Levosimendin is a calcium sensitiser used in the treatment of acute heart failure. It works by:

1. Sensitising cardiac muscle to calcium, stabilising troponin C in a conformation that triggers and maintains contraction in the presence of calcium ions. Because sensitisation is calcium concentration dependent, the contractile apparatus is sensitised in systole without impairing diastolic relaxation.
2. Opening ATP-sensitive K channels on vascular smooth muscle, causing arteriolar and venous dilatation.
3. Being a selective phosphodiesterase III inhibitor in vitro—probably only occurs in vivo at well above therapeutic range.

Clinical effects include:

1. Increasing cardiac output (typically by 0.4-0.8 L/min) by increasing heart rate and stroke volume.
2. Decreasing systemic vascular resistance and systolic blood pressure tends to decline.
3. Decreasing pulmonary capillary wedge pressure (typically by 4-6mmHg) and pulmonary artery pressure.
4. Decreasing coronary vascular resistance and increasing coronary blood flow.
5. Not increasing and may decrease myocardial oxygen consumption.

Pharmacokinetics:
- 85% oral bioavailability but short half-life requires administration by IV infusion.
- Highly protein bound.
- Extensively metabolised by conjugation with glutathione, with these metabolites eliminated in faeces and urine (half-life is approximately 1 hour).
- 5% of levosimendan is metabolised to the active metabolite OR-1896 with peak concentrations occurring 24-36 hours after a 24 hours infusion. This active metabolite has a half-life of approximately 80 hours and has similar properties to levosimendan.
- Intravenous infusion:
  - Loading dose of 12-24 micrograms/kg followed by 0.1-0.2 micrograms/kg/min for 24 hours adjusted for response and tolerability.

Indications:
- Left ventricular failure complicating acute myocardial infarction.
- Acute decompensated heart failure.
- Possible role in post resuscitation myocardial dysfunction.

Contraindications:
- Headache.
- Nausea.
- Vomiting.
- Hypotension.
- Cardiac arrhythmias.

Side effects:
- Headache.
- Nausea.
- Vomiting.
- Hypotension.
- Cardiac arrhythmias.

Pregnancy & lactation:
- Presumably safe in pregnancy.
- Safety in lactation unknown.

Molecular Pharmacology:
- Sensitises cardiac muscle to calcium.
- Stabilises troponin C in a conformation that triggers and maintains contraction in the presence of calcium ions.
- Because sensitisation is calcium concentration dependent, the contractile apparatus is sensitised in systole without impairing diastolic relaxation.
- Opens ATP-sensitive K channels on vascular smooth muscle, causing arteriolar and venous dilatation.
- Selective phosphodiesterase III inhibitor in vitro—probably only occurs in vivo at well above therapeutic range.

General:
- A calcium sensitiser used in the treatment of acute heart failure.