

Alert	High risk medicine. Not to be used in patients taking organic nitrates of any form e.g. glyceryl trinitrate, isosorbide mononitrate, sodium nitroprusside.									
Indication	Persistent Pulmonary Hypertension of the Neonate (PPHN): <ul style="list-style-type: none"> - refractory to inhaled nitric oxide (iNO) and other conventional therapies or - those who are persistently unable to be weaned off inhaled nitric oxide or - in situations where inhaled nitric oxide and high frequency ventilation are not available Chronic pulmonary hypertension secondary to respiratory, cardiac or chest wall disease.									
Action	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). cGMP produces smooth muscle relaxation. Sildenafil increases cGMP within pulmonary vascular smooth muscle cells resulting in 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.									
Drug type	Phosphodiesterase type 5 (PDE5) inhibitor.									
Trade name	IV: Revatio Oral: Pharmacy prepared.									
Presentation	IV: Vial for injection containing 10 mg/12.5 mL = 0.8 mg/mL of sildenafil Oral: Pharmacy-prepared oral suspension									
Dose	IV^{1,2} Loading: 0.4 mg/kg administered over THREE (133.33 microgram/kg/hour for three hours) hours followed by: Maintenance: 1.6 mg/kg/day (67 microgram/kg/hour) as a continuous infusion for up to 7 days. ORAL³ Start at 0.5 to 1 mg/kg/dose 6 to 8 hourly. May titrate up to 2 mg/kg/dose according to response. (Refer to special comments)									
Dose adjustment	Therapeutic hypothermia - Limited data in neonates to suggest changes in the dosage. ECMO - Limited data in neonates to suggest changes in the dosage. Renal impairment - Limited data in neonates to suggest changes in the dosage. Hepatic impairment - Limited data in neonates to suggest changes in the dosage.									
Route	IV, Oral									
Preparation	IV load Draw up 5 mL (4000 microgram) of sildenafil and add 15 mL glucose 5% (preferred) or sodium chloride 0.9% to make a final volume of 20 mL with a concentration of 200 microgram/mL. Can also be administered undiluted (800 microgram/mL). IV infusion: Note: Refer to Appendix for tables to assist with concentration selection. Weight suggestions for infusion concentrations below are a guide only. Clinicians may choose infusion concentration different to the suggested based on expected dose and the corresponding 24-hour fluid volumes <table border="1" style="width: 100%; margin-top: 10px; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Infant weight</th> <th style="text-align: center;">< 1.5 kg</th> <th style="text-align: center;">≥ 1.5 kg</th> </tr> </thead> <tbody> <tr> <td style="text-align: left;">Suggested sildenafil concentration</td> <td style="text-align: center;">200 microgram/mL</td> <td style="text-align: center;">800 microgram/mL</td> </tr> <tr> <td style="text-align: left;">67 microgram/kg/hour is equal to</td> <td style="text-align: center;">0.335 mL/kg/hour</td> <td style="text-align: center;">0.084 mL/kg/hour</td> </tr> </tbody> </table>	Infant weight	< 1.5 kg	≥ 1.5 kg	Suggested sildenafil concentration	200 microgram/mL	800 microgram/mL	67 microgram/kg/hour is equal to	0.335 mL/kg/hour	0.084 mL/kg/hour
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	<p>20mL Syringe</p> <p>Draw up sildenafil and add compatible fluid* as per table below to make a final volume of 20 mL</p> <table border="1"> <thead> <tr> <th>Sildenafil concentration</th> <th>200 microgram/mL</th> <th>800 microgram/mL</th> </tr> </thead> <tbody> <tr> <td>Volume of sildenafil (0.8 mg/mL)</td> <td>5 mL (4 mg)</td> <td>20 mL (16 mg)</td> </tr> <tr> <td>Volume of compatible fluid*</td> <td>15 mL</td> <td>Nil</td> </tr> <tr> <td>Total volume</td> <td>20 mL</td> <td>20 mL</td> </tr> </tbody> </table> <p>* Compatible