



Treatment of Vitamin D Deficiency in Adults

Importance of vitamin D

- Vitamin D is essential for skeletal growth and bone health.
- Around 20% of adults and 8 to 24% of children may have low vitamin D status¹.
- Severe deficiency can result in rickets in children and osteomalacia in adults.

Risk factors for vitamin D insufficiency and deficiency

- Infants and children under 5
- Pigmented skin (non-white ethnicity)
- Pregnant and breastfeeding women, particularly teenagers and young women
- Lack of sunlight exposure
- People over 65
- Skin concealing garments or strict sunscreen use
- Multiple, short interval pregnancies
- Elderly or housebound or confined indoors for long periods.
- Vegan / vegetarian or high phytate consumption such as in chapatis
- Malabsorption (e.g., inflammatory bowel disease, coeliac disease, pancreatic insufficiency)
- Use of anticonvulsants, rifampicin, cholestyramine, anti-retrovirals, glucocorticoids
- Certain conditions e.g. liver or renal disease, cystic fibrosis
- Obesity (BMI > 30)

Sources of vitamin D^{2,3}

It is recommended that everyone over one year of age should consume 10 micrograms of vitamin D daily¹. It is essential that everyone, especially those people most at risk (see list above), are aware of the implications of vitamin D deficiency and what they can do to prevent it.⁴

- From March to October ultraviolet B (UVB) rays help people produce vitamin D. Increasing regular UVB sunlight exposure (to forearms, hands & lower legs)⁵, without sunscreen, for 10 to 15 minutes⁶, between 11am to 3pm (people with darker skin will need longer) helps maintain levels.
- From October to March, sunlight contains very little UVB wavelength the skin needs to make vitamin D so people rely on body stores from sunlight exposure in the summer and dietary sources to maintain vitamin D levels. Food sources include oily fish, cod liver oil, red meat, egg yolks and foods fortified with vitamin D: All infant & toddler formula milk, some breakfast cereals, soya products, dairy products, powdered milks and fat spreads e.g. margarine. Note: Increasing the dietary intake of vitamin D alone will not avoid the need for supplementation in patients with vitamin D deficiency.
- Pregnant women especially need to ensure their own requirement for vitamin D is met and that their baby is born with enough vitamin D for early infancy.

Prevention of vitamin D deficiency and insufficiency

It is important that people who find it hard to get enough vitamin D from the sun and their diet take a vitamin D supplement. Specific groups who may benefit from vitamin D supplementation are listed in the table below (Department of Health recommendations):

People at risk of vitamin D deficiency ^{2,3}	Daily vitamin D supplement
All pregnant and breastfeeding women	400 International Units (10 micrograms) / day
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 International Units (10 micrograms) / day
People aged 65 years and over (see elderly patients section)	400 International Units (10 micrograms) / day

Please Note: 1 microgram is equivalent to 40 International Units



Patients can be advised to buy over the counter vitamin D supplements or signposted to Healthy Start Clinics where Healthy Start Women's vitamins are available. These contain folic acid 400 micrograms, vitamin D 10 micrograms [400 International Units] and vitamin C 70 mg, and are suitable for vegetarians, free from milk, egg, gluten, soya and peanut residues. For more details of the scheme see: www.healthystart.nhs.uk

Clinical features of vitamin D deficiency

- Muscle pain
- Proximal muscle weakness
- Rib, hip, pelvis, thigh and foot pain are typical
- Fractures

Assessing the patient

Patient characteristics	Advice and management
Healthy, no risk factors, symptom free	No investigations required Lifestyle advice
Risk factors only	Lifestyle advice Consider long term preventative therapies
Risk factors AND clinical features (see management flowchart - Appendix 1)	Lifestyle advice Investigations Therapeutic intervention Long term preventative treatment

Investigations

Test	Reason
Renal function tests (U&E, eGFR)	To exclude renal failure. See note below on renal patients.
Liver function tests (including ALP)	To exclude hepatic failure.
FBC	Anaemia may be present if there is malabsorption.
PTH	To exclude primary hyperparathyroidism.
Calcium	To exclude hypercalcaemia and provide a baseline for monitoring. Hypocalcaemia may indicate long standing vitamin D deficiency.
Phosphate	Hypophosphataemia may indicate long standing vitamin D deficiency.
25-OH Vitamin D levels*	To determine vitamin D status

* Only measure if patient is symptomatic and has risk factors for Vitamin D deficiency.

