

Vitamin D

Nationally £31.8 million is spent annually on prescribing vitamin D as colecalciferol (D3) or ergocalciferol (D2); approximately £2 million of this is spent on special order products; £28.1 million on low or moderate dose ($\leq 20,000$ units) vitamin D preparations. (NHSBSA July to September 2020).

Medicines optimisation projects in this area focus on reducing the prescribing of unlicensed or special versions of vitamin D products and health supplements for cost and safety reasons by reviewing the continued need and deprescribing where appropriate, recommending self care or switching to a cost-effective, licensed preparation now that more are available.

This bulletin offers advice on the treatment and prevention of deficiency with recommendations for self care, where appropriate, for organisations considering reviewing vitamin D as a medicines optimisation project. Vitamin D and its role in COVID-19 is also discussed.

Recommendations

- Do not routinely test for vitamin D deficiency unless the patient is symptomatic, at very high risk of deficiency or there is a clinical reason to do so. When a vitamin D test is indicated, use plasma 25-hydroxyvitamin D [25(OH)D] to measure vitamin D status.
- Self care with over the counter (OTC) licensed vitamin D supplements should be recommended, if appropriate, for those who are at risk of vitamin D deficiency, patients that are insufficient and for the general UK population as maintenance therapy, especially during autumn and winter months.
- A Reference Nutrient Intake (RNI) of 400 IU/daily (10 micrograms daily) vitamin D, throughout the year, for everyone in the general UK population aged four years and above is recommended. This includes pregnant and lactating women and population groups at increased risk of vitamin D deficiency.
- A 'Safe Intake' of 340-400 IU/daily (8.5-10 micrograms daily) for ages 0-1 year (including exclusively breast fed and partially breast fed infants, from birth); and 400 IU/daily (10 micrograms daily) for ages one to four years is recommended.
- Babies receiving more than 500ml per day of infant formula do not require vitamin D supplements.
- For the treatment of vitamin D deficiency (plasma 25(OH)D < 25 nmol/L), agree local vitamin D guidelines with local clinicians based on Scientific Advisory Committee on Nutrition (SACN), NICE PH56 and the Royal Osteoporosis Society (ROS) guidance to ensure that all healthcare professionals are recommending cost effective products, prescribed by brand name, appropriate doses and duration of treatment to treat deficiency. Consideration should be given to patients with special dietary needs. (see attachments 2 and 3 for locally adaptable templates).
- Where a treatment course is needed this should be prescribed as an acute medication, do not prescribe this on repeat.
- The Royal Osteoporosis Society recommends that oral vitamin D3 is the treatment of choice in vitamin D deficiency and therefore oral colecalciferol should be prescribed.

Recommendations

- Rapid correction of vitamin D deficiency is recommended for people that are symptomatic or are about to start treatment with a potent antiresorptive agent (zoledronic acid, denosumab or teriparatide).
- Once vitamin D deficiency has been corrected, maintenance therapy is recommended. This does not need to be prescribed; vitamin D supplements can be bought cheaply and easily. Only prescribe if self care is not appropriate, e.g. patient is not capable, diagnosed and documented long term conditions (osteoporosis).
- Review all patients on long-term high dose treatment for continued need. If a treatment course has been completed, discontinue treatment and advise the patient to continue maintenance treatment as self care, if appropriate (as above).
- Some people inadequate in vitamin D (confirmed plasma 25(OH)D 25nmol/L- 50nmol/L) may be prescribed vitamin D only if self care is not appropriate, e.g. patient is not capable, diagnosed and documented long term conditions (osteoporosis) or certain concurrent medications (antiresorptive medication; antiepileptic drugs, e.g. carbamazepine; oral glucocorticoids, e.g. dexamethasone).
- Consider the risks and benefits of prescribing licensed preparations or food supplements for vitamin D deficiency. These should be prescribed by brand to ensure the correct product and dose is issued. Unlicensed specials for vitamin D should not be prescribed as there are now many licensed products available. Consider GMC Guidance on prescribing unlicensed medicines.
- Consider patient compliance and concordance when selecting a vitamin D preparation for the treatment of an established deficiency.

Background

Vitamin D is a fat-soluble vitamin that regulates calcium and phosphate homeostasis and is therefore vital for musculoskeletal health. There are two main forms: vitamin D3 (colecalciferol) and D2 (ergocalciferol). Vitamin D3 is synthesised in the skin by the action of sunlight. Both vitamin D3 and D2 can be obtained from natural foods (which are limited and are mostly from animal sources), fortified foods, and food supplements.¹ Vitamin D can be expressed in international units (IU) and micrograms; [an online tool](#) can be used for conversions.

Dietary and cutaneous vitamin D are biologically inactive and require enzymatic conversion. Firstly, in the liver to 25-hydroxyvitamin D (25(OH)D) (the main circulating metabolite), then to 1,25-hydroxyvitamin D (1,25(OH)2D) (the active metabolite), in the kidneys and other tissues.¹

Severe vitamin D deficiency can result in rickets in children. There have been concerns that rickets may be re-emerging among children in the UK. It can also result in osteomalacia in children and adults and hypocalcaemia in children. In addition, low vitamin D status has been associated with some diseases and other long-term conditions such as osteoporosis, diabetes and some cancers, although the evidence is inconclusive.²

Dietary sources of vitamin D are limited, and oily fish is the only significant source. Small amounts are provided by egg yolk, red meat and fortified foods, such as formula milks for infants and toddlers, some breakfast cereals and fat spreads (margarine). The major natural source is from skin synthesis following exposure to sunlight. However, from October to the beginning of April in the UK there is no ambient ultraviolet sunlight of the appropriate wavelength for skin synthesis of vitamin D. During this time, the population relies on both body stores from sun exposure in the summer and dietary sources to maintain vitamin D status. National surveys suggest that around one fifth of adults and 8% to 24% of children (depending on age and gender) may have low vitamin D status.³

Vitamin D status and its role in the COVID-19 pandemic

Vitamin D may have immune supporting properties through modulation of both the adaptive and innate immune system through cytokines and regulation of cell signalling pathways. It has been hypothesised that vitamin D status may influence the severity of responses to COVID-19 and the prevalence of vitamin D deficiency in Europe will be closely aligned to COVID-19 mortality.⁴ The evidence for any association between vitamin D status and the development of COVID-19 is covered later in this bulletin.

The current advice from the NHS is for all children over the age of one year and adults to consider taking a supplement of 400 IU/(10micrograms) of vitamin D daily. Babies up to the age of one year need 8.5 to 10 micrograms of vitamin D a day, except formula-fed babies having >500mls formula a day, as infant formula is fortified with vitamin D. This is to help keep bones, teeth and muscles healthy and decrease the risk of rickets and osteomalacia, due to insufficient vitamin D from sunlight, if they are indoors most of the day; it is not because vitamin D reduces the risk of COVID-19, as the evidence is currently inconclusive – see discussion of evidence later in this bulletin.^{5,6}

National guidance

Who should be tested for vitamin D deficiency?

