Vitamin E
Newborn use only

2020

Alert	This formulary covers oral vitamin E. Vitamin E 1 International Unit (hereafter referred to as "units") = 0.67 mg d-alpha-tocopherol.[1] Penta-Vite, a commonly used multi-vitamin supplement doesn't contain vitamin E.
Indication	Prevention and treatment of vitamin E deficiency.
Action	Fat soluble vitamin. It is an antioxidant protecting cell membranes from oxidative stress. Active isomer is α-tocopherol.
Drug type	Fat soluble vitamin.
Trade name	Micel-E oral liquid (Oral liquid SAS product may be available – water soluble liquid, Aqua-E containing 16 mg/mL (20 IU/mL).
Presentation	Micel-E oral liquid: d-alpha-tocopherol 104.7 mg/mL (vitamin E 156 units/mL); 50 mL bottle.
Dose	Vitamin E supplementation in preterm neonates* 8 units/kg daily (6-12 IU/kg/day)[2] *Preterm human milk + Human milk fortifier (HMF) at 170 mL/kg/day provides an average 8 units/kg/day.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No information. Hepatic impairment – No information.
Maximum dose	Doses exceeding 25 units/kg/day ORAL may pose more risk than benefit for preterm neonates.[3]
Total cumulative dose	
Route	Oral
Preparation	No preparation is required.
Administration	Administer undiluted.
Monitoring	Serum vitamin E levels – Not routinely required. Target 1.0-2.0 mg/dL.[4,5]
Contraindications	Hypersensitivity to vitamin E or any component
Precautions	Interacts with iron and other oxidants or any polyunsaturated fatty acids. Increases serum bilirubin.
Drug interactions	Iron - Lowers bioavailability of Vitamin E. Vitamin E may increase the effects of vitamin K antagonists and antiplatelet agents.
Adverse reactions	Sepsis. Intracranial haemorrhage (IV dosing). Necrotising enterocolitis.
Compatibility	Not applicable.
Incompatibility	Not applicable.
Stability	
Storage	Micel E oral liquid: Store below 25^0C (room temperature).
Excipients	Micel-E: Potassium sorbate, citric acid anhydrous, glycerol, PEG-35 castor oil, ethanol, water.
Special comments	
Evidence	**Efficacy** Cochrane review by Brion et al 2003 assessed the effects of routine vitamin E supplementation on morbidity and mortality in preterm infants. Twenty-six randomized clinical trials with over 2000 preterm infants < 37 weeks or < 2500 g were analysed. In very low birth weight (VLBW) infants≤ 1500 g, vitamin E supplementation significantly reduced the risk of severe retinopathy and blindness but significantly increased the risk of sepsis. Subgroup analyses demonstrated (1) an association between intravenous, high-dose vitamin E supplementation and increased risk of sepsis and cerebral haemorrhage; (2) an association between non-intravenous vitamin E route and reduced risk of any or severe intraventricular haemorrhage and (3) an association between serum tocopherol levels greater than 3.5 mg/dl and increased risk of sepsis and reduced risk for severe retinopathy. Author's conclusions: Vitamin E supplementation in preterm infants reduced the risk of intracranial haemorrhage but increased the risk of sepsis. In VLBW infants, vitamin E increased the risk of sepsis, and reduced the risk of severe retinopathy and blindness among those examined. Evidence does not support the routine use of vitamin E supplementation by intravenous route at high doses or aiming at serum tocopherol levels greater than 35 mg/L (81 µmol/L).[6] (LOE I GOR A) **Safety**

