

Use of Levosimendan on the Intensive Care Unit

Key Point

Levosimendan is approved for use in the short-term treatment of severe low cardiac output states or advanced cardiac failure where there is a need for inotropic support to maintain cardiac output. Treatment should be initiated by a consultant experienced in the management of critically ill patients with low cardiac output states.

Version: 3
Date Issued: 1 May 2024
Review Date: April 2027
Key words: Levosimendan, critical care

This is a controlled document. If you are using a printed copy, check it against the guidelines site to ensure you are using the latest edition.

Print copies must be destroyed after use.

Abbreviations

CVVHD	Continuous Veno-Venous HaemoDialysis (CVVHD)
ECG	Echo Cardiogram
SPC	Summary of Product Characteristics

Contents

Mechanism of Action.....	2
Indication & Dose.....	2
Contraindications	2
Cautions.....	2
Renal and Hepatic Impairment.....	3
Administration	3
Monitoring	3
Adverse Effects.....	4
References.....	4
Full version control record.....	5

Mechanism of Action

Levosimendan is a calcium-sensitising drug that exerts its effect by two mechanisms. The main mechanism of action is through calcium dependent binding of levosimendan to the calcium-saturated N-terminal domain of troponin-C in cardiac muscle. This results in stabilisation of the troponin molecule with subsequent increase in contractile force without increasing myocardial oxygen and energy demand. Levosimendan also opens the ATP sensitive potassium channels in both vascular and cardiac tissue producing a vasodilatory effect that decreases preload and increases blood supply to the damaged myocardium therefore reducing ischaemia. The haemodynamic effects of levosimendan persist for at least 24 hours and may be seen up to 9 days after discontinuation of a 24-hour infusion due to the presence of active metabolites that reach maximum plasma concentrations about 48 hours after the infusion has stopped.

Indication & Dose

Levosimendan is currently **unlicensed** in the UK but available on a named patient basis.

Treatment should be initiated by a consultant experienced in the management of critically ill patients with low cardiac output states.

It can be used for the short-term treatment of severe low cardiac output states or advanced cardiac failure where there is a need for inotropic support to maintain cardiac output.

Severe hypovolaemia should be corrected prior to levosimendan infusion.

Current information from the Summary of Product Characteristics recommends:

A continuous infusion of 0.1 microgram/kg/minute increasing to 0.2 micrograms/kg/minute as tolerated for up to 24 hours.

If hypotension or tachycardia develops the rate of the infusion should be reduced to 0.05micrograms/kg/min or discontinued. If the infusion is tolerated well the dose should be increased to the target of 0.2 micrograms/kg/min as soon as possible.

See administration table for further information.

For full information on contraindications; cautions and adverse effects see SPC

Contraindications

- Hypersensitivity to levosimendan or excipients
- Patients not expected to survive 24 hours (moribund) or uncorrectable medical condition/ prior cardiac arrest without demonstrable neurological recovery.
- Significant mechanical obstructions affecting ventricular filling or outflow or both
- History of Torsades de Pointes
- Severe hepatic impairment
- Severe renal impairment (creatinine clearance <30ml/min)

Cautions

- Patients with tachycardia, atrial fibrillation or life threatening arrhythmias.
- When given concomitantly with medicinal products that prolong the QTc interval

Renal and Hepatic Impairment

Impaired hepatic or renal function may lead to increased concentrations of the biologically active metabolite and this may result in a more pronounced and prolonged effect on heart rate. In this situation it may be necessary to monitor patients for up to 5 days. In patients with severely impaired renal function (Creatinine clearance < 30ml/min) or severely impaired hepatic function levosimendan should not be used.

In practice levosimendan has been used in patients undergoing CVVHD. There may be an increased concentrations of the active metabolites, which may result in a more pronounced and prolonged haemodynamic effect and lower doses may be needed.

Administration

The infusion can be made up as 50microgram/ml

Mix one vial (12.5mg in 5ml) with 250ml glucose 5%

Administered via central intravenous route or via large peripheral vein Levosimendan has a low pH and may cause venous irritation and tissue damage. Monitor insertion site and resite at first sign of inflammation.

The following table provides weight based rates of a 50microgram/ml levosimendan infusion:

Patient's weight (kg)	Continuous infusion rate (ml/h)		
	0.05 microgram / kg / minute	0.1 microgram / kg / minute	0.2 microgram / kg / minute
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

Levosimendan should be infused for no more than 24 hours. One vial of levosimendan is adequate for treatment in the majority of cases.

