

# Vitamin A

## Newborn use only

2022

<b>Alert</b>	Vitamin A is expressed as microgram retinol activity equivalents (RAE) or international units (IU) or units. <b>1 microgram RAE = 1 microgram retinol = 3.3 units of retinol.</b> <sup>(1)</sup> Pentavite Infant, a commonly used multi-vitamin supplement in Australia, contains 390 microgram RAE or 1287 units of retinol. Vitamin A for chronic lung disease is beyond the scope of this formulary. Refer to evidence summary.
<b>Indication</b>	Prevention of vitamin A deficiency Neonatal cholestasis Cystic fibrosis
<b>Action</b>	Fat soluble vitamin required for vision, growth and bone development, immune function and maintenance of epithelial cells particularly in the retina and respiratory tract tissues.
<b>Drug type</b>	Fat soluble vitamin
<b>Trade name</b>	Biological Therapies Vitamin A oral solution, Kirkman Mycelized Vitamin A drops
<b>Presentation</b>	Biological Therapies Vitamin A oral solution (50 mL bottle): contains 2500 units vitamin A/0.1 mL Kirkman Mycelized Vitamin A drops (30mL): contains 5025 units vitamin A/0.05mL (0.05mL = 1 drop)
<b>Dose</b>	<p><b>Suggested starting dose</b></p> <p><b>Prophylaxis in preterm infants &lt;1800 g birthweight</b></p> <p>2500 units 24 hourly or 5000 units 48 hourly (Range: 1320-3300 units/kg/day) (Example: Biological Therapies Vitamin A 0.1 mL 24 hourly or Kirkman Mycelized Vitamin A 0.05 mL 48 hourly)</p> <p><b>Neonatal cholestasis: Refer to vitamins in cholestasis formulary</b></p> <p><b>Supplementation for cystic fibrosis<sup>8</sup></b></p> <p>2500 units 24 hourly or 5000 units 48 hourly (Example: Biological Therapies Vitamin A 0.1 mL 24 hourly or Kirkman Mycelized Vitamin A 0.05 mL 48 hourly)</p>
<b>Dose adjustment</b>	Therapeutic hypothermia – No information. ECMO – Not applicable. Renal impairment - No information. Hepatic impairment – No information.
<b>Maximum dose</b>	
<b>Total cumulative dose</b>	
<b>Route</b>	Oral
<b>Preparation</b>	No preparation is required
<b>Administration</b>	Oral: Shake the bottle well before use. Administer undiluted with a feed.
<b>Monitoring</b>	An 'adequate' concentration of plasma vitamin A in VLBW infants is not known. Concentrations below 0.70 µmol/L have been considered deficient in premature infants and concentrations below 0.35 µmol/L indicate severe deficiency and depleted liver stores. <sup>(4)</sup>
<b>Contraindications</b>	Hypersensitivity to vitamin A or any component of the formulation, hypervitaminosis A
<b>Precautions</b>	
<b>Drug interactions</b>	May increase effects of anticoagulant and antiplatelet agents
<b>Adverse reactions</b>	Hypervitaminosis A: Irritability, lethargy, vomiting, bulging fontanelle.
<b>Compatibility</b>	Not applicable
<b>Incompatibility</b>	Not applicable
<b>Stability</b>	
<b>Storage</b>	Protect from light
<b>Excipients</b>	Biological Therapies Vitamin A oral solution: Citric acid monohydrate, dl-alpha-tocopherol (vitamin E), glycerol, Polyethylene glycol-35, castor oil, purified water, sodium benzoate. Avoid exposure to sodium benzoate of >99 mg/kg/day in neonates.

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	Kirkman Mycelized Vitamin A drops – Purified water, castor bean oil, glycerine, citric acid, vitamin E (<1%), potassium sorbate.
Special comments	
Evidence	<p><b>Efficacy</b></p> <p><b><u>Preterm infants &lt;1800 g</u></b></p> <p>Recommended enteral intake in preterm infants &lt;1800 g birthweight (ESPGHAN 2022): 1320-3300 units/kg/day.<sup>(4)</sup> Recommended parenteral intake (ESPGHAN 2018): Preterm neonates – 227-455 microgram/kg/day (700-1500 units/kg/day); Term neonates – 150-300 micrograms/kg/day (495-990 units/kg/day). Alternatively 2300 units (697 micrograms)/day.<sup>(5)</sup></p> <p><b><u>Chronic liver disease</u></b></p> <p>Supplementation with 5000–10,000 IU/day may be needed in children with chronic liver disease.<sup>(2)</sup> The dose in neonates is unclear. It is important to monitor levels in children receiving supplementation, as hypervitaminosis A can lead to potentially fatal hepatotoxicity.<sup>(2)</sup></p> <p><b><u>Prevention of chronic lung disease and neurodevelopmental impairment</u></b></p> <p>Cochrane review by Darlow et al 2016<sup>(3)</sup> evaluated vitamin A supplementation on the incidence of death or chronic lung disease and long-term neurodevelopmental disability in very low birth weight (VLBW) infants compared with a control (placebo or no supplementation). Eleven randomised clinical trials (RCTs) were analysed that included over 1500 VLBW infants, defined as birth weight ≤ 1500 grams or less than 32 weeks' gestation. All except one RCT in this review used <b>intramuscular</b> vitamin A as an intervention. Doses varied among the studies. One of the dosing regimens used in RCT by Tyson et al. was IM vitamin A 5,000 units/dose 3 times weekly initiated within the first 96 hours of life and continued for 4 weeks.<sup>(3,7)</sup> Meta-analysis<sup>(3)</sup> found that vitamin A was associated with a small benefit in reducing death or oxygen use at one month of age and a marginal reduction in oxygen use at 36 weeks' postmenstrual age. However, neurodevelopmental assessment in the largest trial showed no difference at 18 to 22 months corrected age. No adverse effects of vitamin A supplementation were reported, but it was noted that intramuscular injections of vitamin A were painful.</p> <p>ANMF consensus: Clinicians need to balance the clinical benefits against painful intramuscular injections and the decision may depend upon the local incidence of the outcomes. It is not a standard practice in Australia to administer intramuscular vitamin A for prevention of chronic lung disease.</p> <p><b><u>Supplementation in cystic fibrosis</u></b></p> <p>The US Cystic Fibrosis Foundation (CFF) recommends daily supplementation of 1500 IU of vitamin A, 400–500 IU of vitamin D, and 40–50 IU of vitamin E for infants with CF. These dosages increase to 5000 IU of vitamin A, 800–1000 IU of vitamin D, and 80–150 IU of vitamin E for children 1–10 years of age.<sup>(8–10)</sup> A multicenter prospective longitudinal study known as FIRST determined the prevalence of suboptimal vitamins A, D, and E status in infants supplemented with CF foundation recommended vitamin dosages. The prevalence of vitamin A, D and E insufficiency were 3%, 22% and 5% on these dosages. The study found normalisation of serum retinol and α-tocopherol in almost all infants by age 3 years.<sup>(11)</sup></p> <p>ANMF consensus: Bio-Logical Vitamin A oral solution at a dose of 0.1 mL (2500 units/day) is recommended for ease of administration and to prevent any potential insufficiency in accordance with the US Cystic Fibrosis Foundation's recommended dosage.</p>
Practice points	<p>Recommendations for daily supplementation of vitamin A:</p> <p>Recommended enteral intake in preterm infants &lt;1800 g birthweight (ESPGHAN 2010): 400-1000 microgram/kg/day (1320-3300 units/kg/day).<sup>(4)</sup></p> <p>Recommended parenteral intake (ESPGHAN 2018): Preterm neonates – 227-455 microgram/kg/day (700-1500 units/kg/day); Term neonates – 150-300 micrograms/kg/day (495-990 units/kg/day). Alternatively 2300 units (697 micrograms)/day.<sup>(5)</sup></p> <p>Preterm human milk contains 50-400 units of vitamin A/dL. Term human milk contains 60-200 units/dL.<sup>(6)</sup></p> <p>Evaluate vitamin A intake from other sources prior to prescribing e.g. feeds and other concomitant medications or supplements.</p>
References	<ol style="list-style-type: none"> <li>1. <a href="https://dietarysupplementdatabase.usda.nih.gov/Conversions.php">https://dietarysupplementdatabase.usda.nih.gov/Conversions.php</a>. Accessed on 17 November 2021.</li> <li>2. Yang CH, Perumpail BJ, Yoo ER, Ahmed A, Kerner Jr. JA. Nutritional Needs and Support for Children with Chronic Liver Disease. <i>Nutrients</i>. 2017;9(10):1127.</li> </ol>

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