Prescribing Protocol – SESLHDPR/725
Levosimendan

Important information	Levosimendan is an unapproved medicine in Australian and is supplied under Category A of the Special Access Scheme. The prescribing Medical Officer should therefore ensure completion of the following forms, all of which can be found of the SESLHD intranet. 1. Category A Special Access Scheme (SAS) form – Email to TGA. Send printed copy to Pharmacy Department. Photocopy to be retained in patient's medical record. 2. Consent for Exception Use of Medicine – to be filed in patient's medical record.
Areas where Protocol/Guideline applicable	Critical Care Service ICU, CCU and CTICU
Authorised Prescribers	Critical Care Staff Specialist, Cardiology Staff Specialist or Medical Officers under the direct supervision of a Critical Care or Cardiology Staff Specialist
Indication for use	• Acutely decompensated heart failure despite other medical therapy • Low cardiac output syndrome following cardiac surgery • Cardiogenic shock
Contra-indications	• Prior hypersensitivity to levosimendan or racemic simendan[1] • Severe renal impairment (creatinine clearance < 30 mL/min)[1] • Severe hepatic impairment[1] • History of Torsades de Pointes[1]
Precautions	• Should not be used in children or adolescents under 18 years of age • Hypokalaemia. Levosimendan may cause a decrease in serum potassium. Correct prior to administration. • Tachycardia, atrial fibrillation with rapid ventricular response or potentially life-threatening arrhythmias. • Hypotension. Use caution in patients with low baseline systolic or diastolic blood pressure or those at risk for a hypotensive episode. Physician should tailor dose and duration of therapy to the condition and response of the patient. • Continue haemodynamic monitoring for at least 3 days following completion of infusion. • Use with caution in patients with mild to moderate renal impairment. Administration of continuous infusion at lower dosing range is recommended for these patients. Continue haemodynamic monitoring for at least 5 days following completion of infusion. • Use with caution in patients with mild to moderate hepatic impairment. Continue haemodynamic monitoring for at least 5 days following completion of infusion. • Pregnancy. Limited experience. Animal studies have shown toxic effects on reproduction. Use in pregnant women only if the benefits for the mother outweigh the possible risks to the foetus.[1] • Breastfeeding: active metabolites may be excreted in human milk.

Levosimendan

<table>
<tr><td>Place in Therapy</td><td>Used for short-term treatment where conventional therapy is not sufficient.</td></tr>
<tr><td>Dosage</td><td>
A loading dose of 6–12 microgram/kg infused over 10 minutes, followed by a continuous infusion, is recommended by the manufacturer.
However, in practice the loading dose may be omitted due to hypotension.
An initial loading dose of 12 microg/kg (or 6 microg/kg if IV vasodilators or other inotropes in progress) may be given if the patient is haemodynamically stable enough to tolerate it. If systolic blood pressure is < 90 mmHg, consider omitting loading dose.
Use actual body weight up to 120 kg.[3]

Initiation of concentrated infusion:

Commence infusion at 0.05 microg/kg/min and if tolerated, increase to 0.1 microg/kg/min after 1 hour
The usual dose is 0.05 to 0.2 microg/kg/minute
Use actual body weight up to 120kg
Dose changes take 30 to 60 minutes to take effect.[3]

<table>
<tr><th rowspan="2">Patient's Weight (kg)</th><th colspan="2">Loading dose
Given as an infusion over 10 minutes
Loading dose infusion rate (mL/h)</th><th colspan="3">Continuous infusion rate (mL/h)</th></tr>
<tr><th>Loading dose 6 microg/kg</th><th>Loading dose 12 microg/kg</th><th>0.05 microg /kg/min</th><th>0.1 microg /kg/min</th><th>0.2 microg /kg/min</th></tr>
<tr><td>40</td><td>29</td><td>58</td><td>2</td><td>5</td><td>10</td></tr>
<tr><td>50</td><td>36</td><td>72</td><td>3</td><td>6</td><td>12</td></tr>
<tr><td>60</td><td>43</td><td>86</td><td>4</td><td>7</td><td>14</td></tr>
<tr><td>70</td><td>50</td><td>101</td><td>4</td><td>8</td><td>17</td></tr>
<tr><td>80</td><td>58</td><td>115</td><td>5</td><td>10</td><td>19</td></tr>
<tr><td>90</td><td>65</td><td>130</td><td>5</td><td>11</td><td>22</td></tr>
<tr><td>100</td><td>72</td><td>144</td><td>6</td><td>12</td><td>24</td></tr>
<tr><td>110</td><td>79</td><td>158</td><td>7</td><td>13</td><td>26</td></tr>
<tr><td>120</td><td>86</td><td>173</td><td>7</td><td>14</td><td>29</td></tr>
</table>

