

VITAMIN D DEFICIENCY IN CHILDREN AND ADULTS: TREATMENT AND PROPHYLAXIS GUIDELINE

SECTION A. DEFINITION AND DIAGNOSIS

The main source of vitamin D is from the action of UVB sunlight on the skin, which results in the formulation of vitamin D₃ (colecalciferol). The rest comes from diet as either vitamin D₂ (ergocalciferol) from plant sources or vitamin D₃ from animal sources.

Definition

There are currently debates as to the optimal level of serum vitamin D. However, there is a consensus that vitamin D deficiency should be defined as 25-hydroxyvitamin D (25(OH)D) below 25 nanomol/Litre.^{1,2,3,4} This is the level below which the parathyroid hormone (PTH) starts to rise causing increased bone turnover and hence symptoms associated with osteomalacia.

Serum 25-hydroxyvitamin D concentration ^{1,2}	Vitamin D status	Management
Below 25 nmol/L	Deficiency	Treat with high dose vitamin D
25 – 50 nmol/L	Insufficiency	Vitamin D supplementation
50 – 80 nmol/L	Normal	<ul style="list-style-type: none"> • None • Continue supplementation if previously treated for vitamin D deficiency.

The above ranges of vitamin D levels may vary slightly depending on the laboratory where the assay was sent. If necessary, GPs should contact the laboratory to discuss the results and subsequent management of the patient.

SECTION B. WHEN TO TEST: RISK FACTORS FOR VITAMIN D DEFICIENCY

Due to the associated cost of testing for vitamin D levels, tests should be limited to those who are symptomatic with low calcium levels or individuals in the following at risk groups in whom practitioners consider merit investigation:

- Increased demand for vitamin D
 - Pregnant and breastfeeding women
 - Twin and multiple pregnancies
 - Infants
- Adolescents with poor diet and/or limited sun exposure
- Reduced sun exposure (wearing concealing clothing, immobility limiting time spent outside)
- Frequent use of sun-block creams and cosmetics containing sun protection factors
- Dark skin pigmentation
- Poor diet
- Intestinal malabsorption e.g. Coeliac disease, Crohns disease
- Chronic liver disease
- Chronic renal disease
- P450 enzyme inducing drugs e.g. anticonvulsants, anti TB drugs.

SECTION C. MONITORING

Pre treatment	Serum 25-hydroxyvitamin D, calcium, phosphate and urea & electrolytes
Monitoring	<p>Serum calcium, phosphate, alkaline phosphatase, 25-hydroxyvitamin D</p> <p>Re check after 3 months with high dose treatment</p> <p>Not necessary with low dose treatment (supplementation)</p> <p>Parathyroid hormone may be checked if the patient does not respond or relapses</p>
Action	<p>If 25-hydroxyvitamin D is over 80 nmol/L, continue supplementation</p> <p>If 25-hydroxyvitamin D is below 80 nmol/L, continue treatment for another 2-3 months and re-check.</p>

Note, children with severe rickets may require longer treatment until complete radiological resolution of rickets. All children with symptomatic hypocalcaemia must be referred immediately to hospital. Children receiving pharmacological doses of vitamin D should have their plasma-calcium concentration checked at regular intervals (initially once or twice weekly) and whenever nausea or vomiting occur.⁵

SECTION D. AT RISK GROUPS

It is particularly important to counsel patients on how to increase vitamin D through diet (found naturally in oily fish, fortified cereals, eggs etc) and benefits of sufficient sunlight exposure (balanced against risk of skin cancer). It is recommended that between March and October, 10 minutes of sun exposure a day with the head, neck and arms exposed should provide sufficient vitamin D.

The Department of Health advises that people who find it hard to get enough vitamin D from the sun and their diet should take a vitamin D supplement. The recommended daily supplements are as follows:⁶

People at risk of vitamin D deficiency	Daily vitamin D supplement
<ul style="list-style-type: none"> ▪ All pregnant and breastfeeding women 	400 units/day
<ul style="list-style-type: none"> ▪ All infants and children from 6 months to 5 years, unless they are drinking 500ml (a pint) or more of infant formula milk a day at any time during this age range. <ul style="list-style-type: none"> ○ Infants aged 0-6 months may not need supplements as they should get adequate amounts from breast milk or infant formula milk. If there is any doubt about the mother's use of vitamin supplements during pregnancy and/or breastfeeding, breastfed infants will benefit from vitamin D supplements from 1 month. 	6 months to 5 years 280 units/day
<ul style="list-style-type: none"> ▪ People who are not exposed to much sun e.g. people confined indoors for long periods and those who cover their skin for cultural reasons. 	400 units/day
<ul style="list-style-type: none"> ▪ People aged 65 years and over. 	400 units/day

SECTION E. TREATMENT OF VITAMIN D INSUFFICIENCY
Dosage^{1,5,7}

Age	Daily Dose
Neonates	400 units
Child 1 month – 18 years	400 units
Adults	800 units daily, however higher doses of up to 2000 units daily have been cited.

See Section H for information on vitamin D preparations available and corresponding dosage information.

SECTION F. TREATMENT OF VITAMIN D DEFICIENCY

F1. Usual treatment doses: ^{1,2,5,7}

Age	Daily Dose of Colecalciferol or Ergocalciferol
Infant 1 – 6 months	3000 units
Children 6 months – 12 years	6000 units
Over 12 years to adult	6000 – 10,000 units

F2. Vitamin D deficiency in intestinal malabsorption or in chronic liver disease

Age	Daily Dose of Colecalciferol or Ergocalciferol
Child 1 - 12 years	10,000 – 25,000 units adjusted as necessary
Child 12 – 18 years	10,000 – 40,000 units adjusted as necessary
Adult	Up to 40,000 units

Patients with complex medical disorders e.g. liver disease and intestinal malabsorption, requiring higher pharmacological doses of vitamin D require intensive monitoring and should be referred to secondary care for investigation.

See Section H for information on vitamin D preparations available and corresponding dosage information.

F3. Renal and liver disease

Vitamin D requires hydroxylation by the kidney and liver to its active form, the hydroxylated derivatives alfacalcidol or calcitriol should be prescribed for patients with severe renal or liver disease requiring vitamin D therapy. **Alfacalcidol and calcitriol must only be prescribed according to their licensed indications** (see individual Summary of Product Characteristics www.medicines.org.uk). They are ineffective in correcting vitamin D deficiency and may lead to hypercalcaemia ¹.

SECTION G. REFERRAL TO SECONDARY CARE

Practitioners should consider referral to secondary care for the following groups of patients:

- All infants and children with hypocalcaemia, even if asymptomatic
- Any child with delayed gross motor milestones or orthopaedic abnormalities suspected to be rickets
- Adolescents with recurrent muscle pain or fatigue
- Poor response to treatment
- Patients with renal impairment
- Primary hyperparathyroidism