fluid: glucose 5% (preferred) or sodium chloride 0.9%</p> <p>50mL Syringe</p> <p>Draw up sildenafil and add compatible fluid* as per table below to make a final volume of 50 mL</p> <table border="1"> <thead> <tr> <th>Sildenafil concentration</th> <th>200 microgram/mL</th> <th>800 microgram/mL</th> </tr> </thead> <tbody> <tr> <td>Volume of sildenafil (0.8 mg/mL)</td> <td>12.5 mL (10 mg)</td> <td>50 mL (40 mg)</td> </tr> <tr> <td>Volume of compatible fluid*</td> <td>37.5 mL</td> <td>Nil</td> </tr> <tr> <td>Total volume</td> <td>50 mL</td> <td>50 mL</td> </tr> </tbody> </table> <p>* Compatible fluid: glucose 5% (preferred) or sodium chloride 0.9%.</p>	Sildenafil concentration	200 microgram/mL	800 microgram/mL	Volume of sildenafil (0.8 mg/mL)	5 mL (4 mg)	20 mL (16 mg)	Volume of compatible fluid*	15 mL	Nil	Total volume	20 mL	20 mL	Sildenafil concentration	200 microgram/mL	800 microgram/mL	Volume of sildenafil (0.8 mg/mL)	12.5 mL (10 mg)	50 mL (40 mg)	Volume of compatible fluid*	37.5 mL	Nil	Total volume	50 mL	50 mL
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Administration	<p>IV infusion:</p> <p>Infuse loading dose over 3 hours (loading dose of 0.4 mg/kg) followed by maintenance dose.</p> <p>Oral:</p> <p>Shake well before drawing up the dose. Give via intragastric tube, preferably with feed to minimise risk of gastrointestinal irritation. If baby is not on enteral feeds or breast milk is not available, give dose via intragastric tube and flush with 0.5 mL water for injections.</p>																								
Monitoring	<p>Heart rate, blood pressure and oxygenation.</p> <p>Renal and hepatic function.</p> <p>Consider monitoring with echocardiogram.</p>																								
Contraindications	<p>Hypersensitivity to sildenafil</p> <p>Not to be used in patients taking organic nitrates of any form e.g. glyceryl trinitrate, isosorbide mononitrate, sodium nitroprusside.</p> <p>Concurrent use with potent CYP3A4 inhibitors (e.g., macrolides including erythromycin, clarithromycin; ketoconazole, itraconazole, ritonavir) is generally not recommended as they decrease the clearance and increase the potency of sildenafil.</p> <p>Pulmonary hypertension secondary to sickle cell anaemia.</p> <p>Severe hepatic impairment</p>																								
Precautions	<p>Use with caution in neonates with sepsis or uncontrolled hypotension.</p> <p>Sildenafil clearance (in adults) is reduced in hepatic and severe renal impairment.</p>																								
Drug interactions	<p>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.</p> <p>Avoid concomitant use of sildenafil with: Alprostadil (prostaglandin E1), other antihypertensive and vasodilators, as they may have their effects potentiated by sildenafil.</p>																								
Adverse reactions	<p>Most concerning short-term adverse effects: Worsening oxygenation and systemic hypotension. Epistaxis, respiratory symptoms (cough and nasal congestion), diarrhoea and vomiting, gastroesophageal reflux and abdominal pain, headaches, tremors, erections, facial flushing, dizziness, irritability and (rarely) fever, skin disorders, pain in limbs and oedema have been reported in children on sildenafil. The Sildenafil in Treatment-Naïve Children, Aged 1-17 Years, With Pulmonary Arterial Hypertension long-term extension (STARTS-2) trial showed worse survival in children receiving high doses of sildenafil as monotherapy.⁴ A recent study conducted by Roldan and colleagues, found there was a statistically significant increase in adverse drug reaction (ADR) frequency in children receiving higher-than-recommended doses. However, it was not associated with a lower survival rate.⁵ Sildenafil has the potential to adversely affect vision.⁶ Impaired liver function tests.</p>																								