Measurement, status and management (see Appendix 1 for flowchart)

Vitamin D level	Vitamin D status	Health effect	Management
<30 nmol/L	Deficient	Rickets, Osteomalacia	High dose colecalciferol then maintenance treatment
30 - 50 nmol/L	Insufficient	Associated with disease risk	Maintenance vitamin D supplements
50 - 75 nmol/L	Adequate	Healthy	Lifestyle advice
>75 nmol/L	Optimal	Healthy	None



Primary Care Only - Diagnosis and coding

If deficiency diagnosed use the Read code **C28 Vitamin D deficiency** (for audit purposes)

Contraindications for vitamin D

Patients with hypercalcaemia or metastatic calcification.

When to refer to secondary care

Atypical biochemistry	Renal stones
Atypical clinical manifestations or biochemistry	Sarcoidosis
Deficiency due to malabsorption	Short stature and skeletal deformity
Failure to respond to treatment after 3 months	Tuberculosis
Focal bone pain	Unexplained deficiency
Liver disease	Unexplained weight loss
Lymphoma	Parathyroid disorders
Metastatic cancer	

Monitoring

- Vitamin D can unmask previously undiagnosed primary hyperparathyroidism. This is usually done by measuring adjusted serum calcium which should be checked 1 month after completing the loading regimen or after starting vitamin D supplementation (or if symptoms of hypercalcaemia occur).
- For malabsorption patients adjusted serum calcium may need to be checked initially every two weeks.
- Routine monitoring of vitamin D levels is generally unnecessary for patients on long term maintenance vitamin D doses of up to 2,000 International Units/day. If there is a need to monitor vitamin D levels repeat after 3-6 months on recommended replacement therapy.⁷
- Whilst on maintenance vitamin D doses recheck bone profile and vitamin D levels if symptoms suggestive of vitamin D toxicosis or hypercalcaemia (confusion, polyuria, polydipsia, anorexia, vomiting or muscle weakness) are present.
- For patients on potent antiresorptive agent (e.g., denosumab or zoledronic acid) check vitamin D levels annually as per protocol.

Treatment regimes

1. Treatment of deficiency (25-OHD <30 nmol/L) - loading regime of colecalciferol followed by long term maintenance treatment

Used where rapid correction of vitamin D deficiency is required, e.g., symptomatic disease or before starting treatment with a potent antiresorptive agent (zoledronic acid, denosumab).

	Colecalciferol dose – licensed products only	Route	Length of course	Total loading dose	Preparation
First line	40,000 International Units, weekly (two capsules)	Oral	7 weeks	280,000 International Units	Colecalciferol 20,000 International Unit capsules (preferably after food)
First line	50,000 International Units, weekly (one 1ml plastic snap & squeeze ampoule)	Oral	6 weeks	300,000 International Units	Colecalciferol oral solution 50,000 International Units /ml
Second line - option for patients with compliance issues	3,200 International Units, daily (one capsule daily)	Oral	12-13 weeks	280,000 International Units	Colecalciferol 3,200 International Unit capsule



2. Treatment of insufficiency (25-OHD: 30-50 nmol/L) or long term maintenance after deficiency

	Colecalciferol Dose – licensed products only	Route	Duration of treatment	Preparations
First Line	20,000 International Units every four weeks	Oral	Indefinite	Colecalciferol 20,000 International Unit capsules (preferably after food)
First Line	25,000 International Units monthly (one 1ml plastic snap & squeeze ampoule)	Oral	Indefinite	Colecalciferol oral solution 25,000 International Units/ml
Second Line - option for patients with compliance issues	800 – 2,000 International Units daily (occasionally up to 4,000 International Units daily) ⁷	Oral	Indefinite	Colecalciferol 800 International Unit capsules <u>OR</u> advise to purchase over the counter vitamin D treatments.

A wide range of vitamin D preparations, in varying strengths are available to buy over the counter from pharmacies and health food shops. For patients not exempt from prescription charges these supplements are generally less expensive to purchase than to obtain on prescription. These products do not have a UK marketing authorisation and are marketed as nutritional supplements.

When prescribing please ensure that licensed products are used. For Primary Care - please follow advice provided by ScriptSwitch as recommendations are reviewed and amended periodically, indicating the most cost effective licensed products.

Special patient groups

Elderly Patients

The elderly are at increased risk of vitamin D deficiency due to a combination of factors including lower sun exposure and reduced capacity to generate vitamin D. The joint formulary for the management of osteoporosis recommends that calcium and vitamin D supplements should be prescribed routinely for mobile frail, elderly individuals who are housebound or care home patients. The recommended daily dose is Calcium 1 – 1.2g and vitamin D3 800 International Units. Secondary care clinicians should prescribe the formulary choices as indicated on Cerner.

Primary care clinicians should follow ScriptSwitch messages to prescribe the most cost-effective brand.

