



Vitamin D

Guidelines for the treatment and prophylaxis of deficiency and insufficiency in children, adolescents and adults.

This guideline does not address the management of vitamin D deficiency in patients with severe or end-stage chronic kidney disease.

Key messages:

- For the treatment of deficiency and subsequent maintenance, vitamin D should be provided via NHS prescription.
- For the management of insufficiency and the prophylaxis of deficiency vitamin D should be purchased OTC or, if eligible, obtained free of charge via the government's "Healthy Start" scheme www.healthystart.nhs.uk
- Vitamin D **deficiency** is defined as **serum 25(OH)D <30nmol/L**
- Vitamin D **insufficiency** is defined as **serum 25(OH)D 30-50nmol/L**
- Oral vitamin D3 (**colecalfiferol**) is the treatment of choice in vitamin D deficiency.
- Where rapid correction of vitamin D deficiency is required, use a fixed loading dose followed by regular maintenance therapy.
- Where correction of vitamin D deficiency is less urgent maintenance therapy may be started without the use of loading doses.
- Adjusted serum calcium should be checked 1 month, in adults, or 6 months, in children, after completing the loading regimen or after starting vitamin D supplementation, in case primary hyperparathyroidism has been unmasked.
- Prescribe by brand.
- Preferred product choice for adults is InVitaD3.
- See SPC for full prescribing information:
<http://www.medicines.org.uk/emc/medicine/28998>

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Recommended Daily Intake:

The major natural source of vitamin D is from skin photosynthesis following ultraviolet B sunlight exposure. Over 90% of the body's vitamin D is produced from the action of sunlight on the skin. Small amounts of vitamin D are also obtained from oily fish, egg yolks, mushrooms, fortified breakfast cereals, milk and margarine.^{1,2}

Vitamin D supplementation, via OTC purchase or the “Healthy Start” scheme www.healthystart.nhs.uk , if eligible, is recommended in the following groups:

- **Everyone in the general population aged 4 years and older**, and including **pregnant and lactating women**, is recommended to take a supplement which provides the equivalent of **400IU** (international units) a day. **400IU is equivalent to 10 micrograms** of colecalciferol (Vitamin D3) or ergocalciferol (Vitamin D2).
- As a precaution, **all infants and young children** should take a **daily** supplement containing Vitamin D: 340 - 400 IU (8.5 -10 micrograms) for infants from birth to 1 year old (including exclusively breast fed and partially breast fed infants, from birth); 400IU (10 micrograms) for children aged 4 years and upwards. Infants who are fed infant formula will not need vitamin drops until they are receiving less than 500ml of infant formula a day, as these products are fortified with vitamin D.
- These recommendations are taken from the Scientific Advisory Committee on Nutrition's report, “Vitamin D and Health”, July 2016² and are to ensure that the majority of the UK population has satisfactory vitamin D blood levels throughout the year, in order to protect musculoskeletal health.

Risk factors for vitamin D deficiency include:

- Dark/pigments skin colour e.g. black, Asian populations
- Routine use of sun protection factor 15 and above as this blocks 99% of vitamin D synthesis.
- Reduced skin exposure e.g. cultural reasons (clothing)
- Latitude (In the UK, there is no radiation of appropriate wavelength between October and March)
- Chronic ill health with prolonged hospital admissions e.g. oncology patients
- Children and adolescents with disabilities which limit the time they spend outside
- Institutionalised individuals
- Photosensitive skin conditions
- Reduced vitamin D intake
- Maternal vitamin D deficiency
- Infants that are exclusively breast fed
- Dietary habits – low intake of foods containing vitamin D
- Abnormal vitamin D metabolism, abnormal gut function, malabsorption or short bowel syndrome.
- Chronic liver or renal disease
- Medicines including rifampicin, isoniazid and anti-convulsants e.g. phenytoin and carbamazepine, glucocorticoids and highly active anti-retroviral treatment.
- Genetic variation.^{1,2}

Measurement of vitamin D:

Measurement of serum 25(OH)D [25-hydroxyvitamin D] is measured in nanomol per litre (nmol/L).

The lab may reasonably expect the reasons for testing to be provided on the request.

It should be possible to justify that the result of the test will affect clinical management.

It is not recommended to screen the normal population for deficiency.

It is not recommended to screen high risk populations. High risk populations should be offered advice in order to avoid vitamin D deficiency. See Appendix 1.

