Milrinone

MECHANISM OF ACTION/PHARMACOLOGY
Milrinone is a positive inotrope and vasodilator, with little chronotropic activity. Milrinone selectively inhibits PEAK III cAMP (cyclic adenosine monophosphate) phosphodiesterase isozyme in cardiac and vascular muscle, leading to an increase in intracellular ionised calcium and contractile force in cardiac muscle.\(^1,2\) This activity results in left ventricular afterload reduction, with an increase in cardiac output and a reduction in total peripheral resistance.\(^3\)

Onset of action: 5–15 minutes.\(^3\)
Duration of action: 3–5 hours.\(^1\)
Half-life: 2–4 hours, renal impairment prolongs half-life.\(^4\)

INDICATIONS
Cardiogenic shock secondary to acute decompensated systolic heart failure.
Short-term therapy for severe heart failure refractory to other treatment.
Low cardiac output states post cardiac surgery.\(^2,5\)

PRECAUTIONS
- Hypersensitivity to milrinone or other bipyridines\(^2\)
- Hypotension due to uncorrected hypovolaemia
- Severe obstructive aortic or pulmonary valvular disease or hypertrophic subaortic stenosis – milrinone may aggravate outflow tract obstruction\(^2\)
- Risk of systolic anterior motion of the mitral valve and/or dynamic left ventricular outflow tract obstruction
- Supraventricular and ventricular arrhythmias
- Severe renal impairment (CrCl < 30 mL/min) increases the terminal elimination half-life; consider dose reduction.\(^2\)

MEDICATION PRESENTATION
10 mg/10mL ampoule.
**MEDICATION STORAGE**

Store vials below 30°C. Do not freeze.\(^6\)

Infusion solutions are stable for up to 24 hours.\(^6\)

**PREPARATION**

<table>
<thead>
<tr>
<th></th>
<th>IV bag</th>
<th>Syringe driver</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prescribe</strong></td>
<td>20 mg in 100 mL</td>
<td>10 mg in 50 mL</td>
</tr>
<tr>
<td><strong>Make up infusion in</strong></td>
<td>100 mL bag of glucose 5%*</td>
<td>Glucose 5%*</td>
</tr>
<tr>
<td><strong>Volume to be removed from IV bag</strong></td>
<td>20 mL</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Drug dose to be added</strong></td>
<td>20 mg (20 mL)</td>
<td>Draw up 40 mL in the syringe</td>
</tr>
<tr>
<td><strong>Final volume</strong></td>
<td>100 mL</td>
<td>50 mL</td>
</tr>
<tr>
<td><strong>Final concentration</strong></td>
<td>200 microg/mL</td>
<td>200 microg/mL</td>
</tr>
<tr>
<td><strong>1mL/hr =</strong></td>
<td>200 microg/hr</td>
<td>200 microg/hr</td>
</tr>
</tbody>
</table>

* Glucose 5% is preferred for dilution of all inotropes and vasopressors. However, milrinone is also compatible with Hartmann’s and sodium chloride 0.9%.\(^6\)

**ADMINISTRATION – THIS GUIDELINE IS INTENDED FOR CENTRAL ACCESS ONLY**

Administer continuous intravenous infusion through a central access line.\(^6\)

Infusions should be administered via a syringe driver or infusion pump, preferably with medication error reduction software enabled.

Avoid administration via lines where other drugs or fluids may be bolused or flushed.\(^7\)

**DOSING**

Starting rate: 0.1 microg/kg/min.\(^8\)

In common practice the loading dose is omitted as it is associated with hypotension.

Usual rate range: 0.125 to 0.35 microg/kg/min.\(^9\)

Titrating in accordance with haemodynamic and clinical response, with dose adjustments every 2–4 hours due to long half-life.

