Colecalciferol (Cholecalciferol) - Vitamin D3 2020

Newborn use only

Alert	Colecalciferol (Vitamin D3) is the inactive form of vitamin D and converted in the body to the active form, calcitriol (1, 25-$(OH)_2$ vitamin D3). 1 microgram colecalciferol = 40 international units (hereafter referred to as "units") of vitamin D. Vitamin D content in preterm and term human milk and formulas may not provide enough vitamin D to meet the recommended daily intake of vitamin D 400 units /day.(1) Some preparations may contain sodium benzoate - Avoid exposure of >99mg/kg/day in neonates.
Indication	Prevention and treatment of vitamin D deficiency and nutritional rickets (in combination with adequate mineral intake).
Action	Regulating body levels of calcium and phosphorus, and mineralization of bone
Drug type	Fat soluble vitamin
Trade name	Bio-Logical Vitamin D3 Solution Ostelin Vitamin D OsteVit-D Liquid OsteVit-D Vitamin D3 Oral Drops for Children Penta-vite Infant Liquid Multivitamin Oral liquid
Presentation	Ostelin Vitamin D Oral Liquid - 25 microgram vitamin D3 = 1000 units/0.5 mL liquid Penta-vite Infant Liquid Multivitamin Oral Liquid - Per 0.45 mL: **vitamin D3 (colecalciferol) 10.13 microgram = 404 units** Biological Therapies Vitamin D3 Forte ampoules - 600 000 units/mL (15mg/mL) of colecalciferol for intramuscular injection. **The following preparations contain sodium benzoate as an excipient:** Bio-Logical Vitamin D3 Oral Solution – 1000 units per 0.2 mL vitamin D3 OsteVit-D Oral Liquid - 25 microgram vitamin D3 = 1000 units/0.2 mL liquid OsteVit-D Vitamin D3 Oral Drops for Children - 5 microgram = vitamin D3 200 units per drop (0.04 mL)
Dose	**Prevention of rickets and osteomalacia in infants at risk of vitamin D insufficiency/deficiency (see *practice points)***: **Term infants:** colecalciferol 400 units/day (10 micrograms) until 12 months age (2) **Preterm infants:** (3) ≤1500 g: colecalciferol 200-400 units/day. >1500 g: colecalciferol 400 units/day. **Infants with cholestasis:** (Refer to special comments section) (4) Commence on colecalciferol 1200 units/day. Monitor every 1 to 3 months. Increase colecalciferol by 1200 units/day to maximum 8000 units/day to maintain vitamin D sufficiency (25-hydroxy vitamin D ≥ 50 nmol/L). Alternatively, calcitriol at 0.05–0.20 microgram/kg daily. **Treatment of nutritional rickets:** Colecalciferol 2000 units/day (50 microgram) for a minimum of 3 months. (3) Alternatively if oral administration is difficult, consider intramuscular colecalciferol 100000 units (2.5 mg) every 3 months (3 doses). Continue maintenance colecalciferol after resolution of nutritional rickets. Ensure adequate calcium intake – see special comments.
Dose adjustment	Therapeutic hypothermia: no information. ECMO: Adult patients on ECMO were at high risk of vitamin D deficiency and repeated doses of colecalciferol were required to correct the deficiency (5). Renal impairment: Vitamin D supplementation may be offered to patients with chronic kidney disease in whom circulating vitamin D levels have been documented as low. Hydroxylated vitamin D

	agents (eg. calcitriol) may be needed in addition to control progressive secondary hyperparathyroidism (6,7). Hepatic impairment: absorption of fat soluble vitamins is impaired in cholestasis (see infants with cholestasis). (8)
Maximum dose	Dosage to cause toxicity varies with individual sensitivity, but in individuals without malabsorption problems, 10,000 units per day for more than several weeks or months is the maximum dose. A dose of colecalciferol 1600 units/day produced vitamin D toxicity (hypercalcaemia and 25OH vitamin D >250 nmol/L) in 94% of infants. (10) Single doses of colecalciferol 600000 units (15 mg) in infants produced prolonged vitamin D excess and transient hypercalcaemia, whereas doses of 100000 to 200000 units every 3 months did not. (2, 11)
Total cumulative dose	
Route	Oral Intramuscular
Preparation	Administer undiluted.
Administration	Oral: May be administered without regard to meals. Intramuscular: inject slowly into anterolateral thigh.
Monitoring	**Healthy infants**: no routine 25OHD screening recommended (2). **Infants with cholestasis:** monitor 25OHD every 1 to 3 months. Maintain vitamin D sufficiency (25-hydroxyvitamin D ≥ 50 nmol/L).(4, 8) **For very low birth weight or preterm infants with nutritional rickets**: serum phosphate and alkaline phosphatase weekly to achieve serum levels of 1.8 mmol/L for term infants (range 1.2-2.6) and 1.3-1.7 mmol/L for preterm infants. (3) Urine calcium and phosphate may be monitored with the goal of achieving a slight surplus of supply of calcium and phosphate (urinary calcium ≥ 1.2mmol/L and phosphate ≥ 0.4 mmol/L). (9) In daily practice, monitoring can be ceased after the preterm infant is on full feeds of fortified human milk or preterm formula and is > 1500 g body weight. Routine evaluation for nutritional rickets should be considered for infants born <1500 g (3). Biochemical testing should usually be started 4 to 5 weeks after birth, and a serum alkaline phosphatase >800 to 1000 units/L or clinical evidence of fractures should lead to a radiographic evaluation for rickets and management focusing on maximizing calcium and phosphorus intake and minimizing factors leading to bone mineral loss.(3)
Contraindications	Hypersensitivity to colecalciferol, Hypervitaminosis D
Precautions	Hypercalcaemia and hyperparathyroidism - avoid a high calcium intake and limit vitamin D supplementation with colecalciferol. The formulations of colecalciferol available in Australia are unlikely to cause vitamin D toxicity. However, if toxicity from colecalciferol occurs, stopping treatment might not lead to rapid resolution because colecalciferol is stored extensively in fat. In addition to rehydration, oral glucocorticoids can be effective in severe or protracted vitamin D toxicity.
Drug interactions	Magnesium-containing antacids (concurrent use with vitamin D may result in hypermagnaesemia, especially in patients with chronic renal failure). Barbiturates may reduce effect of vitamin D by accelerating metabolism by hepatic microsomal enzyme induction; patients on long-term anticonvulsant therapy may require vitamin D supplementation to prevent osteomalacia. Calcitonin – reduces serum calcium levels. Bisphosphonates (etidronate, pamidronate) prevent bone resorption and act synergistically with vitamin D to increase bone mineral density, but antagonise the effect of vitamin D on serum calcium level. Calcium-containing preparations in high doses. Diuretics, thiazide (concurrent use with vitamin D may increase the risk of hypercalcaemia). Cholestyramine, colestipol and mineral oils may interfere with fat soluble vitamin absorption. Corticosteroids - vitamin D supplementation may be recommended for prolonged corticosteroids use, because corticosteroids may interfere with vitamin D action.