	Routine vitamin E supplementation significantly reduced the risk of intraventricular haemorrhage but increased the risk of sepsis in preterm neonates. In VLBW infants (≤ 1500 g), vitamin E supplementation significantly increased the risk for sepsis and cerebral haemorrhage. (LOE I GOR A) A retrospective analysis has shown a significant association between pharmacologic oral doses of vitamin E in VLBW infants and necrotizing enterocolitis[7] but this effect was not evident in meta-analysis.[6]
Practice points	Vitamin E content in preterm human milk: 0.64 units/dL (0.43 mg/dL) Average human milk fortifier (HMF) at 80 kcal/100 mL provides additional 4-4.5 units/dL. Preterm human milk + HMF at 170 mL/kg/day provides an average 8 units/kg/day. **Recommended dietary allowances** Colostrum and preterm human milk contains 2-3 times more alpha-tocopherol in mature milk.[2,8] Vitamin E supplements for the preterm infant less than 1000 g birth weight are recommended to be 2.8 to 3.5 units/kg/day parenterally and 6 to 12 units/kg/day enterally.[2,3,9,10] (LOE III-3 GOR B) Recommended parenteral vitamin E for preterm neonates: 3 units/kg/day (2.8-3.5 units/kg/day).[2,10] SMOFlipid 20% contains 163 – 225 mg dl-alpha-tocopherol per 1000 mL. Vitalipid-N Infant contains 0.64 mg dl-alpha-tocopherol per 1 mL.[11] The current Australasian consensus parenteral nutrition provides 2.8 IU/kg/day at 150 mL/kg/day.[12]
References	1. https://dietarysupplementdatabase.usda.nih.gov/Conversions.php. 2. Greer FR. Vitamin metabolism and requirements in the micropremie. Clin Perinatol 2000;27:95-118. 3. Greer FR. Vitamins A, E and K. In Nutrition of the Preterm Infant. Ed by Tsang R, Uauy R, Koletzko B, Zlotkin S. Second edition 2005. 4. Johnson L, Bowen FW, Abbasi S, Herrmann N, Weston M, Sacks L, Porat R, Stahl G, Peckham G, Delivoria-Papadopoulos M, Quinn G. Relationship of prolonged pharmacologic serum levels of vitamin E to incidence of sepsis and necrotizing enterocolitis in infants with birth weight 1,500 grams or less. Pediatrics. 1985;75(4):619-38. 5. Amorde-spalding KA, D'harlingue AE, Phillips BL, Byrne WI, Cheng KS, Cook NE, Irias JJ. Tocopherol levels in infants≤ 1000 grams receiving MVI pediatric. Pediatrics. 1992;90(6):992-4. 6. Brion LP, Bell EF, Raghuveer TS. Vitamin E supplementation for prevention of morbidity and mortality in preterm infants. Cochrane Database of Systematic Reviews 2003, Issue 4. Art. No.: CD003665. DOI: 10.1002/14651858.CD003665. 7. Finer NN, Peters KL, Hayek Z, Merkel CL. Vitamin E and necrotizing enterocolitis. Pediatrics 1984;73:387-93. 8. Moran JR, Vaughan R, Stroop S, Coy S, Johnston H, Greene HL. Concentrations and total daily output of micronutrients in breast milk of mothers delivering preterm: a longitudinal study. JPGN 1983;2(4):629-34. 9. Agostoni C, Buonocore G, Carnielli VP, De Curtis M, Darmaun D, Decsi T, Domellöf M, Embleton ND, Fusch C, Genzel-Boroviczeny O, Goulet O. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. JPGN 2010;50(1):85-91. 10. Greene_HL, Hambidge_M, Schanler_R, Tsang_RC. Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and chidren receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of the American Society for Clinical Nutrition. American Journal of Clinical Nutrition 1988; **48:1324**-42. 11. Australian Product Information – Vitalipid N Adult and Vitalipid N Infant (Retinol Palmitate, Ergocalciferol, DL-Alpha-Tocopherol, Phytomenadione), Revised February 2020, Fresenius Kabi Australia Pty Limited. 12. Bolisetty, S., Osborn, D., Schindler, T. et al. Standardised neonatal parenteral nutrition formulations – Australasian neonatal parenteral nutrition consensus update 2017. BMC Pediatr 20, 59 (2020). https://doi.org/10.1186/s12887-020-1958-9.

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