Vitamin A
Newborn use only

2022

Alert	Vitamin A is expressed as microgram retinol activity equivalents (RAE) or international units (IU) or units. **1 microgram RAE = 1 microgram retinol = 3.3 units of retinol.**[1] 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.
Indication	Prevention of vitamin A deficiency Cholestatic liver disease Cystic fibrosis
Action	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.
Drug type	Fat soluble vitamin
Trade name	Bio-Logical Vitamin A oral solution
Presentation	Bio-Logical Vitamin A oral solution (50 mL bottle): Contains retinol palmitate 1.375 mg per 0.1 mL (750 microgram RAE or 2500 units vitamin A/0.1 mL)
Dose	**Suggested starting dose** **Prophylaxis in preterm infants <1800 g birthweight:** Bio-Logical Vitamin A oral solution: 0.1 mL/day (2500 units/day) Range: 1320-3300 units/kg/day **Supplementation for cholestatic liver disease*** Bio-Logical Vitamin A oral solution: 0.1 mL/day (2500 units/day) *Please refer to Vitamins in cholestasis formulary[2] (ANMF consensus) **Supplementation for cystic fibrosis*** Bio-Logical Vitamin A oral solution: 0.1 mL/day (2500 units/day)[8-11] (ANMF consensus) *Pentavite 0.45 mL twice daily provides 2574 units/day.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – Not applicable. Renal impairment - No information. Hepatic impairment – No information.
Maximum dose	
Total cumulative dose	
Route	Oral
Preparation	No preparation is required
Administration	Oral: Administer undiluted with a feed
Monitoring	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.[4]
Contraindications	Hypersensitivity to vitamin A or any component of the formulation, hypervitaminosis A
Precautions	
Drug interactions	May increase effects of anticoagulant and antiplatelet agents
Adverse reactions	Hypervitaminosis A: Irritability, lethargy, vomiting, bulging fontanelle.
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	
Storage	Protect from light
Excipients	Sodium benzoate. Avoid exposure to sodium benzoate of >99 mg/kg/day in neonates.
Special comments	

Evidence	**Efficacy** **<u>Preterm infants <1800 g</u>** Recommended enteral intake in preterm infants <1800 g birthweight (ESPGHAN 2010): 400-1000 microgram/kg/day (1320-3300 units/kg/day).[4] 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.[5] **<u>Chronic liver disease</u>** Supplementation with 5000–10,000 IU/day may be needed in children with chronic liver disease.[2] 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.[2] **<u>Prevention of chronic lung disease and neurodevelopmental impairment</u>** Cochrane review by Darlow et al 2016[3] 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 **intramuscular** 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.[3,7] Meta-analysis[3] 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. 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. **<u>Supplementation in cystic fibrosis</u>** 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.[8-10] 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.[11] 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.
Practice points	Recommendations for daily supplementation of vitamin A: Recommended enteral intake in preterm infants <1800 g birthweight (ESPGHAN 2010): 400-1000 microgram/kg/day (1320-3300 units/kg/day).[4] 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.[5] Preterm human milk contains 50-400 units of vitamin A/dL. Term human milk contains 60-200 units/dL.[6] Evaluate vitamin A intake from other sources prior to prescribing e.g. feeds and other concomitant medications or supplements.
References	1. https://dietarysupplementdatabase.usda.nih.gov/Conversions.php. Accessed on 17 November 2021. 2. Yang CH, Perumpail BJ, Yoo ER, Ahmed A, Kerner Jr. JA. Nutritional Needs and Support for Children with Chronic Liver Disease. Nutrients. 2017;9(10):1127. 3. Darlow BA GP, Rojas-Reyes MX. Vitamin A supplementation to prevent mortality and short- and long-term morbidity in very low birth weight infants. Cochrane Database of Systematic Reviews 2016, Issue 8. Art. No.: CD000501.

4. Agostoni C, Buonocore G, Carnielli V, De Curtis M, Darmaun D, Decsi T, et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. Journal of pediatric gastroenterology and nutrition. 2010;50(1):85-91.
5. Bronsky J, Campoy C, Braegger C, Braegger C, Bronsky J, Cai W, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. Clinical Nutrition. 2018;37(6):2366-78.
6. Greer Frank R. Vitamins A, E and K. In Nutrition of the preterm infant. Scientific basis and practical guidelines. Second edition. Eds Tsang RC, Uauy R, Koletzko B, Zlotkin SH. . 2005:141-72.
7. Tyson JE, Wright LL, Oh W, Kennedy KA, Mele L, Ehrenkranz RA, et al. Vitamin A supplementation for extremely-low-birth-weight infants. New England Journal of Medicine. 1999;340(25):1962-8.
8. Borowitz D, Robinson KA, Rosenfeld M, et al. Cystic fibrosis foundation evidence-based guidelines for management of infants with cystic fibrosis. J Pediatr. 2009;155(6 Suppl):S73-S93.
9. Tangpricha V, Kelly A, Stephenson A, et al. Cystic Fibrosis Foundation. Vitamin D Evidence-Based Review Committee. An update on the screening, diagnosis, management, and treatment of vitamin D deficiency in individuals with cystic fibrosis: evidence-based recommendations from the Cystic Fibrosis Foundation. J Clin Endocrinol Metab. 2012;97(4):1082-1093.
10. Lahiri T, Hempstead SE, Brady C, et al. Clinical practice guidelines from the Cystic Fibrosis Foundation for preschoolers with cystic fibrosis. Pediatrics. 2016;137(4):1-26. doi:10.1542/peds.2015-1784.
11. Lai HJ, Chin LH, Murali S, Bach T, Sander D, Farrell PM, FIRST Study Group. Vitamins A, D, E status as related to supplementation and lung disease markers in young children with cystic fibrosis. Pediatric pulmonology. 2022;1-10. DOI: 10.1002/ppul.25825.

VERSION/NUMBER	DATE
Original 1.0	17/02/2022
Current 2.0	21/07/2022
REVIEW	21/07/2027

Authors Contribution

Original author/s	Renee Dimond, Srinivas Bolisetty
Evidence Review	Srinivas Bolisetty
Expert review	Karel Allegaert
Nursing Review	Priya Govindaswamy, Kirsty Minter, Eszter Jozsa, Sarah Neale
Pharmacy Review	Cecilia Peng
ANMF Group contributors	Nilkant Phad, Bhavesh Mehta, John Sinn, Mohammad Irfan Azeem, Rebecca Barzegar, Helen Huynh, Thao Tran, Cecilia Peng, Stephanie Halena
Final editing and review	Thao Tran
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty