribing information side effects and uses. Drugs.com
4. MIMS Online, CIAP: NSW Health Department, Copyright MIMS Australia Pty Ltd 2015. [http://www.mims.hcn.net.au/](http://www.mims.hcn.net.au/)

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