The Royal Osteoporosis Society (ROS) has produced the following guidance:

- Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management.⁷
- Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. The quick guide, (for use in conjunction with full guideline), available via <https://theros.org.uk/clinical-publications-and-resources/>
- Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management in Children and Young People.⁸

These guidelines recommend that the measurement of plasma 25-hydroxyvitamin D (25(OH)D) is the best way of estimating vitamin D status. Routine monitoring of 25(OH)D status is not required in either asymptomatic healthy individuals or those at higher risk of vitamin D deficiency. The ROS guidelines recommend that the following adults should be tested for vitamin D deficiency:⁷

- Patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency.
- Patients suspected of having bone diseases that may be improved with vitamin D treatment.
- Patients with bone diseases, prior to specific treatment where correcting vitamin D deficiency may be necessary.

However, in most cases routine vitamin D testing is unnecessary in patients with osteoporosis or fragility fracture, who may be co-prescribed vitamin D supplementation with an oral antiresorptive treatment.⁷

The ROS guidelines for children and young people recommend that routine vitamin D testing is not recommended in children and young people unless there is a clear indication for measurement, including where there are/is:⁸

- Symptoms and signs of rickets, e.g. progressive bowing of legs and knock knees, wrist swelling, rachitic rosary, craniotabes, delayed tooth eruption and enamel hypoplasia.
- Other symptoms or conditions associated with vitamin D deficiency, e.g. unexplained bone pain >3 months, muscular weakness, tetany, seizures and cardiomyopathy.
- Abnormal investigations, e.g. low plasma calcium or phosphate, high alkaline phosphatase, radiographs showing osteopenia, rickets or pathological fractures.
- Chronic disease that may increase risk of deficiency, e.g. chronic renal and/or liver disease, malabsorption syndromes (e.g. coeliac disease, Crohn's disease, cystic fibrosis).
- Treatment with bone-targeted drugs that require vitamin D sufficiency, e.g. bisphosphonates.

See attachments 2 and 3 for locally adaptable Vitamin D pathways which include guidance on when it is necessary to test vitamin D levels.

The National Institute for Health and Care Excellence (NICE) have produced a Public Health guideline (PH56 Vitamin D: supplement use in specific population groups), which aims to increase supplement use to prevent vitamin D deficiency in specific population groups. This guidance also recommends that vitamin D status should not be routinely tested unless; there are symptoms of deficiency, people are at high risk of deficiency (for example, they have very low exposure to sunlight) or there is a clinical reason to do so (for example, they have osteomalacia or have had a fall).²

Who will benefit from vitamin D supplements?

The ROS guidance proposes that the following vitamin D thresholds are adopted by UK practitioners in respect to bone health:⁷

- Plasma 25(OH)D < 25 nmol/L is **deficient**: treatment is recommended.
- Plasma 25(OH)D of 25–50 nmol/L may be **inadequate (insufficient)** in some people – see further discussion below
- Plasma 25(OH)D > 50 nmol/L is **sufficient** for almost the whole population. For these patients, provide reassurance and give appropriate advice regarding maintaining vitamin D levels, through safe sun exposure and diet.

For patients that are **insufficient** and have a plasma 25(OH)D of between 25–50 nmol/L treatment with vitamin D is recommended in patients with the following:⁷

- Fragility fracture, documented osteoporosis or high fracture risk.
- Treatment with antiresorptive medication, e.g. zoledronic acid for bone disease.
- Symptoms suggestive of vitamin D deficiency.
- Increased risk of developing vitamin D deficiency in the future because of reduced exposure to sunlight, religious/cultural dress code, dark skin, etc.
- Raised parathyroid hormone.
- Medication with antiepileptic drugs, (e.g. carbamazepine), or oral glucocorticoids, (e.g. dexamethasone).

Where rapid correction of vitamin D **deficiency** (plasma 25(OH)D < 25 nmol/L), for patients that are symptomatic or who are about to start treatment with a potent antiresorptive agent (zoledronic acid or denosumab or teriparatide), ROS guidelines recommend a treatment regimen based on fixed loading doses followed by regular maintenance therapy as follows:⁷

- A loading regimen to provide a total of approximately 300,000 IU (7,500 micrograms) vitamin D, given either as separate weekly or daily doses over six to ten weeks.

The following options are suggested:⁷

- 50,000 IU (1,250 micrograms) tablets, capsules or liquid once weekly for six weeks (300,000 IU / 7,500 micrograms).
- 40,000 IU (1,000 micrograms) given weekly for seven weeks (280,000 IU / 7,000 micrograms).
- 1,000 IU (25 micrograms) tablets, four a day for ten weeks (280,000 IU / 7,000 micrograms).
- 800 IU (20 micrograms) capsules, five a day given for ten weeks (280,000 IU / 7,000 micrograms).
- Maintenance therapy comprising vitamin D in doses equivalent to 800–2,000 IU/daily (20 – 50 micrograms daily) occasionally up to a maximum of 4,000 IU/daily (100 micrograms), given either daily or intermittently at higher doses. Maintenance regimens should generally be started one month after the loading regimen has been completed.⁷

When correction of vitamin D deficiency is less urgent and when co-prescribing vitamin D supplements with an oral anti-resorptive agent, maintenance therapy may be started without the use of a loading dose(s).⁷

The SACN reviewed the dietary reference values (DRVs) for vitamin D intake in the UK population in 2016.⁹ They recommended that the serum 25(OH)D concentration of all individuals in the UK should not fall below 25nmol/L at any time of the year. The people at increased risk of having a serum 25(OH)D concentration <25nmol/L are those:

- With minimal sunshine exposure as a result of not spending time outdoors (e.g. frail and institutionalised people)
- Habitually wearing clothing that covers most of the skin while outdoors
- From minority ethnic groups with dark skin.⁹

England guidance

Based on the SACN recommendations Public Health England (PHE) advises a reference nutrient intake (RNI) for vitamin D of 400 IU/daily (10 micrograms daily), throughout the year, for everyone in the general UK population aged four years and above. This is the average amount needed by 97.5% of the population to maintain a serum 25(OH)D concentration \geq 25nmol/L when UVB sunshine exposure is minimal. It refers to average intake over a period of time (e.g. a week) and takes account of day-to-day variations in vitamin D intake. The recommendation includes pregnant and lactating women and the population groups at increased risk of having a serum 25(OH)D concentration <25nmol/L. There is insufficient data to set RNIs for infants and children aged under four years so as a precaution, SACN recommended a 'Safe Intake' of vitamin D of 340-400 IU/daily (8.5-10 micrograms daily) for ages 0 up to one year (including exclusively breast fed and partially breast fed infants, from birth); and 400 IU/daily (10 micrograms daily) for ages one to four years.⁹ Babies receiving infant formula do not require supplements if receiving more than 500ml of formula per day.⁹

The RNI/'Safe Intake' for vitamin D refers to intakes from all dietary sources: natural food sources; fortified foods (including infant formula milk); and supplements. Since it is difficult to achieve the RNI/'Safe Intake' from natural food sources alone, the SACN recommended that the UK Government gives consideration to strategies for the UK population to achieve the recommended levels.⁹ Vitamin D supplements or vitamin drops containing vitamin D (for under 5s) can be bought in many shops, including pharmacies and supermarkets. Women and children who qualify for the Healthy Start scheme can get free supplements containing the recommended amounts of vitamin D.⁵ The [Healthy Start website](#) has full details on the scheme.

From January 2021 in England, all care homes will automatically receive four months' supply of vitamin D supplements for their residents to last through the winter. Individuals on the clinically extremely vulnerable list will receive a letter inviting them to opt in for a supply of vitamin D supplements to be delivered directly to their homes starting in January 2021. Anyone who is able to purchase a vitamin D supplement should start taking them immediately if advised to do so, even if they are eligible for a delivery from January.¹⁰ The [Vitamin D and clinically extremely vulnerable \(CEV\) guidance](#) provides further information.

Scottish guidance

The Scottish Intercollegiate Guidelines Network (SIGN)/Health Improvement Scotland guidelines for the management of osteoporosis and the prevention of fragility fractures advise that adults and children over five years old should consider taking daily vitamin D supplementation 400 IU/daily (10 micrograms daily) from October to March.¹¹ Also, people at greatest risk of vitamin D deficiency should be advised to take a daily supplement of 340-400 IU/daily (8.5-10 micrograms daily) of vitamin D throughout the year. However, there is insufficient evidence to support widespread vitamin D supplementation or fortification

of foodstuffs with vitamin D for the general population due to possible long-term harms from raised vitamin D levels.¹¹ The Scottish Government factsheet advises that everyone (including children - unless receiving more than 500ml of infant formula a day) should consider taking a daily supplement containing 400 IU/daily (10 micrograms daily), specifically if higher risk of vitamin D deficiency.¹²

Wales guidance

The Welsh Government have also issued advice on vitamin D based on the SACN recommendations and advise the following in relation to how vitamin D should be obtained:¹³

- Infants and babies should have a supplement unless they receive more than 500mls of formula a day.
- Children aged one to four should be given a daily supplement containing 400 IU/daily (10 micrograms daily) vitamin D and some children aged up to four may be entitled to free Healthy Start® vitamin drops.
- Ages five years and above:
 - » Between late March/early April and September, the majority of people will probably obtain sufficient vitamin D from sunlight and foods so they might choose not to take a vitamin D supplement during these months.
 - » From October to March everyone will need to rely on dietary sources of vitamin D. Since vitamin D is found only in a small number of foods, everyone, including pregnant and breastfeeding women, should consider taking a daily supplement containing 400 IU/daily (10 micrograms daily) of vitamin D.
- Some groups of people with very little or no sunshine exposure will not obtain enough vitamin D from sunlight. People from these groups should take a daily supplement containing 400 IU/daily (10 micrograms daily) vitamin D throughout the year.

They are:

- » People who are seldom outdoors such as frail or housebound individuals and those who are confined indoors e.g. in institutions such as care homes.
- » People who habitually wear clothes that cover most of their skin while outdoors.
- » People from minority ethnic groups with dark skin such as those of African, African-Caribbean and South Asian origin might not get enough vitamin D from sunlight in summer so they should consider taking a daily supplement containing 400 IU/daily (10 micrograms daily) vitamin D throughout the year.¹³

Families who are not eligible for free Healthy Start® vitamins can be signposted to their local pharmacy for help with choosing an appropriate product. Most families will need to purchase these rather than have them prescribed by a GP.¹³

Table 1: Summary of national guidance.^{7,8,11-13}

Guidance	25(OH)D <25nmol/L	25(OH)D 25–50nmol/L	25(OH)D >50nmol/L
ROS and NICE PHE Guidance ^{2,7}	Treatment recommended	Treatment recommended in certain patients	Reassurance and advice on maintaining adequate vitamin D levels.
SACN & NHS Guidance ^{5,9}	Not considered as part of SACN Review	Not considered as part of SACN review	340-400 IU/daily (8.5-10 micrograms daily) for ages 0 up to one year and 400 IU/daily (10 micrograms daily) >1 year bought over the counter.

Guidance	25(OH)D <25nmol/L	25(OH)D 25–50nmol/L	25(OH)D >50nmol/L
SIGN ^{11,12}	Not considered as part of SIGN guidance	Not considered as part of SIGN guidance	400 IU/daily (10 micrograms daily) from October to March. People at greatest risk of vitamin D deficiency should take 340-400 IU/daily (8.5-10 micrograms daily) every day, throughout the year.
Scottish Government Factsheet ¹²			340-400 IU/daily (8.5-10 micrograms daily) for ages 0 to one year and 400 IU/daily (10 micrograms daily) specifically if at higher risk of vitamin D deficiency.
Welsh Government ¹³	Based on SACN review, therefore not considered	Based on SACN review, therefore not considered	340-400 IU/daily (8.5-10 micrograms daily) for ages 0 to one year and 400 IU/daily (10 micrograms daily) one to four years bought over the counter. Late March to September, the majority of people will probably obtain sufficient vitamin D from sunlight and foods so they might choose not to take a vitamin D supplement. From October to March everyone should consider taking a daily supplement containing 400 IU (10 micrograms) of vitamin D.

Clinical effectiveness - Vitamin D and COVID-19

The novel disease COVID-19, caused by severe acute respiratory syndrome coronavirus SARS-CoV-2, is now a pandemic with devastating implications for populations, healthcare systems, and economies globally.¹⁴ COVID-19 mortality disproportionately impacts older people, people in care homes, males, and BAME (Black, Asian and Minority Ethnic) UK individuals (specifically Bangladeshi, Chinese, Indian, Pakistan, Other Asian, Black Caribbean, and Other Black ethnicity).¹⁵ Concerns about a possible association between ethnicity and outcome were raised after the first 10 doctors in the UK to die from COVID-19 were identified as being from ethnic minorities. These concerns were confirmed by observational data from the Intensive Care National Audit and Research Centre, showing that a third of COVID-19 patients admitted to critical care units are from an ethnic minority background.¹⁴ Obesity is also a strong COVID-19 risk factor, as are co-morbidities, including diabetes, hypertensive diseases, chronic kidney disease, chronic obstructive pulmonary disease and dementia.¹⁵

Evidence of the link of vitamin D to COVID-19 is still being researched with larger scale trials needed.¹⁵ Some of the evidence gathered is discussed below.

In 2017, Adrian Martineau et al, conducted a systematic review and meta-analysis of individual participant data from 25 randomised controlled trials with a total of 11,321 participants (aged 0 to 95 years) assessed the overall effect of vitamin D supplementation on the risk of acute respiratory tract infections. Outcome data for the primary analysis of proportion of participants experiencing at least one acute respiratory tract infection were obtained for 10,933 (96.6%) of the randomised participants. Vitamin D supplementation was associated with a statistically significant reduction in the proportion of participants experiencing at least one acute respiratory tract infection; (adjusted odds ratio 0.88, 95% confidence interval 0.81 to 0.96; P=0.003; P for heterogeneity <0.001). In subgroup analysis, n=5133 participants; protective effects were seen in those receiving daily or weekly vitamin D without additional bolus doses (adjusted odds ratio 0.81, 95% CI 0.72 to 0.91) p<0.001, but not in those receiving one or more bolus doses (n= 5800, adjusted odds ratio 0.97, 95% CI 0.86 to 1.10; P=0.067 within subgroup, P for interaction=0.05). Among those receiving daily or weekly vitamin D, protective effects were stronger in those with baseline 25(OH)D levels <25nmol/L (n=234; adjusted odds ratio 0.30, 95% CI 0.17 to 0.53; P<0.001) than in those with baseline 25(OH)D levels ≥25nmol/L (n=1603; adjusted odds ratio 0.75, 95% CI 0.60 to 0.95; P=0.02 for subgroup analysis, P for interaction=0.006). Vitamin D did not influence the

proportion of participants experiencing at least one serious adverse event ($n=11224$; adjusted odds ratio 0.98, 95% CI 0.80 to 1.20, $P=0.83$). The body of evidence contributing to these analyses was assessed as being of high quality. The review authors concluded that vitamin D supplementation was safe, and it protected against acute respiratory tract infection overall. Patients who were very vitamin D deficient and those not receiving bolus doses experienced the most benefit.¹⁶

Grant et al. reviewed the evidence that vitamin D supplementation could reduce the risk of influenza and COVID-19 infections and deaths. They concluded that the evidence which supported the role of vitamin D in reducing risk of COVID-19 included:¹⁷

- The outbreak occurred in winter, a time when 25(OH)D concentrations are lowest.
- The numbers of cases in the Southern hemisphere near the end of summer are low.
- Vitamin D deficiency has been found to contribute to acute respiratory distress syndrome.
- Case-fatality rates increase with age and with chronic disease comorbidity, both of which are associated with lower 25(OH)D concentration.

To reduce the risk of infection, it is recommended that people at risk of influenza and/or COVID-19 consider taking 10,000 IU/daily (250 micrograms daily) of vitamin D3 for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5,000 IU/daily (125 micrograms daily). The goal should be to raise 25(OH)D concentrations above 100–150nmol/L. For treatment of people who become infected with COVID-19, higher vitamin D3 doses might be useful.¹⁷

Randomised controlled trials and large population studies should be conducted to evaluate the recommendation that a vitamin D supplementation could possibly improve clinical outcomes of patients infected with COVID-19.¹⁷

University Hospital, Angers France is currently conducting a multicentre randomised controlled trial of high dose versus standard dose vitamin D3 in high-risk COVID-19 patients; (CoVitTrial). This trial due to be completed in April 2021. It is hoping to recruit 260 high risk participants aged 65 years and older either receiving colecalciferol 200,000 IU ((5,000 micrograms) high dose) or colecalciferol 50,000 IU ((1,250 micrograms) standard dose) and aims to assess if high-dose vitamin D supplementation improves the prognosis of older patients diagnosed with COVID-19 compared to a standard dose of vitamin D.¹⁸

In the UK, the COVIDENCE observational study aims to investigate how diet and lifestyle factors might influence transmission of SARS-CoV-2, severity of COVID-19 symptoms, speed of recovery, and any long-term effects. It is currently recruiting at least 12,000 people and to obtain interim results by the summer.^{19,20}

A recent report from researchers at Trinity College, Dublin found that vitamin D may play a role in preventing serious respiratory infections and supporting immune functions.²¹ The authors hoped by compiling the report, the information could help in the mitigation of the negative health consequences of COVID-19 and concluded that, if vitamin D status is sufficient, it could benefit vulnerable adults in particular those aged 70+ years and older who are 'cocooning' during the COVID-19 outbreak.²²

A literature review completed and published by the University of Oxford conversely concluded that there was no evidence related to vitamin D deficiency predisposing to COVID-19, nor were there studies of supplementation for preventing or treating COVID-19. There is some evidence that daily vitamin D3 supplementation over weeks to months may prevent other acute respiratory infections, particularly in people with low or very low vitamin D status. This evidence has limitations, including heterogeneity in study populations, interventions, and definitions of respiratory infections that include upper and lower respiratory tract involvement.²³

NICE

NICE have also published a COVID-19 rapid evidence summary looking at the association between vitamin D status and development of COVID-19. They reviewed evidence from five published studies in peer reviewed journals. One was an observational cohort study, three were observational prognostic studies involving published data sets using correlation or regression analysis and one was a retrospective case-control survey. None of the studies were intervention trials.²⁴

Four of the studies found an association or correlation between a lower vitamin D status and subsequent development of COVID-19. However, confounders such as body mass index (BMI) or underlying health conditions, which may have independent correlations with vitamin D status or COVID-19, were not adjusted for. The largest UK study found an association between vitamin D status and COVID-19 only in a univariable analysis (with this single potential causative factor). Importantly, no causal relationship between vitamin D status and COVID-19 was found after adjustment for confounders such as comorbidity, socio-demographics, ethnicity, BMI and other baseline factors.²⁴

The rapid evidence summary concluded that there is no evidence to support taking vitamin D supplements to specifically prevent or treat COVID-19.²⁴ However, all people should continue to follow UK Government advice on daily vitamin D supplementation to maintain bone and muscle health during the COVID-19 pandemic.^{5,24}

Clinical effectiveness - Vitamin D and calcium

A recent review considered the evidence for vitamin D and calcium for osteoporosis in older people. Vitamin D and calcium are often thought of together and frequently co-prescribed, but they are fundamentally different entities so the adequacy of supply of each should be considered separately.²⁵

Circulating parathyroid hormone (PTH) levels are inversely related to calcium intake, so an increase in calcium intake result in falls in both PTH and bone turnover. As a result, calcium supplementation increases bone mineral density (BMD) by about 1% in the first year of use, but there is no further increase subsequently. This non-cumulative benefit probably represents a filling in the osteoclastic bone resorption space. Meta-analyses of the effects of vitamin D supplementation on BMD have been negative, but recent studies demonstrate that when baseline circulating levels of 25(OH)D is <30nmol/L, increases in BMD of 1-2% result from vitamin D supplementation. Individuals starting above this level show no BMD response to supplementation, indicating that they are vitamin D replete. Therefore, vitamin D supplements only improve BMD and prevent fractures when marked deficiency is present.²⁵

Seven larger trials of supplementation with calcium (with or without vitamin D) were reviewed, one study found a substantial reduction in the incidence of both hip and total fractures, whereas none of the other studies reproduced this finding. The one trial where fracture was reduced was carried out in severely vitamin D-deficient, elderly women living in nursing homes. Mean levels of 25(OH)D in the placebo group during the study were about 14nmol/L. This implies that many of these women were at risk of osteomalacia and that the dramatic fracture response to the intervention represents the effects of treatment of osteomalacia rather than of osteoporosis. Trials of vitamin D supplementation alone do not show reduced fracture risk, but it should be noted that most studies were in populations that would not currently consider to be vitamin D deficient. In general, these results are consistent with the BMD findings, indicating that in the presence of demonstrable vitamin D deficiency, supplementation with vitamin D is beneficial. In other circumstances, calcium, vitamin D or their combination is without effect.²⁵

Safety

Until recently there have been limited licensed vitamin D products available, but now there is a much larger range of licensed vitamin D products listed in the British National Formulary (BNF).²⁶ The term 'unlicensed medicine' is used to describe medicines that are used outside the terms of their UK licence (sometimes described as 'off-license/label') or which have no licence for use in the UK. Licensed products

should always be considered first line over unlicensed alternatives, unless there is a good clinical reason, which makes an unlicensed medicine the most appropriate option for an individual patient. Consequently, unlicensed specials for vitamin D should not be prescribed in-line with the General Medical Council (GMC) Guidance on prescribing unlicensed medicines See GMC Guidance for further information on prescribing unlicensed medicines.²⁷

People with the following should not take systemic vitamin D and analogues as they are contraindicated:^{26,28}

- Hypercalcaemia and/or hypercalciuria
- Metastatic calcification
- Calcium nephrolithiasis
- Nephrocalcinosis
- D-hypervitaminosis
- Severe renal impairment

Prescribers should take care to ensure that the correct dose is prescribed in infants.²⁶

Renal impairment

Vitamin D may be given to patients with impaired renal function with caution. In this case monitoring of calcium and phosphate levels is necessary, and the risk of soft tissue calcification should be taken into consideration.^{26,28} In severe renal deficiency, colecalciferol is not metabolised and other forms of vitamin D should be used.²⁸

Pregnancy and breastfeeding

The recommended daily intake for pregnant women is 400 IU (10 micrograms), however, in women who are considered to be vitamin D deficient a higher dose may be required, and the advice of a medical practitioner should be followed.²⁸ Daily vitamin D intake during pregnancy should not exceed 600 IU (15 micrograms). Overdoses of vitamin D have been shown to have teratogenic effects in animal experiments, but therapeutic doses are unlikely to be harmful.²⁸

Caution is required with high doses when breastfeeding as this may cause hypercalcaemia in the infant; serum-calcium concentration should be monitored.²⁶

Side-effects

Common or very common side effects of colecalciferol include abdominal pain; headache; hypercalcaemia; hypercalciuria; nausea and skin reactions. Uncommon side-effects are decreased appetite; constipation; thirst and vomiting.²⁶ Hypersensitivity reactions such as angio-oedema or laryngeal oedema have also been reported.²⁸

Interactions

There is a potential severe interaction between colecalciferol/ergocalciferol and digoxin. Colecalciferol/ergocalciferol is predicted to increase the risk of toxicity when given with digoxin and the manufacturer's advice is to monitor ECG and calcium levels.^{26,28}

Thiazide diuretics (bendroflumethiazide, chlorothiazide, chlortalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, metolazone, xipamide) increase the risk of hypercalcaemia when given with colecalciferol/ergocalciferol. This is a moderate interaction and manufacturers make no recommendations.²⁶ Regular monitoring of the serum calcium level is necessary in the case of concomitant use with thiazide diuretics or with calcium containing products taken in large doses because of the increased risk of hypercalcaemia.²⁸

Antiepileptic medications (carbamazepine, fosphenytoin, phenobarbital, phenytoin and primidone) moderately decrease the effects of colecalciferol / ergocalciferol.²⁶

Clotrimazole and ketoconazole are predicted to decrease the exposure to colecalciferol, but not ergocalciferol.²⁶

Overdose

Overdose may cause hypervitaminosis, hypercalcaemia and hyperphosphatemia. Symptoms of hypercalcaemia include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, confusion, polydipsia, polyuria, bone pain, calcification in the kidneys, kidney stones, vertigo, and cardiac arrhythmia in severe cases. Hypercalcaemia in extreme cases may lead to coma or even death. Persistently high levels of calcium may cause irreversible renal impairment and soft tissue calcification.²⁸

Monitoring

For all systemic vitamin D and analogues, all patients receiving pharmacological doses of vitamin D should have their plasma-calcium concentration checked at intervals (initially once or twice weekly) and whenever nausea or vomiting occur. For patients prescribed high doses of colecalciferol / ergocalciferol plasma-calcium concentration should be monitored.²⁶

During long-term treatment, serum calcium level, urinary calcium excretion and renal function should be monitored by measuring the serum creatinine level. Monitoring is especially important for elderly patients who concomitantly take cardiac glycosides or diuretics, and in the case of hyperphosphataemia, as well as for patients with an increased risk of lithiasis.²⁸

Local specialists can advise on the frequency of calcium monitoring required.

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. If the patient is still symptomatic after treatment, wait at least three months, preferably six months, before re-testing serum 25(OH)D.⁷

Product and cost comparisons

The total annual spend across England and Wales for vitamin D is £31.8 million (NHSBSA July to September 2020).

Many clinicians prescribe vitamin D generically as either ergocalciferol or colecalciferol, in a wide range of strengths and formulations. Unlicensed specials are sometimes used to fulfil prescriptions written generically. Approximately £2 million is spent annually on vitamin D specials across England and Wales (NHSBSA July to September 2020). There are numerous licensed preparations and health supplements available in a wide variety of doses and forms and so it should rarely be necessary to fulfil a vitamin D order with a special. Whilst the health supplements are generally inexpensive, if a special is dispensed against a generically written prescription, costs can vary immensely. Licensed preparations or health supplements should be prescribed by brand to ensure the correct product and dose is dispensed.

The Drug Tariff (DT) lists various formulations and strengths of colecalciferol as illustrated in Table 2. Most of them are category C and so the price is based on a particular brand, manufacturer or supplier.²⁹ The products listed in Table 2 are all licensed products and listed on the electronic Medicines Compendium (eMC).³⁰ NB: It is accepted that one unit of vitamin D is equivalent to 25 nanograms of colecalciferol or ergocalciferol. An [online tool](#) can be used for conversions.