Calcium and Vitamin D Preparations

Generally (apart from elderly patients, as above) clinicians should avoid giving combined calcium and vitamin D preparations in the long term because the calcium component is unnecessary and unpalatable, reducing concordance. There may be an increased risk of some cardiovascular events in postmenopausal women who use calcium and vitamin D supplements to prevent osteoporotic fractures but no change to prescribing practice is currently recommended.⁸ Prescribers should provide calcium and vitamin D treatment for osteoporotic fractures in line with NICE guidance and should consider offering these supplements to patients who receive treatment for osteoporosis (e.g., with bisphosphonates), unless they are confident that the patient has an adequate calcium intake and is vitamin D replete.

Renal Patients

Patients with CKD should have their native Vitamin D replaced as per these guidelines, the exception being when they are also taking Vitamin D analogues (such as alfacalcidol) and in end stage renal failure, where advice should be sought from a renal consultant regarding replacement and monitoring requirements.

For further information please see - NICE clinical guideline CG182 on chronic kidney disease, published in 2014, which advises on which vitamin D preparations should be used and when, according to the stage of renal impairment. Available at <http://www.nice.org.uk/guidance/CG182>



Intestinal Malabsorption

Vitamin D deficiency caused by intestinal malabsorption or chronic liver disease usually requires vitamin D in pharmacological doses. A suggested regime for adult patients would be to use Ergocalciferol 300,000 IU by intramuscular injection, rechecking levels again after 3 months and repeating if required. Sometimes patients have been reversed at this stage so monthly injections for 3 months are not prescribed but repeat levels would always be checked before giving another injection.

Patients on Anti-epileptic medication

Long-term use of anti-epileptic drugs (in particular carbamazepine, phenytoin, phenobarbital, primidone and sodium valproate)⁹ is associated with decreased bone mineral density that may lead to osteopenia, osteoporosis, and increased fractures in at-risk patients. Vitamin D status should be assessed and patients treated according to their level (see Appendix 1). NICE clinical guideline CG137 on epilepsy, published in 2012, advises full blood count, electrolytes, liver enzymes, vitamin D levels, and other tests of bone metabolism (e.g., serum calcium and alkaline phosphatase) every 2–5 years for adults taking enzyme-inducing drugs. Available at <http://www.nice.org.uk/guidance/CG137>