SECTION H. VITAMIN D PREPARATIONS

PREPARATIONS FOR VITAMIN D INSUFFICIENCY OR FOR SUPPLEMENTATION	COMMENTS AND DOSAGE
<p>Healthy Start Vitamins, tablets and drops</p> <p>For women, tablets contain vitamin C, D (providing 400units/day) and 400µg folic acid</p> <p>For children, drops contain vitamins A, C and D</p>	<ul style="list-style-type: none"> ▪ Visit www.healthystart.nhs.uk ▪ Available to women during pregnancy and until their baby is one year old through the Healthy Start Scheme. ▪ Free of charge to children under 4 years through the Healthy Start Scheme; otherwise direct to the public from maternity and child health clinics. ▪ Maybe in short supply* ▪ <u>Dose:</u> Child: 1 month – 5 years: 5 drops daily (5 drops contain vitamin A approx. 700 units, vitamin D approx. 300 units, ascorbic acid 20mg) ▪ Adults: 1 tablet daily
<p>Abidec[®], Dalivit[®] multivitamin oral drops. Contains vitamins A, B, C and D.</p>	<ul style="list-style-type: none"> ▪ Contains 400 units (10µg) of colecalciferol or ergocalciferol in 0.6ml ▪ <u>Dose:</u> Neonate to 1 year: 200 units (0.3ml) daily 1 – 18 years: 400 units (0.6ml) daily <p>Note: doses above are taken from BNF for Children⁵ however, according to the Summary of Product Characteristics for the preparations:^{8,9}</p> <ul style="list-style-type: none"> ▪ Abidec[®] - is not licensed for adults and children over 12 years of age. ▪ Dalivit[®] - is licensed for adults: 0.6ml daily.
<p>Calcium / Vitamin D tablets Various brands available containing colecalciferol 200 – 800 units and calcium 12.5 – 30mmol per tablet e.g. Calceos[®] (currently the most cost effective), Calcichew D3 Forte[®], Adcal D3[®]</p>	<ul style="list-style-type: none"> ▪ For adolescents and adults also requiring calcium supplementation. ▪ There is no plain vitamin D tablet available for treating insufficiency. ▪ <u>Dose:</u> 800 units vitamin D daily.
<p>Vitamins A and D capsules Contains vitamin D 400 units and vitamin A 4000 units</p>	<ul style="list-style-type: none"> ▪ Usually contains gelatin ▪ <u>Dose:</u> 1 capsule daily
<p>Multivitamin capsules Contains vitamin D 300 units and ascorbic acid 15mg, nicotinamide 7.5mg, riboflavin 500mcg, thiamine hydrochloride 1mg, vitamin A 2500 units.</p>	<ul style="list-style-type: none"> ▪ Contain gelatin ▪ <u>Dose:</u> Child 1 – 12 years: 1 capsule daily Child ≥ 12 years and adults: 2 capsules daily
<p>Forceval capsules Contains vitamin D 400 units and vitamins A, B group, C, E and minerals.</p>	<ul style="list-style-type: none"> ▪ Contain gelatin ▪ <u>Dose:</u> 1 capsule daily, one hour after a meal ▪ Not recommended for children under 12 years of age. ▪ Currently more expensive than alternatives listed above
<p>Forceval Junior capsules Contains vitamin D 200 units and vitamins A, B group, C, E and minerals.</p>	<ul style="list-style-type: none"> ▪ Contain gelatin ▪ <u>Dose:</u> Child 5 – 12 years: 2 junior capsules daily.

NB. There are a number of preparations which contain vitamin D available to purchase from community pharmacies and health stores. These products are marketed as nutritional supplements and vary in their vitamin content and strength of vitamin D. Monitoring parameters in Section C will apply to patients who purchase these preparations.

PREPARATIONS FOR VITAMIN D DEFICIENCY	COMMENTS AND DOSAGE
<p>First line Ergocalciferol injection 300,000 units/ml</p>	<ul style="list-style-type: none"> ▪ This is a licensed product ▪ For intramuscular injection ▪ Drug Tariff price (October 2010): <ul style="list-style-type: none"> ○ 1mL amp = £8.50 ○ 2mL amp = £9.84 ▪ <u>Dose</u>²: <ul style="list-style-type: none"> ○ 6 months to 12 years = 150,000 units ○ ≥ 12 years and adults = 300,000 units ▪ Given every 3 months, however one dose may be sufficient (re check vitamin D level every 3 months)
<p>Second line – when intramuscular injection is not available Colecalciferol capsules (Dekristol®) 20,000 units (500 micrograms)</p>	<ul style="list-style-type: none"> ▪ Unlicensed special order product that is obtained through a company in the UK with a license to import ▪ Contains gelatin. ▪ Available from IDIS: 1pack (50 capsules): £24.09 ▪ <u>Dose</u>^{1,10}: 60,000 units (3 x 20,000 units) weekly.
<p>Ergocalciferol tablets 10,000 units (250 micrograms)</p>	<ul style="list-style-type: none"> ▪ This is a licensed product ▪ Current supply problems* ▪ See section I for information on cost ▪ <u>Dose</u>: see section F
<p>Colecalciferol liquid special order product 3000 units/ml</p>	<ul style="list-style-type: none"> ▪ Unlicensed special order product ▪ Short shelf life, often 28 days once the bottle is opened (> 1yr expiry from the date of manufacture) ▪ First choice vitamin D liquid special – longer shelf life ▪ See section I for information on cost ▪ <u>Dose</u>: see section F
<p>Ergocalciferol liquid special order product 3000 units/ml</p>	<ul style="list-style-type: none"> ▪ Unlicensed special order product ▪ Very short shelf life, 28 days from the date of manufacture ▪ Current supply problems* ▪ See section I for information on cost ▪ <u>Dose</u>: see section F
<p>Colecalciferol liquid special order product 300,000units/10ml</p>	<ul style="list-style-type: none"> ▪ Unlicensed special order product ▪ St. George's Hospital (SGH) formula ▪ 7 day shelf life ▪ <u>Dose</u>: 10ml as a single dose