Ergocalciferol preparations are higher cost than colecalciferol preparations. The Royal Osteoporosis Society recommends that oral vitamin D3 (colecalciferol) is the treatment of choice in vitamin D deficiency and therefore oral colecalciferol should be prescribed.^{6,31}

Table 2: Costs of colecalciferol tablets & capsules listed in the DT (December 2020)^{29,30}

Products (IU)	DT Category	Quantity per pack	Cost in DT	DT price based on brand:	Other Licensed Products
Colecalciferol 400 IU capsules	C	28	£1.85	InVita D3®	
Colecalciferol 800 IU capsules	C	30	£3.60	Fultium-D3®	Strivit-D3®, InVita D3®
Colecalciferol 800 IU tablets	A	30	£4.59		Desunin®, Consilient Health Ltd
Colecalciferol 1,000 IU capsules	C	30	£10.00	Colonis Pharma Ltd	
Colecalciferol 1,000 IU tablets	C	28	£2.95	Stexerol-D3®	
Colecalciferol 3,200 IU capsules	C	30	£13.32	Fultium-D3®	Strivit-D3®
Colecalciferol 4,000 IU tablets	C	70	£15.90	Desunin®	
Colecalciferol 5,600 IU capsules	C	4	£2.50	InVita D3®	Plenachol D3®, Strivit-D3®
Colecalciferol 20,000 IU capsules	C	15	£17.04	Fultium-D3®	
		30	£29.00		
Colecalciferol 25,000 IU capsules	C	3	£3.95	InVita D3®	
Colecalciferol 25,000 IU tablets	C	12	£17.00	Stexerol-D3®	
Colecalciferol 40,000 IU capsules	C	10	£15.00	Plenachol D3®	
Colecalciferol 50,000 IU capsules	C	3	£4.95	InVita D3®	

Self care with over the counter (OTC) preparations and dietary insufficiency

£28.1 million annually is spent on low or moderate dose ($\leq 20,000$ units) vitamin D preparations across England and Wales (NHSBSA July to September 2020). NHS England and NHS Clinical Commissioners issued guidance for CCGs on “Conditions for which over the counter items should not routinely be prescribed in primary care.” This guidance included vitamin D and recommended prescribing for medically diagnosed vitamin or mineral deficiency (not insufficiency) in-line with the Advisory Committee on Borderline Substances (ACBS) guidance. The guidance had feedback during the consultation process from the pharmaceutical industry that maintenance treatment for vitamin D therapy should be an exception as it is included in PHE guidance. The guidance working group considered this feedback and agreed that whilst maintenance therapy is recommended, there is no indication that this needs to be prescribed as vitamin D supplements can be bought cheaply and easily. The PHE guidance also does not distinguish between the general public and at-risk patients and therefore it was not included as an exemption.^{29,32}

For the general population:

- Maintenance therapy does not need to be prescribed, vitamin D supplements can be bought cheaply and easily. However, if self care is not appropriate and prescribing is required then the most cost-effective maintenance dose is either Invita D3® capsules 400IU daily (10 micrograms daily) or 800IU daily (20 micrograms daily). The most cost-effective maintenance dose liquid formulation is Invita D3® drops 2,400IU daily (60 micrograms daily).
- The most cost-effective 300,000IU (7,500 micrograms) treatment course is Invita D3® capsules 50,000IU (1,250 micrograms) capsules.
- The most cost-effective liquid preparation 300,000IU (7,500 micrograms) treatment course is Invita D3® 50,000IU (1,250 micrograms) oral solution.

Choice of formulations for specific patient groups

Swallowing difficulties

There are colecalciferol and ergocalciferol liquid preparations and injections listed in the Drug Tariff (Table 3) which may be suitable for people with swallowing difficulties.

Table 3: Costs of colecalciferol liquid preparations & ergocalciferol injection listed in the DT (December 2020)²⁹ and described in the SPCs³⁰

Products in DT (IU)	DT Category	Quantity per pack	Cost	DT price based on:
Colecalciferol 2,400 IU/mL oral drops SF	C	10 mL	£3.60	InVita D3®
Colecalciferol 2,740 IU/mL oral drops SF	C	25 mL	£10.70	Fultium-D3®
Colecalciferol 10,000 IU/mL oral drops SF	C	10 mL	£5.85	Thorens®
Colecalciferol 10,000 IU/mL oral solution SF	C	2.5 mL	£1.55	Thorens®
		10 mL	£5.85	
Colecalciferol 14,400 IU/mL oral drops SF	C	12.5 mL	£8.95	Sapvit-D3® (discontinued 2019)
Colecalciferol 15,000 IU/5mL oral solution	A	100 mL	£144.00	
Colecalciferol 25,000 IU/1mL oral solution unit dose ampoules SF	C	3	£4.45	InVita D3®
Colecalciferol 50,000 IU/1mL oral solution unit dose ampoules SF	C	3	£6.25	InVita D3®
Ergocalciferol 300,000 IU/1mL solution for injection ampoules	A	10	£93.51	

There are some specials and imported unlicensed ergocalciferol products listed in Part VIIIB of the Drug Tariff. These specials have a basic price for a minimum quantity on which payment is calculated and then an additional a price for each subsequent millilitre prescribed over the minimum quantity, see table 4.²⁹

Table 4: Ergocalciferol specials listed in Part VIIIB of the Drug Tariff (December 2020)²⁹

Products in DT (IU)	Minimum quantity	Cost	Price for each extra mL above minimum quantity
Ergocalciferol 1,000 IU/5mL oral solution	100 mL	£45.13	2p
Ergocalciferol 10,000 IU/5mL oral solution	100 mL	£24.99	23p
Ergocalciferol 100,000 IU/5mL oral solution	20 mL	£20.48	1p
Ergocalciferol 3,000 IU/mL oral solution	60 mL	£42.88	24p
Ergocalciferol 6,000 IU/5mL oral solution	100 mL	£42.56	8p

Food intolerance, allergies and special diets

In addition to patients with swallowing difficulties, consideration should be given to which vitamin D formulations are suitable for patients with food intolerance, food allergies (e.g. lactose intolerance, gluten free, nut free), patients who follow certain food choices (e.g. vegetarian, vegan) and patients with religious beliefs around foods (e.g. halal or kosher). Healthy Start® vitamins are suitable for vegetarians and halal diets, and are free from milk, egg, gluten, soya and peanut residues.

Halal or kosher requirements

UK Medicines Information has prepared the document - What factors to consider when advising on medicines suitable for a Halal diet? The aim of this document is to increase awareness of the term 'Halal' in relation to medication and to direct readers towards further sources of information. Halal or kosher certification is dependent on information supplied by product manufacturers and maybe subject to change. It is recommended that individuals verify information on each product with the manufacturers in line with their own religious or belief system. See Table 5 and Table 6 below, which provide a summary of available products and their suitability for a Halal or Kosher diet.

Vegetarian and vegan requirements

Colecalciferol products derived from sheep's wool fat are not acceptable to vegans but are usually suitable for vegetarians, unless this is derived from the wool fat from slaughtered animals (in which case, some vegetarians may object). Ergocalciferol, also known as vitamin D₂, is derived from a substance called ergosterol that comes from yeast and so is suitable for vegans.³³ See Table 5 and Table 6 below, which provide a summary of available products and their suitability for a Halal or Kosher diet.