Sildenafil

Newborn use only

2025

	May increase the risk of severe retinopathy of prematurity if used in extremely preterm neonates.
Overdose	AUSTRALIA: Contact the Poisons Information Centre on 13 11 26 for management. NEW ZEALAND: Contact the National Poisons Centre on 0800 764 766 for management.
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9%. PN at Y-site: Lipid Emulsion (Fat Emulsion - Fish Oil and Plant Based) Y-site: alprostadil, amphotericin B (Liposomal), cefOTAXIME, ciPROFLOXAcin, clonidine hydrochloride, dexMEDETOMIDine hydrochloride, dobutamine hydrochloride, dopamine hydrochloride, fentanyl citrate, flucONAZOLe, gentamicin sulfate, insulin regular, levetiracetam, linEZOLID, metronidazole, midazolam hydrochloride, milrinone lactate, morphine hydrochloride, morphine sulfate, noradrenaline bitartrate (norepinephrine bitartrate), paracetamol, penicillin G sodium, piperacillin sodium-tazobactam sodium, vancomycin hydrochloride, vecuronium bromide
Incompatibility	Fluids: No information PN at Y-site: TPN (2-in-1) Total Parenteral Nutrition Admixture Y-site: flucLOXACILLIN sodium, furosemide, ibuprofen, meropenem, sodium bicarbonate Variable at Y-site: aciclovir, amoxicillin sodium, ampicillin sodium, calcium gluconate, heparin sodium, hydrocortisone sodium succinate, ibuprofen lysine, indometacin (indomethacin) sodium, phenobarbital (phenobarbitone) sodium No data – where possible administer via dedicated line.
Stability	IV – infusion should be changed every 24 hours. Oral suspension – as per pharmacy advice.
Storage	IV – unopened vials at room temperature (20–25°C). Oral suspension – as per pharmacy advice
Excipients	Solution for injection - Glucose monohydrate, water for injections. Oral Suspension – contact local pharmacy
Special comments	Use of 3 mg/kg/dose 6 hourly for short duration (4-5 days) has been reported in resource limited settings, but the safety data are limited. ⁷ In paediatric patients with pulmonary arterial hypertension, an increased mortality risk was associated with long-term (> 2 year) use. The mortality risk of long-term use in neonates is unknown.
Evidence	Efficacy <u>Neonates with pulmonary hypertension</u> Shah et al performed a systematic review on sildenafil compared with placebo or other pulmonary vasodilators, irrespective of dose, route and duration of administration, in neonates with PPHN. ⁸ Three eligible trials that enrolled 77 infants were identified. The methodological quality of the studies indicated low-moderate risk of bias. All studies were performed in resource-limited settings where iNO and high frequency ventilation were not available at the time of study. There was a significant reduction in mortality in the sildenafil group (typical RR 0.20, 95% CI 0.07 to 0.57; typical RD -0.38, 95% CI -0.60 to -0.16; Number needed to treat to benefit 3, 95% CI 2 to 6). Physiological parameters of oxygenation (oxygenation index, PaO ₂) suggested a steady improvement after the first dose of sildenafil. No clinically important side effects were identified. Sildenafil in the treatment of PPHN has significant potential especially in resource limited settings (LOEI, GOR B). Furthermore, combined use of oral sildenafil with milrinone was superior to monotherapy with either drug in reducing estimated pulmonary pressure and oxygenation index in neonates with severe pulmonary hypertension in resource limited setting. ⁹ Interestingly, systolic and diastolic blood pressure were not different pre and post treatment. Updated systematic review by He et al involving 216 neonates showed significant improvement in the pulmonary artery pressure and oxygenation. ¹⁰ The European Paediatric Pulmonary Vascular Disease Network's consensus statement 2016: Oral sildenafil should be considered for treatment of PPHN and PH in BPD, especially if iNO is not available (LOE IIa GOR B). Intravenous sildenafil may be considered for treatment of PH, including PPHN, in critically ill patients, especially in those with an unsatisfactory response to iNO (LOE IIb GOR B). ^{11, 12} However, in one RCT, addition of intravenous sildenafil to 29 neonates with PPHN who had OI > 15 despite 10-20 PPM inhaled nitric oxide did not yield any benefits when compared to placebo. Moreover, addition of sildenafil was associated with hypotension, hypokalaemia, anaemia and was withdrawn in 15-25% neonates. ¹³ <u>Pulmonary hypertension secondary to congenital diaphragmatic hernia</u> Small retrospective reviews, report acute improvement in oxygenation in neonates with congenital diaphragmatic hernia who received sildenafil before surgery. ^{14,15}

