NEONATAL

SILDENAFIL

This document should be read in conjunction with this **DISCLAIMER**

Highly Restricted: Requires neonatologist approval before commencing

Presentation	Ampoule: 10mg/12.5mL (0.8mg/mL) Mixture: 2mg/mL (prepared in KEMH/PCH Pharmacy)
Classification	Selective phosphodiesterase type 5 (PDE5) inhibitor. PDE5 is found in the smooth muscle of the pulmonary vasculature, where it is responsible for the degradation of cyclic guanosine monophosphate (cGMP). Sildenafil increases cGMP within pulmonary vascular smooth muscle cells resulting in smooth muscle relaxation. In patients with pulmonary hypertension, this can lead to selective vasodilatation of the pulmonary vascular bed and, to a lesser degree, vasodilatation in the systemic circulation.
Indication	Sildenafil is a selective pulmonary vasodilator used to treat: Persistent Pulmonary Hypertension of the Neonate (PPHN) where • Refractory to inhaled nitric oxide (iNO) and other conventional therapies or; • Neonate persistently unable to be weaned off inhaled nitric oxide or; • Where inhaled nitric oxide and high frequency jet ventilation are not available or contraindicated. Chronic pulmonary hypertension secondary to respiratory, cardiac or chest wall disease. **Use in <37 weeks:** IV sildenafil is reserved for severe refractory Pulmonary hypertension. Potential risk (pulmonary haemorrhage) should be considered versus overall benefit of therapy.
Precautions	Sildenafil should not be used in patients; • with hereditary degenerative retinal disorders. Use with caution in patients; • receiving nitrates, • with hypotension (or concurrent use with alprostadil) • suspected or confirmed sepsis • with bleeding disorders Concomitant use of CYP 3A4 inhibitors – *see Interactions*

Dose	**<u>Pulmonary hypertension</u>** **IV Continuous Infusion:** **<u><37 Weeks Corrected Gestational Age</u>** **Loading:** 0.1 mg/kg (0.13mg/kg/hour) administered **over 45 minutes** **Maintenance:** 0.5 to 1.2mg/kg/day (0.021 to 0.05mg/kg/hour) as a **continuous infusion** for up to 7 days. **<u>≥ 37 Weeks Corrected Gestational Age</u>** **Loading:** 0.4 mg/kg (0.13mg/kg/hour) administered **over 3 hours** **Maintenance:** 1.6 mg/kg/day (0.067mg/kg/hour) as a **continuous infusion** for up to 7 days. **Oral:** Initially 0.25 – 0.5 mg/kg/dose every 4 to 8 hours, adjust according to response. **Maximum dose of 2mg/kg/dose 6 hourly.** Patients concurrently receiving other vasodilators (including nitric oxide) should start with a lower dose. May require adjustment in renal or hepatic impairment. Treatment should be weaned gradually to prevent withdrawal.
Monitoring	Oxygen saturation must be continuously monitored when commencing sildenafil as it can acutely increase oxygen requirements due to ventilation/perfusion (V/Q) mismatch. Monitor blood pressure twice daily or at least daily as ordered by medical staff Heart rate, left ventricular performance. Renal function and urine output. hepatic function. Consider monitoring with echocardiogram.
Compatible Fluids	Glucose 5% (preferred) or Sodium Chloride 0.9%
Preparation/ Administration	**<u>IV:</u>** **<37 Weeks Corrected Gestational Age** ***Dilution*** Dilute 0.62mg/kg (0.78mL/kg) of sildenafil solution and make to 15mL using compatible fluid. **Loading dose:** 3.2mL/hour (0.1mg/kg) for **45 minutes**

	Maintenance dose: 0.5 to 1.2mL/hour (0.021 to 0.05mg/kg/hour) *Continued over page* **>37 Weeks Corrected Gestational Age** ***Dilution*** Dilute 2mg/kg (2.5mL/kg) of sildenafil solution and make to 15mL using compatible fluid. **Loading dose:** 1mL/hour (0.4mg/kg) for **3 hours** **Maintenance dose:** 0.5mL/hour (0.067mg/kg/hour) **Oral:** Use suspension prepared by Pharmacy. May be given at any time with regard to feeds.
Adverse Reactions	**Common: hypotension,** flushing, dyspepsia, headache, dizziness, visual disturbances, nasal congestion, vomiting, rash. **Serious:** serious cardiovascular disorders (including arrhythmia and sudden cardiac death), raised intra-ocular pressure, swelling of the eyelids**.**
Storage	IV − unopened vials at room temperature (20−25°C). Oral suspension – Store below 30°C
Interactions	Sildenafil metabolism is principally mediated by the cytochrome P450 (CYP) isoforms 3A4 (major route) and 2C9 (minor route). Inhibitors of these isoenzymes may reduce sildenafil clearance and inducers of these isoenzymes may increase sildenafil clearance. Thus, erythromycin and fluconazole may increase concentrations of sildenafil by reducing hepatic clearance and rifampicin may decrease concentrations by inducing its hepatic metabolism. Avoid concomitant use of sildenafil with: Alprostadil (prostaglandin E1), other antihypertensives and vasodilators, as they may have their effects potentiated by sildenafil.
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