Maximum rate: 0.75 microg/kg/min.\(^2\)

Dose based on actual body weight up to a maximum of 120 kg.\(^10\)

Weaning: The infusion should be weaned slowly (2–4-hourly), monitoring for clinical signs of inadequate cardiac output.
**Infusion rate guide:** Maintenance continuous infusion rate for milrinone (mL/hr) (using 200 microg/mL solution).

<table>
<thead>
<tr>
<th>Patient weight (kg)</th>
<th>Infusion rate (mL/hr) 0.05 microg/kg/min</th>
<th>Infusion rate (mL/hr) 0.1 microg/kg/min</th>
<th>Infusion rate (mL/hr) 0.15 microg/kg/min</th>
<th>Infusion rate (mL/hr) 0.2 microg/kg/min</th>
<th>Infusion rate (mL/hr) 0.25 microg/kg/min</th>
<th>Infusion rate (mL/hr) 0.3 microg/kg/min</th>
<th>Infusion rate (mL/hr) 0.35 microg/kg/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.6</td>
<td>1.2</td>
<td>1.8</td>
<td>2.4</td>
<td>3</td>
<td>3.6</td>
<td>4.2</td>
</tr>
<tr>
<td>50</td>
<td>0.75</td>
<td>1.5</td>
<td>2.25</td>
<td>3</td>
<td>3.8</td>
<td>4.5</td>
<td>5.25</td>
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<tr>
<td>60</td>
<td>0.9</td>
<td>1.8</td>
<td>2.7</td>
<td>3.6</td>
<td>4.5</td>
<td>5.4</td>
<td>6.3</td>
</tr>
<tr>
<td>70</td>
<td>1.05</td>
<td>2.1</td>
<td>3.15</td>
<td>4.2</td>
<td>5.3</td>
<td>6.3</td>
<td>7.35</td>
</tr>
<tr>
<td>80</td>
<td>1.2</td>
<td>2.4</td>
<td>3.6</td>
<td>4.8</td>
<td>6</td>
<td>7.2</td>
<td>8.4</td>
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<tr>
<td>90</td>
<td>1.35</td>
<td>2.7</td>
<td>4.05</td>
<td>5.4</td>
<td>6.8</td>
<td>8.1</td>
<td>9.45</td>
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<tr>
<td>100</td>
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<td>3</td>
<td>4.5</td>
<td>6.0</td>
<td>7.5</td>
<td>9</td>
<td>10.5</td>
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<tr>
<td>110</td>
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<td>3.3</td>
<td>4.95</td>
<td>6.6</td>
<td>8.3</td>
<td>9.9</td>
<td>11.55</td>
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<tr>
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<td>1.8</td>
<td>3.6</td>
<td>5.4</td>
<td>7.2</td>
<td>9</td>
<td>10.8</td>
<td>12.6</td>
</tr>
</tbody>
</table>

Calculation:
Infusion rate (mL/hr) = (patient weight (kg) × dose (microg/kg/min) × 60) ÷ infusion strength (microg/mL).

**MONITORING**
Continuous blood pressure and cardiac monitoring for the duration of the infusion. Daily 12-lead ECG.
Monitor fluid balance and electrolytes at least daily.

**SIDE EFFECTS**
- Supraventricular and ventricular arrhythmias
- Hypotension – concomitant vasopressor use may be required
- Mild thrombocytopenia

**COMPATIBILITIES**
Consult the following references, which are available online through the Clinicians Health Channel:
- Australian injectable drugs handbook
- Trissel's™ in IV compatibility (Micromedex) – from the site homepage, select the ‘IV Compatibility’ tab.

**IMPORTANT DRUG INTERACTIONS**
Anagrelide or cilostazol are agents that also inhibit phosphodiesterase III and, in combination with milrinone, may increase the risk of adverse effects.
REFERENCES

2. MIMS [online] (accessed 29 November 2017)
6. Australian injectable drugs handbook (AIDH) [online] (accessed 17 October 2017)

ACKNOWLEDGEMENTS

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