Paediatric pulmonary hypertension

STARTS-1 trial performed by Barst et al studied the effectiveness of oral sildenafil in children with pulmonary arterial hypertension.¹⁶ 238 children with a weight ≥ 8 kg were randomised to low-, medium-, or high-dose sildenafil or placebo orally 3 times daily for 16 weeks. The primary comparison was percent change from baseline in peak oxygen consumption for the 3 sildenafil doses combined versus placebo. Percent change in $PV' O_2$ for the 3 sildenafil doses combined was only marginally significant; however, $PV' O_2$, functional class and haemodynamic improvements with medium and high doses suggest efficacy with these doses.

STARTS-2 was the extension of the STARTS-1 trial.⁴ In STARTS-2, sildenafil-treated patients continued STARTS-1 dosing; placebo-treated patients were randomised to 1 of the 3 sildenafil dose groups. Patients requiring additional pulmonary arterial hypertension-specific therapy discontinued study treatment; survival follow-up was attempted. Hazard ratios for mortality were 3.95 (95% confidence interval, 1.46–10.65) for high versus low and 1.92 (95% confidence interval, 0.65–5.65) for medium versus low dose; however, multiple analyses raised uncertainty about the survival/dose relationship. In summary, although children randomised to higher dose compared with lower sildenafil doses had an unexplained increased mortality, all sildenafil dose groups displayed favourable survival for children with pulmonary arterial hypertension. Combined with STARTS-1 data, the overall profile favoured the medium dose.

Preterm infants at risk of BPD

Konig et al performed an RCT in preterm infants, < 28 weeks gestational age, if they were mechanically ventilated on day 7 of life.¹⁷ Infants were randomised to a 4-week course of either oral sildenafil (3 mg/kg/day) or placebo solution. Twenty infants were randomised, 10 received sildenafil and 10 received placebo. Sildenafil did not reduce length of invasive (median 688 versus 227 h) or non-invasive ventilation (median 1609 versus 1416 h). More infants in the sildenafil group required postnatal steroid treatment. One infant developed hypotension following sildenafil administration and was excluded after three doses. Conclusion: Sildenafil as an early treatment for preterm infants at risk of BPD is not beneficial.

Cohen et al retrospectively reviewed effect of sildenafil in 135 children with pulmonary hypertension associated with BPD. The mean age of commencement of oral sildenafil was 4 months and the children were followed up until 2 years (mean) of age. In 45%, the PH resolved, and sildenafil was discontinued while 7% died due to pulmonary hypertension directly.¹⁸

Prevention of rebound pulmonary HTN after weaning iNO

Namachivayam et al performed an RCT in 30 ventilated infants and children from varying respiratory conditions including BPD (average age 0.4 y) and receiving 10 ppm iNO.¹⁹ They were randomised to either 0.4 mg/kg as a single oral dose of sildenafil or placebo 1 h before discontinuing iNO. Rebound occurred in 10/14 of the placebo group and 0 out of 15 in the sildenafil group. Four placebo patients couldn't be weaned off iNO, whereas all in the sildenafil group were successfully weaned ($p = 0.042$). A single oral dose of sildenafil may be considered for this particular scenario (LOE II, GOR C).

Pre-op oral sildenafil for children with CHD prior to cardiopulmonary bypass

Vassalos et al, in a randomised trial, compared the effects of oral sildenafil (0.5 mg/kg) and placebo, administered the day before cardiac surgery, in 24 children.²⁰ Postoperatively, mean pulmonary vascular resistance and oxygenation index remained unchanged, whilst oxygen delivery and bi-ventricular systolic function were significantly reduced in the sildenafil group. In this trial, pre-operative sildenafil did not affect postoperative pulmonary vascular resistance. There was, however, a negative impact on ventricular function and oxygenation. Therefore, sildenafil is not recommended for this particular indication.

Post-op sildenafil in infants after cardiac surgery

Stocker et al performed an RCT in 16 ventilated infants early after closure of ventricular or atrioventricular septal defects.²¹ They were randomly assigned to one of two groups. Seven infants received iNO (20 ppm) first, with the addition of intravenous sildenafil (0.35 mg/kg over 20 min) after 20 min. Eight infants received sildenafil first, iNO was added after 20 min. Intravenous sildenafil augmented the pulmonary vasodilator effects of iNO in infants early after cardiac surgery. However, sildenafil produced systemic hypotension and impaired oxygenation, which was not improved by iNO. Sildenafil is not recommended for this particular indication.

