# Vitamin E
## Newborn use only

**2020**

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| **Alert** | This formulary covers oral vitamin E.<br>Vitamin E 1 International Unit (hereafter referred to as "units" ) = 0.67 mg d-alpha-tocopherol.[1]<br>Penta-Vite, a commonly used multi-vitamin supplement doesn't contain vitamin E. |
| **Indication** | Prevention and treatment of vitamin E deficiency.<br>Neonatal cholestasis |
| **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<br>(Oral liquid SAS product may be available – water soluble liquid, Aqua-E containing 16 mg/mL (20 units/mL). |
| **Presentation** | Micel-E oral liquid: d-alpha-tocopherol 104.7 mg/mL (vitamin E 156 units/mL); 50 mL bottle. |
| **Dose** | **Supplementation in preterm neonates**\*<br>      8 units/kg daily (6-12 units/kg/day)[2]<br><br>**Neonatal cholestasis:** Refer to vitamins in cholestasis formulary.<br><br>\*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.<br>ECMO – No information.<br>Renal impairment – No information.<br>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.<br>Increases serum bilirubin. |
| **Drug interactions** | Iron - Lowers bioavailability of Vitamin E.<br>Vitamin E may increase the effects of vitamin K antagonists and antiplatelet agents. |
| **Adverse reactions** | Sepsis.<br>Intracranial haemorrhage (IV dosing).<br>Necrotising enterocolitis. |
| **Compatibility** | Not applicable. |
| **Incompatibility** | Not applicable. |
| **Stability** | |
| **Storage** | Micel E oral liquid: Store below 25$^0$C (room temperature). |
| **Excipients** | Micel-E: Potassium sorbate, citric acid anhydrous, glycerol, PEG-35 castor oil, ethanol, water. |
| **Special comments** | |
| **Evidence** | **Efficacy**<br>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 |

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| | 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) <br><br> **Safety** <br> 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) <br> 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) <br> Average human milk fortifier (HMF) at 80 kcal/100 mL provides additional 4-4.5 units/dL. <br> Preterm human milk + HMF at 170 mL/kg/day provides an average 8 units/kg/day. <br> **Recommended dietary allowances** <br> 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) <br> Recommended parenteral vitamin E for preterm neonates: 3 units/kg/day (2.8-3.5 units/kg/day).[2,10] <br> SMOFlipid 20% contains 163 – 225 mg dl-alpha-tocopherol per 1000 mL. <br> Vitalipid-N Infant contains 0.64 mg dl-alpha-tocopherol per 1 mL.[11] <br> The current Australasian consensus parenteral nutrition provides 2.8 units/kg/day at 150 mL/kg/day.[12] |
| **References** | 1. https://dietarysupplementdatabase.usda.nih.gov/Conversions.php. <br> 2. Greer FR. Vitamin metabolism and requirements in the micropremie. Clin Perinatol 2000; 27:95-118. <br> 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. <br> 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. <br> 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. <br> 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. <br> 7. Finer NN, Peters KL, Hayek Z, Merkel CL. Vitamin E and necrotizing enterocolitis. Pediatrics 1984;73:387-93. <br> 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. <br> 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. <br> 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. <br> 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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