Indications for testing:

Children:

Symptoms and signs of rickets/osteomalacia:

- Progressive bowing deformity of legs
- Waddling gait
- Abnormal knock knee deformity (intermalleolar distance > 5 cm)
- Swelling of wrists and costochondral junctions (rachitic rosary)
- Prolonged bone pain (>3 months duration)

Symptoms and signs of muscle weakness

- Delayed walking
- Difficulty climbing stairs
- Cardiomyopathy in an infant

Abnormal bone profile or x-rays

- Low plasma calcium or phosphate
- Raised alkaline phosphatase
- Osteopenia or changes of rickets on x-ray
- Pathological fractures

Disorders impacting on vitamin D metabolism

- Chronic renal failure
- Chronic liver disease
- Malabsorption syndromes, for example, cystic fibrosis, Crohn's disease, coeliac disease
- Older anticonvulsants, for example, phenobarbitone, phenytoin, carbamazepine

Children with bone disease in whom correcting vitamin D deficiency prior to specific treatment would be indicated

- Osteogenesis imperfecta
- Idiopathic juvenile osteoporosis
- Osteoporosis secondary to glucocorticoids, inflammatory disorders, immobility³

Adults:

High risk patients, where vitamin D measurement should be **considered**, include those with the following:

- intestinal malabsorption, for example coeliac disease, Crohn's disease, gastrectomy
- liver or renal disease
- taking medications including anticonvulsants, cholestyramine, rifampicin, glucocorticoids, antiretrovirals, IV bisphosphonates*, denosumab*. [* N.B. Vitamin D and calcium levels **must be replete before** treatment with IV bisphosphonates or denosumab is started.]
- osteoporosis
- falls

Vitamin D deficiency should be **considered** and checked in any patient with the following **symptoms**, and particularly in those at high risk of deficiency:

One or more of the following clinical features AND other causes for symptoms have been excluded, for example myeloma, rheumatoid arthritis, polymyalgia rheumatica and hypothyroidism:

- Insidious onset of widespread or localised bone pain and tenderness (especially lower back and hip pain, but may include rib, thigh or foot pain)
- proximal muscle weakness i.e. in quadriceps and glutei. This may cause difficulty rising from a chair and/ or a waddling gait
- swelling, tenderness and redness at pseudo-fracture sites
- fractures, typically femoral neck, scapula, pubic rami, ribs or vertebrae
- non-specific myalgia especially with a raised Creatine Kinase (CK)

Vitamin D levels, effects on health and management of deficiency ¹.

Serum 25 – (OH) D concentration level	Vitamin D status	Manifestation	Management
< 30 nmol/L	Deficient	Rickets, osteomalacia	Treat with high dose vitamin D
30 – 50 nmol/L	Insufficient	Associated with disease risk	Vitamin D supplementation OTC – Not to be prescribed
50 – 75 nmol/L	Adequate	Healthy	Lifestyle advice
> 75 nmol/L	Optimal	Healthy	None

Management of vitamin D deficiency: i.e. Serum 25(OH)D < 30 nmol/L

Check:

- renal function
- alkaline phosphatase (ALP)
- calcium, phosphate, magnesium (infants)
- urea and electrolytes
- parathyroid hormone.

If no significant renal impairment, calcium is normal (if <2.1mmol/L in infants, refer as risk of seizures) and no other abnormal results of concern

- give lifestyle advice and
- prescribe vitamin D3 (colecalciferol) on FP10.

Vitamin D should preferably be taken with a meal, to aid absorption.

Treatment of vitamin D deficiency is usually managed with fixed loading doses followed by regular maintenance therapy.

The maintenance regime should be considered one month after the loading dose.⁴

Colecalciferol and ergocalciferol are traditionally considered equal in potency. However, **colecalciferol is preferred to ergocalciferol** as it has been reported to raise serum Vitamin D levels more effectively than ergocalciferol². Colecalciferol should be prescribed unless this is unacceptable to the patient.

Ergocalciferol (vitamin D2) has a different side chain than colecalciferol and is commercially made by irradiating and then purifying the ergosterol extracted from yeast. Yeast derived products are acceptable to vegetarians and vegans.

Source of colecalciferol:

Colecalciferol is commercially synthesised from an animal source such as lanolin/wool fat from sheep's wool. The wool is usually taken from live sheep and the lanolin is extracted by squeezing the wool. 7-dehydrocholesterol is then purified out from the lanolin and irradiated with UV-B in order to generate the vitamin D3.

Vegans:

It is advised that the source of vitamin D3 be discussed with vegans in order for them to make an informed choice as to whether this is acceptable to them or not.

Vegetarians:

Although vitamin D3 is sourced from an animal, if the animal is not harmed in the manufacture of the raw vitamin D3, the product could be considered suitable for vegetarians.

Monitoring:

The prescriber who initiates vitamin D treatment is responsible for making the arrangements for subsequent monitoring.

In adults, **adjusted serum calcium** should be checked **1 month after** completing the loading regimen or after starting vitamin D supplementation in case primary hyperparathyroidism has been unmasked.⁴ **In children**, calcium can be checked **after 6 months**, providing the baseline bloods (Ca, phosphate, PTH) were normal; otherwise, after 3 months.

Routine monitoring of serum 25(OH)D is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption and where poor compliance with medication is suspected.

Vitamin D has a relatively long half-life (21-30 days for 25(OH)D) and levels of 25(OH)D will take 3-6 months to reach steady state after a loading dose. **Vitamin D levels should be checked at 6 months**; if still deficient, seek advice.

A daily supplement of 800 to 1000IU calciferol will cause an increase in 25(OH)D of 24-29nmol/L after 3 to 6 months of treatment.

Treatment of vitamin D deficiency and subsequent maintenance:

ADULTS:

1st line formulary choice:

InVita D3 25,000IU/ml oral solution (See SPC for full prescribing information: <http://www.medicines.org.uk/emc/medicine/28998>)

1ml contains 0.625mg colecalciferol, equivalent to 25,000 IU vitamin D, in an olive oil-based oral solution presented in 1ml single dose “snap and squeeze” plastic ampoules.

One pack of 3 x 25,000IU/1ml ampoules costs £4.45.

The product is licensed in the UK for

- the prevention and treatment of vitamin D deficiency in adults and children and
- as an adjunct to osteoporosis therapy.

The full contents of the ampoule should be either emptied into the mouth and swallowed orally or emptied onto a spoon and taken orally.

InVitaD3 can also be taken by mixing with a small amount of cold or lukewarm food immediately prior to use.

Vegetarians and certain religious groups:

As InVita D3 does not use any ingredients from slaughtered animals, and does not contain gelatine or porcine sourced materials, the product is potentially suitable for vegetarians and patients following a halal or kosher diet.

InVita D3 as a whole finished product however has not been certified as halal or kosher.

2nd line formulary choice:

Fultium D3 3,200IU soft gelatine capsule, (£13.32/30) if a daily dose is required e.g. for elderly/ confused patients using Monitored Dosage Systems (MDS).

Beware early formulations contain arachis oil and so unsuitable for those with allergy to peanut or soy.

3rd line formulary choice:

Desunin 800IU tablet, (£3.60/30) if a daily dose is required and unable to take gelatine or allergic to ingredients of Fultium D3 capsule.

Vitamin D treatment and maintenance options for adults.

Treatment Options	Product (prescribe as brand)	Dosage	Total cost of loading regime	Total Units of Vitamin D	Medico-legal category
1	InVitaD3 25,000IU/ml unit dose ampoule	2 x1ml (50,000IU) by mouth every week for 6 doses	£17.80	300,000IU	Licensed medicine. POM
2 if daily dose required e.g. frail, elderly using MDS	Fultium D3 3200IU soft gelatine capsule	1 capsule (3,200IU) by mouth daily for 12 weeks	£37.30	268,800IU	Licensed medicine. POM
3 If sensitivity to ingredients in Fultium D3 and daily dose is required.	Desunin 800IU tablet	4 tablets (3,200IU) by mouth daily for 12 weeks	£40.32	268,800IU	Licensed medicine. POM
4 Hospital Only (Red Drug) if compliance issues or malabsorption suspected.	Colecalciferol injection 300,000IU	300,000IU via I.M. injection once per month for 3 months.	£5.16, only if obtained from Mawdsleys.	900,000IU	Unlicensed special.
Maintenance Options	Product (prescribe as brand)	Dosage	Cost of maintenance for one year	Average daily dose of vitamin D	Medico-legal category
1	InVitaD3 25,000IU/ml unit dose ampoule	1ml (25,000IU) by mouth once every month	£17.80	833IU	Licensed medicine. POM
2 if daily dose required e.g. frail, elderly using MDS	Fultium D3 800IU soft gelatine capsule	1 capsule daily	£43.80	800IU	Licensed medicine. POM
3 If sensitivity to ingredients in Fultium D3 and daily dose is required.	Desunin 800IU tablet	1 tablet daily	£43.80	800IU	Licensed medicine. POM
4 Hospital Only (Red Drug) if compliance issues or malabsorption suspected.	Colecalciferol injection 300,000IU	300,000IU via I.M. injection once every 6- 12 months.	£1.72-£3.44	822-1644IU	Unlicensed special.

CHILDREN:

The treatment doses for children are based on the guidance from the Royal College of Paediatrics and Child Health "GUIDE FOR VITAMIN D IN CHILDHOOD" October 2013. <http://www.rcpch.ac.uk/guide-vitamin-d-childhood>

There is no licensed medicinal product containing vitamin D which can provide the RCPCH dose regimes, only unlicensed nutritional products or "specials" whose cost can be unpredictable.

InVita D3 is a medicine licensed for all ages; it is a high-dose product (25,000IU/ml) and the total loading dose for treatment of vitamin D deficiency with InVitaD3 is lower than those recommended by the RCPCH. For those reasons, low-medium strength solutions of colecalciferol, prescribed as the **specified brand** ("**Aciferol**" for treatment and "**ProD3**" drops for maintenance - see chart below), at a daily dose, are recommended as first line.

If compliance with the daily dose regime is not possible, InVitaD3, used at off-label dose regimes (see chart), is an option for older children. InVitaD3 can be mixed with a small amount of children's foods, yogurt, milk, cheese, or other dairy products. The parents should be warned not to mix InVitaD3 into a large quantity of milk or food in case the child does not consume the full portion and so does not receive the full dose.

Vitamin D treatment and maintenance options for children 0-18years.

Age	Options	Product (prescribe as brand)	Dosage	Total cost of loading regime	Total Units of Vitamin D	Medico-legal category
0-6 months	Dose Regime		3000IU daily for 4 – 8 weeks.		84,000IU-168,000IU	
Loading dose	1	Aciferol D3 3,000IU/ml solution	1ml (3,000IU) daily for 4-8 weeks.	£19.99 (after discount)	84,000-168,000IU	Unlicensed
6 months to 12 years	Dose Regime		6,000IU daily for 4-8 weeks		168,000-336,000IU	
Loading dose	1	Aciferol D3 3,000IU/ml solution	2ml (6,000IU) daily for 4-8 weeks.	£19.99-£38.98 (after discount)	168,000-336,000IU	Unlicensed
	2 if compliance problems with daily dose	InVitaD3 25,000IU/ml unit dose ampoule	1ml (25,000IU) by mouth every 2 weeks for 8 doses	£11.87	200,000IU	Off-label use of licensed product P.O.M.
12 years to 18 years	Dose Regime		10,000IU daily for 4-8 weeks		280,000-560,000IU	
Loading dose	1	Aciferol D3 tablet 10,000IU	1 tablet daily for 4-8 weeks	£11.19-£22.38 (after discount)	280,000-560,000IU	Unlicensed
	2, if compliance problems with daily dose	InVitaD3 25,000IU/ml unit dose ampoule	1ml by mouth every 2 weeks for 12 doses	£17.80	300,000IU	Off-label use of licensed product P.O.M.
Age	Options	Product (prescribe as brand)	Dosage	Cost of maintenance for one year	Average daily dose of vitamin D	Medico-legal category
0-1 year maintenance	1	ProD3 Liquid Drops 100IU/drop	4 drops daily	£32.00	400IU	Unlicensed medicine. Nutritional supplement. Available OTC.
1 to 18 years maintenance	1	ProD3 Liquid Drops 100IU/drop	4 drops daily	£32.00	400IU	Unlicensed medicine. Nutritional supplement. Available OTC.
	2 if compliance problems with daily dose	InVitaD3 25,000IU/ml unit dose ampoule	1ml (25,000IU) by mouth every 8 weeks	£12.83	446IU	Licensed product being used at off-label dose regime. P.O.M.