The European Paediatric Pulmonary Vascular Disease Network Consensus 2016: Beneficial haemodynamic effects of sildenafil have also been demonstrated in failing Fontan circulations.²² Sildenafil improved max. oxygen consumption (VO_2 max.) and pulmonary blood flow in patients with

	<p>Fontan circulation. Another randomised, crossover study showed that sildenafil therapy improved exercise tolerance and ventilatory efficiency in Fontan patients.</p> <p>Pharmacokinetics</p> <p>Steinhorn et al performed a multicentre, open-label, dose-escalation, pilot, pharmacokinetics study of 36 near-term and term neonates with echo-confirmed idiopathic PHN or secondary PHN with MAS, RDS, sepsis or pneumonia and OI ≥ 15.¹ The study included 8 sequential “step-up” dosing groups. Most infants received a loading dose of sildenafil to bring the plasma concentration of sildenafil to a target, followed by a maintenance infusion for the remainder of the study. The duration of IV sildenafil was for at least 48 hours and up to 7 days. They found sildenafil to be well tolerated, particularly with a dosing regimen comprising a loading dose of 0.4 mg/kg delivered over 3 hours, followed by a maintenance infusion at 1.6 mg/kg/day. In 23 neonates with congenital diaphragmatic hernia and pulmonary hypertension, Cochius-den et al found appropriate sildenafil plasma levels with the above dosage.² In an open-label trial by Mukherjee et al, 36 term neonates with PPHN or hypoxemia were administered IV sildenafil for up to 7 days starting within 72 h of birth. Sildenafil clearance increased threefold from the first day after birth to values similar to those in adults by the first week. Volume of distribution of sildenafil in neonates was fourfold higher than in adults, resulting in a longer terminal half-life in neonates (48-56 h) compared to adults.²⁴</p> <p>Sildenafil and retinopathy of prematurity</p> <p>Sildenafil is 10 x more selective for PDE5 as compared to PDE6. PDE6 is found in the retina. If used in extremely preterm neonates, sildenafil may increase the risk of severe retinopathy of prematurity. A retrospective, case-controlled study (n = 68) in neonates born before 30 weeks gestation showed sildenafil use did not increase the risk of retinopathy of prematurity.²³</p>
<p>References</p>	<ol style="list-style-type: none"> Steinhorn RH, Kinsella JP, Pierce C, et al. Intravenous sildenafil in the treatment of neonates with persistent pulmonary hypertension. <i>J Pediatr</i> 2009 Dec; 155(6):841-847. Cochius-den, Kipfmüller F, Allegaert K, et al. Pharmacokinetic modelling of intravenous sildenafil in newborns with congenital diaphragmatic hernia. <i>Eur J Clin Pharmacol</i>. 2020 Feb; 76(2):219-227. Huddleston AJ, Knoderer CA, Morris JL, Ebenroth ES. Sildenafil for the treatment of pulmonary hypertension in pediatric patients. <i>Pediatr Cardiol</i>. 2009 Oct; 30(7):871-82. Barst RJ, Beghetti M, Pulido T, et al. STARTS-2: long-term survival with oral sildenafil monotherapy in treatment-naïve pediatric pulmonary arterial hypertension. <i>Circulation</i> 2014; 129(19):1914-23. Roldan T, Deiros L, Romero JA, et al. Safety and tolerability of targeted therapies for pulmonary hypertension in children. <i>Pediatric cardiology</i>. 2014 Mar 1; 35(3):490-8. Dhariwal AK, Bavdekar SB. Sildenafil in pediatric pulmonary arterial hypertension. <i>J Postgrad Med</i>. 2015 Jul-Sep; 61(3):181-92. Vargas-Origel A, Gomez-Rodriguez G, Aldana-Valenzuela C, et al: The use of sildenafil in persistent pulmonary hypertension of the newborn. <i>Am J Perinatol</i> 2010; 27(3):225-230 Shah PS, Ohlsson A. Sildenafil for pulmonary hypertension in neonates. <i>Cochrane Database Syst Rev</i>. 2011 Aug 10 ; (8):CD005494. El-Ghandour M, Hammad B, Ghanem M, Antonios MAM. Efficacy of Milrinone Plus Sildenafil in the Treatment of Neonates with Persistent Pulmonary Hypertension in Resource-Limited Settings: Results of a Randomized, Double-Blind Trial. <i>Paediatr Drugs</i>. 2020 Dec; 22(6):685-693. He Z, Zhu S, Zhou K, et al. Sildenafil for pulmonary hypertension in neonates: An updated systematic review and meta-analysis. <i>Pediatr Pulmonol</i>. 2021 May 13. Hansmann G, Apitz C. Treatment of children with pulmonary hypertension. Expert consensus statement on the diagnosis and treatment of paediatric pulmonary hypertension. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK. <i>Heart</i> 2016; 102 Suppl 2:ii67-85. Hilgendorff A, Apitz C, Bonnet D, Hansmann G. Pulmonary hypertension associated with acute or chronic lung diseases in the preterm and term neonate and infant. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK. <i>Heart</i> 2016; 102 Suppl2 49-56. Pierce CM, Zhang MH, Steinhorn RH et al. Efficacy and Safety of IV Sildenafil in the Treatment of Newborn Infants With, or at Risk of Persistent Pulmonary Hypertension of the Newborn (PPHN): A Multicenter, Randomized, Placebo-Controlled Trial. <i>J Pediatr</i>. 2021 May 27:S0022-3476 Kipfmüller F, Schroeder L, Berg C, et al. Continuous intravenous sildenafil as an early treatment in neonates with congenital diaphragmatic hernia. <i>Pediatr Pulmonol</i>. 2018 Apr; 53(4):452-460.