Patients >90kg may require a second vial in order to complete the 24 hour infusion.

It is a consultant decision if a second vial is required to complete the 24 hour infusion.

Monitoring

Continuous: blood pressure, heart rate and ECG.

As clinically appropriate: cardiac output monitoring, urine output and serum potassium.

These parameters should be monitored for at least 3 days or until the patient is clinically stable.

Haemodynamic will likely persist for at least 24hrs and may be seen up to 9 days after discontinuation of the infusion.

Adverse Effects

- Headache
- Hypotension, dizziness
- Extrasystoles, tachycardia, atrial fibrillation, ventricular tachycardia, palpitations, myocardial ischaemia
- Reduced haemoglobin
- Hypokalaemia
- Nausea and vomiting.

References

- Colucci, W.S. (2024) 'Inotropic agents in heart failure with reduced ejection fraction', in T.W. Post (ed.) *UpToDate*. Available at: <https://www.uptodate.com/contents/inotropic-agents-in-heart-failure-with-reduced-ejection-fraction> (Accessed: 23 February 2024)
- Orion Pharma (2010) *Simdax summary product characteristics*. Available at: <https://www.simdax.com/siteassets/simdax-spc.pdf> (Accessed: 23 February 2024).
- Follath, F. *et al.* (2002) 'Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial', *Lancet*, 360(9328), pp. 196-202. Available at: [https://doi.org/10.1016/s0140-6736\(02\)09455-2](https://doi.org/10.1016/s0140-6736(02)09455-2)
- Mebazza, A. *et al.* (2007) 'Levosimendan vs dobutamine for patients with acute decompensated heart failure: the SURVIVE Randomized Trial', *JAMA*, 297(17), pp. 1883-1891. Available at: <https://doi.org/10.1001/jama.297.17.1883>
- Packer, M. *et al.* (2013) 'Effect of levosimendan on the short-term clinical course of patients with acutely decompensated heart failure', *JACC Heart Failure*, 1(2), pp. 103-111. Available at: <https://doi.org/10.1016/j.jchf.2012.12.004>
- Gong B, Li Z, Yat Wong PC (2015) Levosimendan treatment for heart failure; a systematic review and meta-Analysis. *Journal of Cardiothoracic and Vascular Anesthesia*. 29(6),pp.:1415-25 Available at <https://doi.org/10.1053/j.jvca.2015.03.023>
- Cardiff Critical Care Services (2020) *Levosimendan in ICU*. Available at <https://cardiffcriticalcare.co.uk/wp-content/uploads/2020/11/Levosimendan-ICU-SOP-020.pdf> Accessed 23 February 2024
- University Hospitals Sussex NHS Foundation Trust (2023) *Levosimendan: guide to use in critical care [unlicensed drug]*. Available at: <https://www.bsuh.nhs.uk/library/wp-content/uploads/sites/8/2023/10/Levosimendan-in-Critical-Care-ICU-2023.pdf>. Accessed 23 February 2024
- Injectable Medicines Guide Levosimendan monograph accessed 23th February 2024

Full version control record

Version:	3
Guidelines Lead(s):	Laura Johnson, Lead Critical Care Pharmacist, FPH Dr David Hunt, Consultant Anaesthetist and Intensivist
Contributor(s):	
Lead Director / Chief of Service:	Dr Sudodh Tote, CoS for Anaesthetics, Theatres and Critical Care
Library check completed:	19/03/2024
Ratified at:	Critical Care Clinical Governance, 25 April 2024
Date Issued:	1 May 2024
Review Date:	April 2027
Pharmaceutical dosing advice and formulary compliance checked by:	Laura Johnson / Katherine Lee
Key words:	levosimendan, critical care

This guideline has been registered with the Trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Caution is advised when using guidelines after the review date.

This guideline is for use in Frimley Health NHS Foundation Trust hospitals only. Any use outside this location will not be supported by the Trust and will be at the risk of the individual using it.

Version History

Version	Date	Guideline Lead(s)	Status	Comment
2	Jan 2018	David Hunt	Final	
3	Mar 2024	Laura Johnson	Final	Updated to remove 12.5mg in 500ml as per ICS standard concentration. Multiple changes in content.

Related Documents

None