SILDENAFIL

Read in conjunction with Disclaimer

HIGH RISK Medication

Formulary: Highly Restricted
Requires neonatologist approval before commencing

Presentation	**Ampoule:** 10 mg/12.5 mL (0.8 mg/mL) **Oral Suspension:** 2 mg/mL (prepared in KEMH/PCH Pharmacy)
Drug Class	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.

Indications	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.

Special Considerations	**Use in less than 37 weeks:** IV sildenafil is reserved for severe refractory pulmonary hypertension. Potential risk (pulmonary haemorrhage) should be considered versus overall benefit of therapy. Sildenafil should not be used in patients; • with hereditary degenerative retinal disorders • severe hepatic impairment Use with caution in patients: • receiving nitrates ((e.g. glyceryl trinitrate, isosorbide mononitrate, sodium nitroprusside) • with hypotension (or concurrent use with alprostadil) • suspected or confirmed sepsis • with bleeding disorders Concomitant use of CYP 3A4 inhibitors – *see Interactions* Use extreme caution when titrating dosage and changing lines/fluids as sudden changes to rates can result in blood pressure fluctuations.

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.
Compatibility	**Fluids:** Glucose 5% (preferred), Sodium Chloride 0.9%. Refer to KEMH Neonatal Medication Guideline: Y-Site IV Compatibility in Neonates.
Interactions	Sildenafil metabolism is principally mediated by the CYP3A4 (major route) and CYP2C9 (minor route). • Erythromycin and fluconazole may increase concentrations of sildenafil by reducing hepatic clearance. • Rifampicin may decrease concentrations of sildenafil 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.
Side Effects	**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 & Stability	**Vial:** Store unopened vials at room temperature (20 to 25°C). Discard open vials after use. **Oral Suspension:** Store at room temperature (below 30°C).

ORAL

Presentation (for oral use)	**Oral Suspension**: 2 mg/mL (prepared in KEMH/PCH Pharmacy)
Dose	**Pulmonary hypertension** Initially 0.25 to 0.5 mg/kg/dose every 4 to 8 hours, adjusting according to response. **Maximum dose of 2 mg/kg/dose 6 hourly**. **Dose adjustment** • Patients concurrently receiving other vasodilators (including nitric oxide) should start with a lower dose. • Treatment should be weaned gradually to prevent withdrawal • Renal and/or hepatic impairment: adjustment may be required, limited data.
Administration	• Shake well before use. • Draw prescribed dose into oral/enteral syringe. • Can be given Oral/OGT/NGT. • May be given anytime in relation to feeds.

INTRAVENOUS INFUSION

Presentation (for IV use)

Vial: 10mg/12.5 mL (0.8 mg/mL)
Available from CIVAS (KEMH Only)

Dosage

Pulmonary hypertension

Intravenous Continuous Infusion

Less than 37 Weeks Corrected Gestational Age	
Loading	0.1 mg/kg (0.13 mg/kg/hour) administered **over 45 minutes** then reduce to maintenance infusion rate,
Maintenance	0.5 to 1.2 mg/kg/day (0.021 to 0.05 mg/kg/hour) as a **continuous infusion** for up to 7 days.

37 Weeks Corrected Gestational Age or greater	
Loading	0.4 mg/kg (0.13 mg/kg/hour) administered **over 3 hours** then reduce to maintenance infusion rate,
Maintenance	1.6 mg/kg/day (0.067 mg/kg/hour) as a **continuous infusion** for up to 7 days.

Dose adjustment

- Patients concurrently receiving other vasodilators (including nitric oxide) should start with a lower dose.
- Treatment should be weaned gradually to prevent withdrawal.
- Renal and/or hepatic impairment: adjustment may be required, limited data.

Preparation

Less than 37 Weeks CGA
Dilute 0.62 mg/kg (0.78 mL/kg) of sildenafil solution and make to 15 mL using compatible fluid.

37 Weeks CGA or greater
Dilute 2 mg/kg (2.5 mL/kg) of sildenafil solution and make to 15 mL using compatible fluid.

Administration

IV Continuous Infusion:
Infuse via syringe driver pump:

Less than 37 Weeks CGA

- **Loading dose:** 3.2 mL/hour (0.1 mg/kg) for **45 minutes**
- **Maintenance dose:** 0.5 to 1.2 mL/hour (0.021 to 0.05mg/kg/hour)

37 Weeks CGA or greater

- **Loading dose:** 1 mL/hour (0.4 mg/kg) for **3 hours**
- **Maintenance dose:** 0.5 mL/hour (0.067 mg/kg/hour)

Related Policies, Procedures, and Guidelines

CAHS Neonatology Guidelines:

Persistent Pulmonary Hypertension of the Newborn (PPHN)

Nitric Oxide Therapy (iNO)

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