Supplements (unlicensed) may be considered for people with particular dietary needs, for example SunVit-D3® Vegan tablets, Pro D3® Vegan capsules and Pro D3® Vegan liquid. Attachment 5 shows the different supplements available (listed in the BNF) and their costs.²⁶

Table 5: Comparison of licensed vitamin D products currently available^{33,34-45}

Product & strength (IU)	Suitability in food allergies?	Suitable for vegetarians?*	Suitable for vegan?*†	Suitable for halal?	Suitable for kosher?	Comments
Colecalciferol capsules – Colonis Pharma (1,000 IU)	<ul style="list-style-type: none"> • Capsules are peanut and soya free. • Gluten free. • Lactose free. 	X	X	X	X	<ul style="list-style-type: none"> • Contains gelatine from a bovine or porcine source. • No specific halal or kosher accreditation has been sought by the manufacturer.
Desunin® tablets (800, 4,000 IU)	<ul style="list-style-type: none"> • Does not contain soya or peanut oil. • Gluten free. • Lactose free. <p>Note: the manufacturers cannot guarantee the suitability of the product for soya, peanut, gluten or lactose allergy sufferers as it may have come into contact with such allergens during transit.</p>	√	X	X	X	<ul style="list-style-type: none"> • Colecalciferol derived from lanolin from the wool of sheep. • Does not contain gelatine. • Desunin® does not hold a religious certification for halal or kosher.
Ergocalciferol injection (300,000 IU/1mL)	<ul style="list-style-type: none"> • Does not contain any soya or nuts. • Gluten free. • Lactose free. <p>Note: It is not made in a nut or soya free facility but there should not be any nut or soya contamination within the injection.</p>	√	√	√	√	<ul style="list-style-type: none"> • Ergocalciferol is derived from ergosterol that comes from yeast. • Neither the excipient, nor the active ingredient is derived from animal products. It is therefore suitable for vegetarian, vegan, kosher and halal diet.
Fultium-D3® capsules (800, 3,200, 20,000 IU)	<ul style="list-style-type: none"> • Capsules are peanut and soya free. • Gluten free. • Lactose free. 	X	X	√	√	<ul style="list-style-type: none"> • Contains gelatine from a bovine or porcine source. • Manufacturer states that gelatine is halal and kosher compliant.

Product & strength (IU)	Suitability in food allergies?	Suitable for vegetarians?*	Suitable for vegan?*†	Suitable for halal?	Suitable for kosher?	Comments
Fultium-D3® Drops (2,740 IU/mL)	<ul style="list-style-type: none"> Does not contain peanuts, tree-nuts or any soy-derived ingredients. Gluten free. Lactose free. 	✓	X	✓	✓	<ul style="list-style-type: none"> Contains colecalciferol derived from lanolin from the wool of sheep. Does not contain gelatine. The product only contains medium-chain triglycerides (from coconut oil and palm kernel oil).
InVita D3® capsules (400, 800, 5,600, 25,000, 50,000 IU)	<ul style="list-style-type: none"> Capsules are peanut and soya free. Gluten free. Lactose free. 	X	X	✓	✓	<ul style="list-style-type: none"> Contains gelatine from a bovine or porcine source. Manufacturer states that gelatine is halal and kosher compliant.
InVita D3® oral drops (2,400 IU/mL)	<ul style="list-style-type: none"> Drops are peanut and soya free. Gluten free. Lactose free. 	✓	X	✓	✓	<ul style="list-style-type: none"> Contains colecalciferol derived from lanolin from the wool of sheep. Does not contain gelatine. No halal or kosher certification. The product does not contain any ingredients from slaughtered animals or any other prohibited ingredients.

Product & strength (IU)	Suitability in food allergies?	Suitable for vegetarians?*	Suitable for vegan?*†	Suitable for halal?	Suitable for kosher?	Comments
InVita D3® oral solution (25,000, 50,000 IU/1mL)	<ul style="list-style-type: none"> • Products are peanut and soya free. • Gluten free. • Lactose free. 	√	X	√	√	<ul style="list-style-type: none"> • Contains colecalciferol derived from lanolin from the wool of sheep. • Does not contain gelatine. • No halal or kosher certification. The product does not contain any ingredients from slaughtered animals or any other prohibited ingredients.
Plenachol D3® capsules (20,000, 40,000 IU)	<ul style="list-style-type: none"> • Does not contain soya or peanut constituents. • Gluten free. • Lactose free. <p>Note: the manufacturers cannot guarantee the suitability of the product for soya, peanut, gluten or lactose allergy sufferers as it may have come into contact with such allergens during the manufacturing process.</p>	√	X	√	√	<ul style="list-style-type: none"> • Contains colecalciferol derived from lanolin from the wool of sheep. • Does not contain gelatine. • Manufacturer states halal and kosher certified.
Stexerol-D3® tablets (1,000 25,000 IU)	<ul style="list-style-type: none"> • Does not contain ingredients sourced from nuts or soya derivatives. • Gluten free. • Lactose Free. (Note: it cannot be guaranteed that they are manufactured in a nut or soya free environment) 	√	X	√	√	<ul style="list-style-type: none"> • Contains colecalciferol derived from lanolin from the wool of sheep. • Does not contain gelatine. • Manufacturer states halal and kosher certified.

Product & strength (IU)	Suitability in food allergies?	Suitable for vegetarians?*	Suitable for vegan?*†	Suitable for halal?	Suitable for kosher?	Comments
Strivit-D3® capsules 800, 3,200, 20,000 IU)	<ul style="list-style-type: none"> Does not contain soya or peanut constituents. Contains gluten and lactose. 	X	X	✓	✓	<ul style="list-style-type: none"> Contains gelatine from a bovine or porcine source. The capsules are suitable for halal and kosher diets as they do not contain pork or alcohol derivatives.
Thorens® oral drops (10,000 IU/mL)	<ul style="list-style-type: none"> Does not contain nut or soya derived ingredients and are deemed to be suitable for patients with nut or soya allergies. Gluten free. Lactose free. 	✓	X	✓	✓	<ul style="list-style-type: none"> Contains colecalciferol derived from lanolin from the wool of sheep. Does not contain gelatine. The colecalciferol is halal and kosher certified.
Thorens® oral solution (10,000, 25,000 IU/mL)	<ul style="list-style-type: none"> Does not contain nut or soya derived ingredients and are deemed to be suitable for patients with nut or soya allergies. Gluten free. Lactose free. 	✓	X	✓	✓	<ul style="list-style-type: none"> Contains colecalciferol derived from lanolin from the wool of sheep. Does not contain gelatine. The colecalciferol is halal and kosher certified.

Notes for Table 5

*Confirmed by manufacturers to be suitable for vegan or vegetarian diets as per the definitions of vegetarian and vegan by the European Vegetarian Union.

† Table 5 compares licensed vitamin D products, however supplements (unlicensed) may be considered for people with particular dietary needs, for example SunVit-D3® Vegan tablets, Pro D3® Vegan capsules and Pro D3® Vegan liquid. Attachment 5 shows the different supplements available (listed in the BNF)²⁶ and their costs.