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Appendix

Infusion tables to assist concentration selection

Table 1: Infusion rates when using sildenafil concentration **200 microgram/mL** (suggested for weight <1.5 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	40	80	120	160	200	240	280	320	360	400
1	20	40	60	80	100	120	140	160	180	200
1.5	13	27	40	53	67	80	93	107	120	133
2	10	20	30	40	50	60	70	80	90	100
2.5	8	16	24	32	40	48	56	64	72	80
3	7	13	20	27	33	40	47	53	60	67
3.5	6	11	17	23	29	34	40	46	51	57
4	5	10	15	20	25	30	35	40	45	50
4.5	4	9	13	18	22	27	31	36	40	44
5	4	8	12	16	20	24	28	32	36	40

Table 2: Infusion rates when using sildenafil concentration **800 microgram/mL**
(suggested for weight ≥ 1.5 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	160	320	480	640	800	960	1120	1280	1440	1600
1	80	160	240	320	400	480	560	640	720	800
1.5	53	107	160	213	267	320	373	427	480	533
2	40	80	120	160	200	240	280	320	360	400
2.5	32	64	96	128	160	192	224	256	288	320
3	27	53	80	107	133	160	187	213	240	267
3.5	23	46	69	91	114	137	160	183	206	229
4	20	40	60	80	100	120	140	160	180	200
4.5	18	36	53	71	89	107	124	142	160	178
5	16	32	48	64	80	96	112	128	144	160

$$\text{Dose (microgram/kg/hour)} = \frac{\text{Rate (mL/hr)} \times \text{Concentration (microgram/mL)}}{\text{Weight (kg)}}$$

$$\text{Rate (mL/hr)} = \frac{\text{Dose (microgram/kg/hour)} \times \text{Weight (kg)}}{\text{Concentration (microgram/mL)}}$$

VERSION/NUMBER	DATE
Original 1.0	16/10/2016
Version 1.1	20/02/2017
Version 2.0	29/07/2021
Version 2.1	12/02/2025
Version 2.2	5/12/2025
Version 3.0	5/03/2026
Current 3.1	16/04/2026
REVIEW	5/03/2031

This standard concentration formulary has been developed by the ANMF standard concentration working group. The working group (in alphabetical order): Mohammad Irfan Azeem, Susannah Brew, Cindy Chen, Michelle Jenkins, Kerrie Knox, Rebecca O'Grady

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