* Please note that information on product supply is subject to change and GPs should check availability with community pharmacies before prescribing.

SECTION I. RECOMMENDATIONS WHEN PRESCRIBING ERGOCALCIFEROL OR COLECALCIFEROL LIQUID SPECIAL ORDER PRODUCTS

- Due to intermittent supply problems with licensed vitamin D preparations, vitamin D liquid preparations as special order products are available. Special order products do not have a product license in the UK and hence are unlicensed products which have not been assessed for safety, quality and efficacy as for licensed products. Clinicians take on full responsibility when prescribing these products. They should only be prescribed when all other licensed options have been considered. The cost can vary depending on the manufacturer supplying the product and the volume and strength required. **Specials can be very costly as there is currently no price regulation.**
- The **strength** prescribed should remain the same to maintain product consistency and to avoid dosing errors particularly as some patients remember dosing in terms of volume rather than strength
- It is recommended that the **manufacturer** remain the same to ensure product consistency.
- The **quantity prescribed** should take into account the product shelf life and duration of treatment
- Prescribers should be aware that delivery of stock to community pharmacies may take up to 5 days.

SECTION J. INFORMATION FOR COMMUNITY PHARMACISTS

GPs may forward the following information to community pharmacies if queries arise from pharmacists who have been asked to source vitamin D special order products:

The following manufacturers can supply vitamin D liquid special order products:

- Cardinal Health Martindale Products
Essex
0800 137 627
- The Specials Laboratory
Northumberland
0800 028 4925
- Colecalciferol liquid special 300,000units in 10ml
SGH formula
St George's Healthcare NHS Trust
(020) 8725 1770/1768

The following companies have a license to import medicines in the UK:

- IDIS
01932 824 000
www.idispharma.com
- Martindale Pharma
0800 137 627
www.martindalepharma.co.uk
- Mawdsley Unlicensed Medicines
01302 553000
www.mawdsleys.co.uk/unlicensedMedicines.asp

References

1. Diagnosis and management of vitamin D deficiency. BMJ 340: b5664, January 2010.
2. Treatment and Prophylaxis Guidelines for Vitamin D deficiency in Infants, Children and Adolescents, Imperial College Healthcare and NHS Westminster, June 2010.
3. Primary vitamin D deficiency in adults. Drugs and Therapeutics Bulletin; April 2006, 44(4).
4. Update on Vitamin D: position statement by the Scientific Advisory Committee on Nutrition, 2007. www.sacn.gov.uk
5. BNF for Children 2010-2011 www.bnfc.org
6. Department of Health: Vitamin D, an essential nutrient for all...but who is at risk of vitamin D deficiency? January 2010. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_115370
7. BNF 59 March 2010 www.bnf.org
8. Abidec® Summary of Product Characteristics. Date of revision of text 16th June 2008.
9. Dalivit® Summary of Product Characteristics. Date of first authorisation/renewal of authorisation 20th January 2005.
10. Vitamin D deficiency and insufficiency: available products. East and South East England Specialist Pharmacy Services. October 2010.

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Although every effort is made to ensure the accuracy of the information in this guideline, the authors cannot accept responsibility for errors or omissions. The information contained is the best available from the resources at our disposal at the time of writing.