85% oral bioavailability but short half life requires administration by iv infusion highly protein bound - extensively metabolised by conjugation with glutathione a calcium sensitiser used in with these metabolites eliminated in faeces & urine (half life General Pharmacokinetics the treatment of acute heart failure is approximately 1 hour) - 5% of levosimendan is metabolised to the active metabolite OR-1896 with peak concentrations occuring 24-36 hrs after 1. sensitises cardiac muscle to calcium a 24 hours infusion. This active metabolite has a half life of - stabilises troponin C in a conformation that triggers approximately 80 hrs and has similar properties to levosimending & maintains contraction in the presence of calcium ions - because sensitisation is calcium concentration dependent the contractile apparatus is sensitised in systole without Molecular 1. left ventricular failure complicating acute myocardial infarction impairing diastolic relaxation Pharmacology 2. acute decompensated heart failure Indications 2. opens ATP-sensitive K channels on vascular smooth muscle: 3. possible role in post resuscitation myocardial dysfunction - causes arteriolar & venous dilatation 3. a selective phosphodiesterase III inhibitor in vitro intravenous infusion: - probably only occurs in vivo at well above therapeutic range levosimendia - loading dose of 12-24 micrograms/kg loading dose Dosage followed by 0.1-0.2 micrograms/kg/min for 24 hours adjusted for response and tolerability 1. increases cardiac output (typically by 0.4-0.8 L/min) by increasing heart rate and stroke volume 2. decreases systemic vascular resistance Contraindications and systolic blood pressure tends to decline Clinical 3. decreases pulmonary capillary wedge pressure (typically by 4-6mmHg) and pulmonary artery pressure effects 1. headache 4. decreases coronary vascular resistance 2. nausea and increases coronary blood flow 3. vomiting Side effects 4. hypotension 5. does not increase and may decrease myocardial 5. cardiac arrhythmias oxygen consumption Pregnancy & lactation