

# Levosimendan

## APPLICABLE AREAS

THIS SECTION WILL BE LEFT BLANK FOR EACH HOSPITAL TO COMPLETE IN ACCORDANCE WITH LOCAL PRACTICE. EXAMPLES: ICU, ED, OR, WARD 2B

## MECHANISM OF ACTION/PHARMACOLOGY

Levosimendan is an inodilator, which increases myocardial contractility by enhancing cardiac sensitivity to calcium. Despite the improvement in ventricular function, levosimendan does not increase myocardial oxygen uptake significantly.<sup>1</sup> Intracellular calcium is unaffected, thus limiting arrhythmic potential. The positive inotropic effect is independent of  $\beta$  receptors and cAMP (cyclic adenosine monophosphate).

Levosimendan also opens ATP-sensitive vascular potassium channels, causing vasodilation in veins, arteries and coronary arteries. This results in afterload reduction.<sup>1</sup>

Onset of action: Rapidly distributed. Peak plasma concentration of active metabolite (OR-1986) in 48–78 hours.<sup>1</sup>

Duration of action: Haemodynamic effects sustained for approximately one week after cessation of parent drug.<sup>2</sup>

Half-life: 1 hour (parent drug); 80 hours (active metabolite OR-1986).<sup>2</sup>

## INDICATIONS

Severe decompensated heart failure unresponsive to other therapies.

Cardiogenic shock post cardiac surgery in patients with left ventricular ejection fraction less than 40%.

Evidence of mortality benefit for these indications is lacking.<sup>3,4</sup>

## PRECAUTIONS

- Hypersensitivity to levosimendan or any of the excipients<sup>5</sup>
- Hypotension due to uncorrected hypovolaemia<sup>5</sup>
- Significant mechanical obstruction affecting ventricular filling, outflow or both<sup>5</sup>
- Hypertrophic obstructive cardiomyopathy<sup>5</sup>
- Atrial fibrillation with rapid ventricular response, ventricular tachycardia, history of Torsades de Pointes, long QTc or concomitantly on medications that prolong the QTc interval<sup>5</sup>
- Ongoing coronary ischaemia<sup>5</sup>
- Heart failure due to diastolic dysfunction – unlikely to benefit

- Severe hepatic impairment may result in more pronounced and prolonged effects<sup>6</sup>
- Severe renal impairment may result in more pronounced and prolonged effects.<sup>7</sup>

## MEDICATION PRESENTATION

12.5 mg/5mL vial.

Stock not registered in Australia – will require completion of a Special Access Scheme Category A form.

## MEDICATION STORAGE

Refrigerate (2–8°C). Do not freeze. During storage, concentrate in vial is clear/yellow to orange. May turn more orange during storage, which does not indicate a loss of potency (may still be used until labelled expiry date).<sup>5,8</sup>

Infusion solution is stable for 24 hours at 25°C.<sup>8</sup>

## PREPARATION

Dilute 12.5 mg (5 mL) in 250 mL glucose 5%.

	Infusion pump
<b>Prescribe</b>	12.5 mg in 250 mL
<b>Make up infusion in</b>	250 mL bag of glucose 5%
<b>Volume to be removed from IV bag</b>	5 mL
<b>Drug dose to be added</b>	12.5 mg (5 mL)
<b>Final volume</b>	250 mL
<b>Final concentration</b>	50 microg/mL
<b>1mL/hr =</b>	0.83 microg/min

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

Administer continuous intravenous infusion through a central access line.

Infusions should be administered via an infusion pump, preferably with medication error reduction software enabled.

Avoid administration in lines where other drugs or fluids may be bolused or flushed.

## DOSING

In common practice the loading dose is omitted as it is associated with hypotension.<sup>9</sup>

Usual dose range: 0.05 to 0.2 microg/kg/min. Dose based on actual body weight up to a maximum of 120 kg.<sup>5</sup>

**Commence infusion at 0.05 microg/kg/min.** If the initial rate is tolerated, consider increasing the maintenance rate to 0.1 microg/kg/min after 60 minutes. If the patient remains haemodynamically stable, further increase the dose to 0.2 microg/kg/min for the remainder of the infusion.

If the patient is haemodynamically unstable, postpone the dose increase for several hours or consider returning to previously stable dose. When adjusting the dose rate, take into account the long half-life of the active metabolite.

The infusion is usually ceased at 24 hours without weaning the infusion rate. Experience with use of infusions beyond 24 hours, and with repeat doses, is limited.<sup>1,4</sup>

**Infusion rate guide:** Continuous infusion rate (mL/hr) (using 50 microg/mL solution)

Patient's weight (kg)	Infusion rate (mL/hr) 0.05 microg/kg/min	Infusion rate (mL/hr) 0.1 microg/kg/min	Infusion rate (mL/hr) 0.2 microg/kg/min
40	2	5	10
50	3	6	12
60	4	7	14
70	4	8	17
80	5	10	19
90	5	11	22
100	6	12	24
110	7	13	26
120	7	14	29

## MONITORING

- Continuous blood pressure and cardiac monitoring for the duration of the infusion
- Continue monitoring ECG, blood pressure, heart rate and electrolytes for 7–10 days after infusion completion. Extended periods of monitoring may be needed in patients with renal or hepatic impairment.<sup>4</sup>

## SIDE EFFECTS

- Hypotension<sup>1</sup>
- Headache<sup>1</sup>
- Hypokalaemia<sup>4</sup>
- Arrhythmias including tachycardia, atrial fibrillation and ventricular tachycardia.<sup>4</sup>

## 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 INTERACTION

**Isosorbide mononitrate** – significant potentiation of orthostatic hypotension.<sup>4</sup>

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## ACKNOWLEDGEMENTS

We would like to thank the pharmacists involved in writing the guidelines: Melissa Ankravs, Melanie Kowalski, Rachel Fyfe, Robyn Ingram, Annalie Jones, Susan Trevillian, and Lucy Sharrock.

To receive this publication in an accessible format phone 9096 1384, using the National Relay Service 13 36 77 if required, or email [info@safercare.vic.gov.au](mailto:info@safercare.vic.gov.au)

Printed copies of this document may not be the most recent version.

Authorised and published by the Victorian Government, 1 Treasury Place, Melbourne.

© State of Victoria, Australia, Safer Care Victoria, December 2018

ISBN 978-1-76069-717-4 (online/print)

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