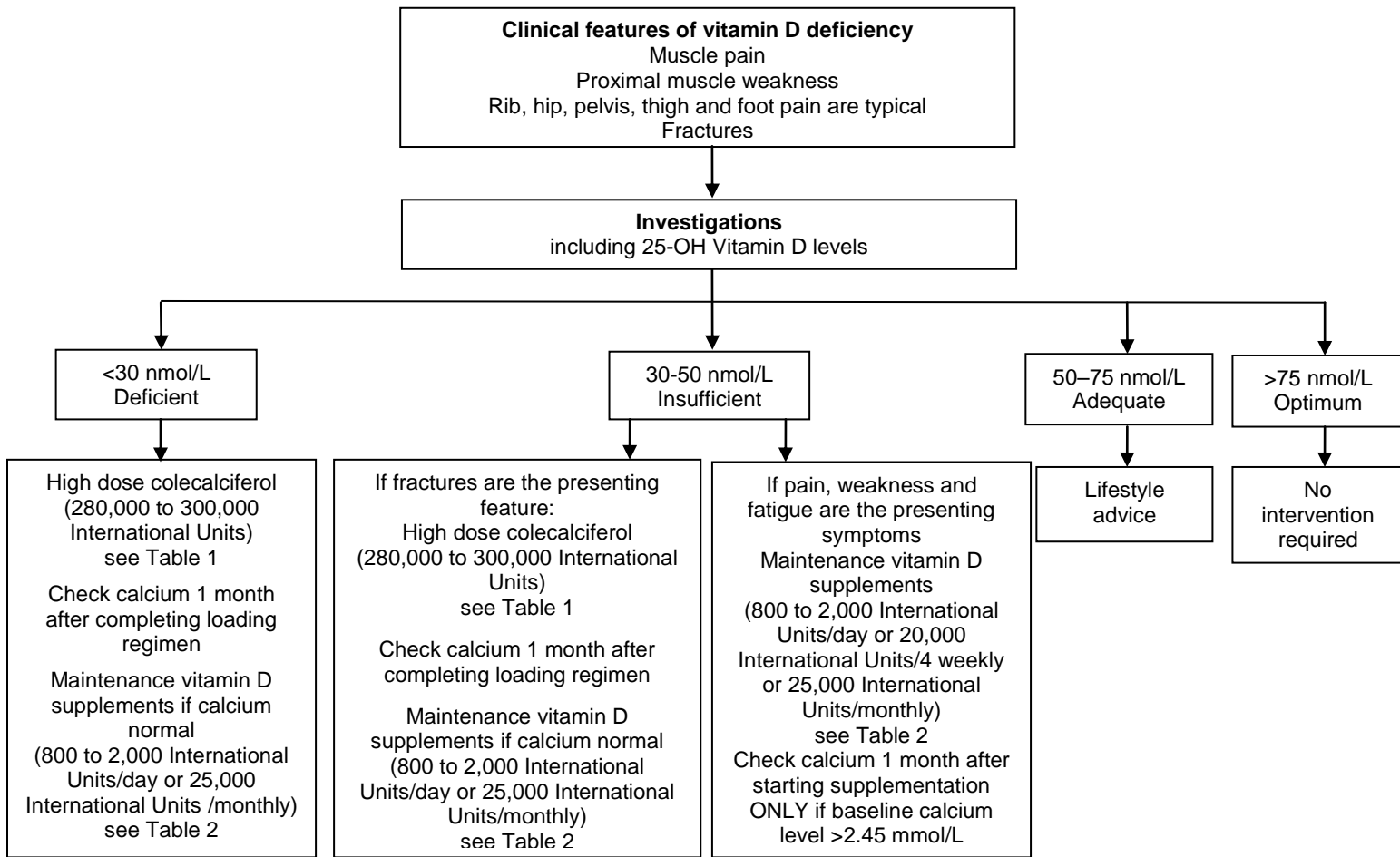
Other Drugs

In addition to anti-epileptic medication, there is an increased breakdown of vitamin D with other drugs including rifampicin, highly active antiretroviral treatment and glucocorticoids.

References

1. NICE public health guidance 56. Vitamin D: increasing supplement use among at-risk groups. National Institute for Health and Clinical Excellence. Published November 2014. Last Updated May 2017. Available at: www.nice.org
2. Public Health England. Vitamin D - Important information for healthcare professionals. December 2014. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390393/A5_Vitamin_D_leaflet_HCP_FINAL_19.12.14_.pdf
3. UK Chief Medical Officers Communication. Vitamin D advice on supplements for at risk groups, 2 Feb 2012. Accessed via <https://www.cas.dh.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=101726>
4. Update on Vitamin D: Position statement by the Scientific Advisory Committee on Nutrition, 2007. Accessed via; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/339349/SACN_Update_on_Vitamin_D_2007.pdf
5. NICE guidance (NG34). Sunlight Exposure: risks and benefits National Institute for Health and Clinical Excellence. February 2016. Available at: <https://www.nice.org.uk/guidance/ng34>
6. NHS Choices. How to get vitamin D from sunlight. Accessed via; <http://www.nhs.uk/Livewell/Summerhealth/Pages/vitamin-D-sunlight.aspx>
7. National Osteoporosis Society. Vitamin D and Bone Health: A practical clinical guideline for patient management. April 2013. <https://nos.org.uk/media/2073/vitamin-d-and-bone-health-adults.pdf>
8. Drug Safety Update April 2009; vol 2, issue 9
9. Drug Safety Update Oct 2011; vol 5, issue 3

Appendix 1: Quick guide to vitamin D levels and management (for patients with risk factors AND clinical features)



Hypercalcaemia

If calcium levels are elevated:

1. Stop any calcium containing vitamin D supplements.
2. Delay further vitamin D loading, and repeat calcium levels 2 weekly until normalises.
3. Continue loading and check calcium levels every 4 weeks until loading completed.
4. If calcium levels are persistently elevated despite stopping calcium containing supplements check PTH and refer to endocrinology (possibly unmasked primary hyperparathyroidism).

Table 1

	Colecalciferol dose – licensed products only	Route	Length of course	Total loading dose	Preparation
First line	40,000 International Units weekly (two capsules)	Oral	7 weeks	280,000 International Units	Colecalciferol 20,000 International Unit capsules (preferably after food)
First line	50,000 International Units weekly (one ampoule)	Oral	6 weeks	300,000 International Units	Colecalciferol oral solution 50,000 International Units/ml (1ml plastic snap & squeeze ampoule)
Second line*	3,200 International Units daily (one capsule)	Oral	12-13 weeks	280,000 International Units	Colecalciferol 3,200 International Unit capsules

Table 2

	Colecalciferol Dose – licensed products only	Route	Duration of treatment	Preparations
First Line	20,000 International Units every four weeks	Oral	Indefinite	Colecalciferol 20,000 International Unit capsules (preferably after food)
First Line	25,000 International Units monthly	Oral	Indefinite	Colecalciferol oral solution 25,000 International Units /ml (1ml plastic snap & squeeze ampoule)
Second Line*	800 – 2,000 International Units daily (occasionally up to 4,000 International Units daily) ⁷	Oral	Indefinite	Colecalciferol 800 International Unit capsules <u>OR</u> advise to purchase over the counter vitamin D treatments.

*NB - option for patients with compliance issues.