The following events should lead to a consideration of either a dose reduction or temporary discontinuation of infusion:

Decrease in systolic blood pressure ≤ 85 mmHg or symptomatic hypotension
Persistent heart rate ≥ 140 for over 10 minutes
Angina or new ECG changes consistent with myocardial ischemia
Development of new tachyarrhythmia

</td></tr>
<tr><td>Duration of therapy</td><td>Treatment is generally continued for 24 hours after which infusion is turned off without weaning. Note: IPU required for treatment > 24 hours.
Duration of effect is up to 9 days after stopping the infusion and half-life is 80 hours (active metabolite).</td></tr>
<tr><td>Important Drug Interactions</td><td>Use caution when used with other intravenous vasoactive medicinal products due to a potentially increased risk of hypotension.</td></tr>
</table>

Levosimendan

Presentation & Storage	Each vial contains 12.5 mg in 5 mL (2.5 mg/mL) Store at 2 – 8°C in refrigerator. Do not freeze. Protect from light.
Administration instructions	The concentrate is intended for single use only. Dilute prior to use. **IV Infusion:** • Mix 12.5 mg of levosimendan into 250 mL Glucose 5% **(concentration 50 microg/mL)** • Use a central line and infusion pump. A peripheral line can be used if required.[3] Y-site compatible: digoxin, furosemide, glyceryl trinitrate.[3] No information available with any other drugs or sodium chloride 0.9%.
Monitoring requirements	• **Continuous haemodynamic monitoring (ECG, HR, BP).** BP must be measured at least hourly for the duration of the infusion and for 24 hours post infusion. • Monitor urine output hourly. • Continue haemodynamic monitoring for at least 3 days following completion of infusion. In patients with mild to moderate renal or mild to moderate hepatic impairment monitoring is recommended for at least 5 days.
Adverse effects	• Tachycardia • Hypotension (most common) • Chest pain • Headache • Atrial & ventricular arrhythmias
Basis of Protocol/Guideline	SGH ICU CLIN025 Clinical (Drug Information) Business Rule Prescribing and Administration of Levosimendan in Intensive Care Services St George Hospital POWH Cardiac Service Intravenous Drug Protocols – Levosimendan
References	1. Simdax. NZ product Information. Auckland. New Zealand: Pharmacy Reatiling (NZ) Limited. May 2019. 2. Aidonidis G, Kanonidis I, Koutsimanis V, Nuemann T, Erbel R, Sakadamis G. Efficiency and safety of prolonged levosimendan infusion in patients with acute heart failure. Cardiol Res Pract 2011; Mar 31. DOI: 10.4061/2011/342302. 3. The Society of Hospital Pharmacists of Australia. Australian Injectable Drugs Handbook, 8th Ed. [Online] 2021. 4. Standardised inotrope and vasopressor guidelines. Levosimendan. Safer Care Victoria. Updated 04/12/2018. Accessed 14/10/2021. 5. Truvan Health Analytics Inc. Micromedex Solutions. Levosimendan. [Online] 2021. 6. Postpartum Cardiomyopathy and Considerations for Breastfeeding Laura Kearney,1 Paul Wright,2 Sadeer Fhadil2 and Martin Thomas, Cardiac Failure Review 2018;4(2):112–18.

Groups consulted in development of this protocol	Pharmacy SGH & POWH ICU CNC SGH & POWH

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GOVERNANCE	
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Chairperson, QUM Committee	Dr John Shephard
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