	Digitalis glycosides - hypercalcaemia caused by vitamin D may potentiate the effects of digitalis glycosides resulting in cardiac arrhythmias. Phosphorus containing preparations in high doses may cause hyperphosphataemia as vitamin D enhances of phosphate absorption. Vitamin D and analogs - concurrent use with another analog, especially calcifediol, is not recommended because of additive effects and increased potential for toxicity.
Adverse reactions	A dose of colecalciferol 1600 units/day produced vitamin D toxicity (hypercalcaemia and 25-hydroxy vitamin D >250 nmol/L) in 94% of infants (10). Single doses of colecalciferol 600000 units (15 mg) in infants produced prolonged vitamin D excess and transient hypercalcaemia, whereas doses of 100000 to 200000 units every 3 months did not. (2, 11) Ingestion of excessive doses of vitamin D over prolonged periods 2000 to 4000 units a day for several months in children can result in severe toxicity. Acute excessive doses of vitamin D can also result in severe toxicity. Chronic vitamin D induced hypercalcaemia may result in generalized vascular calcification, nephrocalcinosis, and other soft tissue calcification that may lead to hypertension and renal failure. These effects are more likely to occur when the hypercalcaemia is accompanied by hypophosphatemia. Growth may be arrested in children, especially after prolonged administration of 1800 units of ergocalciferol per day. Death may occur as a result of renal or cardiovascular failure caused by vitamin D toxicity. Symptoms (all age groups) may include bone pain, constipation, diarrhoea, drowsiness, dry mouth, headache (continuing), increased thirst, increase in frequency of urination (especially at night) or in the amount of urine, loss of appetite, metallic taste, muscle pain, nausea or vomiting, unusual tiredness or weakness, cloudy urine, conjunctivitis (calcific), decreased libido, ectopic calcification, high fever, high blood pressure, increased sensitivity of eyes to light or irritation of eyes, irregular heartbeat, itching of skin, lethargy, loss of appetite, pancreatitis, psychosis (overt), rhinorrhoea, and weight loss.
Compatibility	No information – do not mix.
Incompatibility	No information
Stability	No information
Storage	VITAMIN D3 FORTE – store below 25^{O}C. For other brands – refer to product information.
Excipients	Sodium benzoate: Some vitamin D preparations contain sodium benzoate. Avoid exposure of >99mg/kg/day in neonates. Ostelin Vitamin D Oral Liquid – contains orange flavour Bio-Logical Vitamin D3 Solution – contains sodium benzoate OsteVit-D Oral Liquid - contains sodium benzoate; caramel flavour OsteVit-D Vitamin D3 Oral Drops for Children - contains sodium benzoate 2 mg/mL; butterscotch flavour. Penta-vite Infant Liquid Multivitamin Oral Liquid - contains sodium saccharin; pineapple flavour. Biological Therapies Vitamin D3 Forte Injection - contains ethyl oleate
Special comments	Vitamin D content in preterm and term human milk averages 8 and 6 units/100 mL, respectively with median intake averaging 77 units/day (interquartile range 55 to 110).(12) For human milk fed preterm or low birthweight infants, the addition of a human milk fortifier may not reach the recommended daily intake of vitamin D 400 units/day.(1) Penta-vite Infant 0.45 mL contains 404 units vitamin D3. The adequate calcium intake for term infants based on breast milk calcium content is 200 mg/day and 260 mg/day for babies from 0–6 and 6–12 months of age, respectively. (2) The recommended intake for very low birth weight infants are: Calcium 150–220 mg/kg/day; and Phosphorous 75–140 mg//kg/day.(3) For treatment of nutritional rickets, oral calcium 500 mg/day, either as dietary intake or supplements, should be routinely used in conjunction with vitamin D in the treatment regardless of age or weight. (2)

	Recommendations in cholestasis: In daily practice, if the infant has severe cholestasis from parenteral nutrition, it is often not possible to achieve vitamin D sufficiency with 1200-8000 IU/day cholecalciferol and alternative is to commence calcitriol at a dose of 0.1 microgram/kg daily and follow parathyroid hormone (PTH) and 25-OHD. This is safe, effective and requires less monitoring. Hypercalcemia doesn't occur at this dose.(Expert opinion)
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

VERSION/NUMBER	**DATE**
Original	**15/11/2016**
Revised 2.0	**15/10/2020**
REVIEW (5 years)	15/10/2025

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