Management of vitamin D insufficiency:
serum 25(OH)D 30-50 nmol/L

- Patients to purchase products OTC; NOT to be prescribed.
- Products can be purchased from pharmacies, health food shops and on the internet.
- Some patients, e.g. pregnant women or parents of children under 4 years old, and some people on certain benefits or tax credits, are eligible for supplements via the government's Healthy Start scheme. For details see www.healthystart.nhs.uk
- Doses as per maintenance regimes following treatment of deficiency.
- Give lifestyle advice – see Appendix 1

Calcium supplementation:

The use of combined calcium and vitamin D3 supplementation has been found to reduce fracture rates in older people in residential/nursing homes and sheltered accommodation. Anti-fracture studies in patients with osteoporosis being treated with bisphosphonates show that combined calcium and vitamin D supplementation is associated with an improvement in mortality, which is not observed with vitamin D supplementation alone.⁶

The evidence based doses are 1g per day of calcium and around 800IU vitamin D.

Consideration should be given to the patient's dietary intake of calcium, possibly by using "calcium calculators" e.g. <http://www.rheum.med.ed.ac.uk/calcium-calculator.php>

- 1 pint of milk (skimmed, semi-skimmed or whole)) contains approximately 700mg calcium.
- 1 matchbox-sized serving of cheese contains approximately 200mg calcium.
- 1 small pot of yogurt contains approximately 150mg calcium.
- Sardines in oil contain 500mg calcium per 100g
- Tuna in oil contains 12mg calcium per 100g

If adult patients with osteoporosis are found not to be consuming at least 700mg calcium per day, calcium supplementation is recommended.⁴

- Calcium supplements are notoriously unpalatable for many patients, resulting in poor compliance. If this is the case, consider prescribing vitamin D alone and advise an increase in dietary calcium intake.
- Combined calcium and vitamin D preparations should not be used for the treatment of vitamin D deficiency as the high dose of vitamin D required will result in excess calcium being consumed.
- Refer to the formulary on Pathfinder <http://www.plain.pathfinder-rf.net/media/581846/primary-care-drug-formulary-september-14.pdf> [BNF Chapter 9] for the choice of combined calcium and vitamin D3 product to be prescribed.
- Generic "Calcium and Ergocalciferol tablets" should NOT be prescribed; the dose of calcium is inadequate (97mg per tablet), the vitamin D is ergocalciferol not colecalciferol, and they are expensive.

Vitamin D side-effects and toxicity:

Excessive intake of vitamin D leads to the development of raised plasma calcium and phosphate.

Symptoms of hypercalcaemia include anorexia, nausea and vomiting, headache, dry mouth, fatigue, muscle weakness, lassitude, diarrhoea or constipation, weight loss, polyuria, sweating, vertigo.

Vitamin D at doses below 10,000IU/day is not usually associated with toxicity; doses equal to or above 50,000IU/day for several weeks or months are frequently associated with toxicity.

Toxicity is not seen at serum vitamin D levels < 250nmol/L and is not usually a problem until serum 25(OH)D>500nmol/L.

The European Food Safety Authority concluded that an upper limit of 4000IU a day is safe for adults and children over 11 years of age.

Exercise caution if there is a history of renal calculi, renal impairment (CKD 3 or 4), or parathyroid disorders; refer for secondary care advice.

Yearly high-dose vitamin D is ineffective and may cause increased risk of fracture.⁵

Appendix 1

Lifestyle Advice:

Sunlight

- Exposure of face, arms and legs for 5-10 mins (15-25 mins if dark pigmented skin) would provide good source of Vitamin D. In the UK, April to September, between 11am and 3pm, will provide the best source of UVB.
- Application of sunscreen will reduce the Vitamin D synthesis by >95%. Advise to avoid sunscreen for the first 20-30 minutes of sunlight exposure.
- Persons wearing traditional black clothing can be advised to have sunlight exposure of face, arms and legs in the privacy of their garden.

Diet

- Vitamin D can be obtained from dietary sources (salmon, mackerel, tuna, egg yolk) fortified foods (cow, soy or rice milk) and supplements.
- There are no plant sources that provide a significant amount of Vitamin D naturally.

See also:

<https://www.gov.uk/government/publications/vitamin-d-for-healthcare-professionals-and-the-public>

for leaflets to download.

Direct links to the PDF documents:

- Leaflet for healthcare professionals:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390393/A5_Vitamin_D_leaflet_HCP_FINAL_19.12.14_.pdf
- Leaflet for the public:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390394/A5_Vitamin_leaflet_public_FINAL_22_12_14.pdf

To print in the form of an A5 leaflet, please select the 'booklet' option when printing from the PDF documents.

Appendix 2: Vitamin D Flow chart summary

Appendix 3: Patient leaflet for purchasing vitamin D OTC

References

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Approved by NPAG

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