See individual Summary of Product Characteristics (SPC) for full prescribing information: <https://www.medicines.org.uk/emc/>

Table 6: Cost of oral and injectable treatments suitable for halal and kosher diets. DT (December 2020)^{26,29}

Preparation	Low dose – cost per dose (IU)	High dose - Cost of 300,000-IU course
Fultium-D3® capsules	£0.12 (800IU), £0.44 (3,200IU)	
Fultium-D3® oral drops	£0.43 (2,740IU)	
Invita D3® capsules	£0.07 (400IU), £0.09 (800IU)	£33.48 (5,600IU), £15.80 (25,000IU), £9.90 (50,000IU)
Invita D3® oral drops	£0.36 (2,400IU)	
Invita D3® oral solution		£17.80 (25,000IU), £12.50 (50,000IU)
Plenachol D3® capsules		£11.25 (40,000IU)
Stexerol-D3® capsules	£0.11 (1,000IU)	£17.00 (25,000IU)
Strivit-D3® capsules	£0.08 (800IU), £0.31 (3,200IU)	£14.40 (20,000IU)
Thorens® oral drops		£17.55 (10,000IU)
Thorens® oral solution		£17.55 (10,000IU)
Ergocalciferol injection		£9.35 (300,000IU)

Notes for table 6

- Maintenance therapy does not need to be prescribed, vitamin D supplements can be bought cheaply and easily. However, if self care is not appropriate and prescribing is required then the most cost-effective product suitable for halal and kosher diets is Invita D3® capsules 400IU daily (10 micrograms daily) or 800IU daily (20 micrograms daily). The most cost-effective maintenance dose liquid formulation suitable for halal and kosher diets is Invita D3® drops 2,400IU daily (60 micrograms daily).
- The most cost-effective 300,000IU (7,500 micrograms) treatment course suitable for halal and kosher diets is Invita D3® capsules 50,000IU (1,250 micrograms) capsules.
- The most cost-effective liquid preparation 300,000IU (7,500 micrograms) treatment course suitable for halal and kosher diets is Invita D3® 50,000IU (1,250 micrograms) oral solution.

Table 7: Cost of oral and injectable treatments suitable for vegetarians. DT (December 2020)[26,29]

Preparation	Low dose – cost per dose (IU)	High dose - Cost of 300,000-IU course
Desunin® capsules	£0.12 (800IU), £0.23 (4,000IU)	
Fultium-D3® oral drops	£0.43 (2,740IU)	
Invita D3® oral drops	£0.36 (2,400IU)	
Invita D3® oral solution		£17.80 (25,000IU), £12.50 (50,000IU)
Plenachol D3® capsules		£11.25 (40,000IU)
Stexerol-D3® capsules	£0.11 (1,000IU)	£17.00 (25,000IU)
Thorens® oral drops		£17.55 (10,000IU)
Thorens® oral solution		£17.55 (10,000IU)
Ergocalciferol injection		£9.35 (300,000IU)

Notes for table 7

- Maintenance therapy does not need to be prescribed, vitamin D supplements can be bought cheaply and easily. However, if self care is not appropriate and prescribing is required then the most cost-effective product suitable for vegetarians is either Stexerol-D3® capsules 1,000IU daily (25 micrograms daily) or Desunin® capsules 800IU daily (20 micrograms daily). The most cost-effective maintenance dose liquid formulation suitable for vegetarians is Invita D3® drops 2,400IU daily (60 micrograms daily).

- The most cost-effective 300,000IU (7,500 micrograms) treatment course suitable for vegetarians is Plenachol D3® 40,000IU (1,000 micrograms) capsules.
- The most cost-effective liquid preparation 300,000IU (7,500 micrograms) treatment course suitable for vegetarians is Invita D3® 50,000IU (1,250 micrograms) oral solution.

The only licensed product suitable for vegans is the ergocalciferol injection, however there are some colecalciferol food supplements (unlicensed) available in tablets, capsules, liquid and drop formulations that are suitable for vegans, for example SunVit-D3® Vegan tablets, Pro D3® Vegan capsules and Pro D3® Vegan liquid - see attachment 5 for details.

Other (gluten, lactose)

All products are gluten free and lactose free except Strivit-D3® capsules.

Savings

The following savings on vitamin D prescribing are available including:

- Converting all low or moderate dose ($\leq 20,000$ units) vitamin D preparations to self care requiring purchasing OTC would save **£28.1 million annually across England and Wales or £44,508 per 100,000 patients.**
- Discontinuing all unlicensed vitamin D specials and recommending OTC purchase where indicated would result in **savings of £ 1,985,081 across England and Wales or £3,140 per 100,000 patients.**
- Reviewing patients at the end of their treatment loading doses ($>20,000$ units daily) of vitamin D and switching to a maintenance dose of vitamin D which is purchased OTC in 20% of patients currently on treatment doses of vitamin D would result in **savings of £341,946 annually across England and Wales or £541 per 100,000 patients.**

Summary

Plasma 25-hydroxyvitamin (OH)D should be used to measure vitamin D status in patients that are symptomatic, at very high risk of deficiency or if there is a clinical reason to do so.^{2,6} SACN recommends that the serum 25(OH)D concentration of all individuals in the UK should not fall below 25 nmol/L at any time of the year.⁷

A RNI of 400 IU/daily (10 micrograms daily) of vitamin D should be taken throughout the year by everyone in the general UK population aged 4 years and above.⁷ A 'Safe Intake' of 340-400 IU/daily (8.5-10 micrograms daily) is recommended for ages 0 up to one year (including exclusively breast fed and partially breast-fed infants, from birth) unless more than 500ml of infant formula per day is taken. For ages one to four years 400 IU/daily (10 micrograms daily) is recommended.^{7,8} Vitamin D should be prescribed for people with a medically diagnosed deficiency, however self care should be recommended for maintenance therapy for both at risk patients and the general public, if appropriate.³²

Consideration should be given to the risks and benefits of prescribing licensed preparations or food supplements for vitamin D deficiency. Unlicensed specials for vitamin D should not be prescribed in-line with the GMC Guidance on prescribing unlicensed medicines⁸ as there are now many licensed products available. Whilst health supplements are generally inexpensive, if a special is dispensed against a generically written prescription, costs can vary hugely.

Guidelines for the treatment of vitamin D deficiency should be agreed with local clinicians. These should be based on national guidance and recommendations from NICE (PH56),² SACN and PHE.⁷ They should include recommendations regarding cost-effective products, which should be prescribed and specified by brand name, appropriate doses and duration for patients to treat deficiency. Consideration should be given to patients with special dietary needs.




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Additional PrescQIPP resources

 Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-275-vitamin-d/
 Implementation tools	
 Data pack	https://data.prescqipp.info/?pdata.u/#/views/B275_VitaminD/Front-Page?:iid=1

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