Vitamin D Deficiency in Adults: Primary Care Guideline

The prevalence of vitamin D deficiency in the UK is 16% and around 50% of the UK adult population have vitamin D insufficiency in winter and spring. Vitamin D is essential for musculoskeletal health.

Nomenclature: The term vitamin D is used for a range of compounds. Vitamin D2 is known as ergocalciferol. Vitamin D3 is known as colecalciferol (the recommended International Nonproprietary Name) when referring to the drug and as cholecalciferol when referring to the analyte.

Conversion factors: 10ug (micrograms) vitamin D = 400IU vitamin D
2.5 nmol/L serum 25OHD = 1 ng/mL serum 25OHD

Achieving adequate vitamin D status

Ultraviolet B sunlight exposure is the main source of vitamin D. During summer two or three exposures (of at least the face and arms without sunscreen and not behind glass) of 20 to 30 minutes each week between 10am and 3pm should provide adequate amounts of vitamin D for most individuals. Due to the latitude in the UK, from October to April sun exposure is not adequate for synthesis of vitamin D.

Oily fish such as sardines, mackerel, salmon and tuna are the best dietary source of vitamin D. Egg yolks, mushrooms and liver contain small amounts of vitamin D. Liver is also a rich source of vitamin A, therefore consumption should be limited to once a week to avoid toxicity and avoided entirely in pregnancy. There are also some foods such as margarines, cereals that are fortified with vitamin D (refer to product labels).

In the UK, a recommended dietary intake has not been set for those leading a normal lifestyle where they are exposed to solar radiation. The Chief Medical Officer for England, Wales, Northern Ireland, and Scotland has recommended routine daily supplementation with 10 mcg of vitamin D for pregnant and breastfeeding women, people aged 65 years and over, and people who are not exposed to much sun. The Healthy Start Programme is available for eligible pregnant women and children under 4 years.

Risk Factors

- Pregnancy and breastfeeding
- Older people, aged 65 years and over
- Low exposure to sun, e.g. routine covering of skin, housebound
- Darker skin, e.g. African, African-Caribbean or South Asian origin
- Conditions resulting in intestinal malabsorption, e.g. coeliac, Crohn’s
- Liver or renal disease
- Vegan or vegetarian diet
- Medications including anticonvulsants, cholestyramine, rifampicin, glucocorticoids, antiretrovirals

Symptoms

Symptoms of vitamin D deficiency are unfortunately vague and it can be difficult to ascertain whether a low vitamin D is causal or a surrogate marker. The symptoms are primarily those associated with osteomalacia such as bone, joint and muscle pain or tenderness, muscle weakness, waddling gait.
Testing Recommendations

Measurement of serum 25 OHD is the most reliable way of determining vitamin D status.

Routine testing of vitamin D levels is not recommended. Given the large proportion of the population who may have insufficient levels and uncertainty as to whether low levels relate to a patient’s condition there needs to be a clear clinical indication for testing.

Categories:
1. Patients with bone diseases that may be improved with vitamin D treatment
   • Predominantly osteomalacia where symptoms include bone, joint and muscle pain or tenderness, muscle weakness, waddling gait
   • Correction is required prior to some antiresorptive treatment, e.g. zoledronate, denosumab or bisphosphonate in Paget’s disease
   • For osteoporosis and fragility fractures, testing is unnecessary where an oral bisphosphonates with calcium/vitamin D supplementation is prescribed as recommended by NICE Guideline. It may be appropriate for patients that sustain a fragility fracture despite adhering to treatment or where fracture healing is delayed.

2. Patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency
   • If patients are having symptoms such as those associated with osteomalacia or have chronic widespread pain, then testing may be considered as part of their clinical and laboratory assessment, particularly those with risk factors.
   • Other causes for symptoms should be excluded, for example myeloma, rheumatoid arthritis, polymyalgia rheumatica and hypothyroidism.

3. Asymptomatic individuals at higher risk of vitamin D deficiency.
   • Testing is not recommended.
   • There are a number of risk factors in asymptomatic individuals that predispose to lower levels of 25OHD.

4. Asymptomatic healthy individuals
   • Testing is not recommended
   • There is no evidence to support population screening.

Assessment of vitamin D status should also include serum calcium (to exclude hypercalcaemia and provide a baseline), alkaline phosphatase (ALP) and phosphate. Additional tests if indicated: renal function (to exclude renal failure), liver function tests (to exclude hepatic failure), full blood count (anaemia may be present if there is malabsorption) and thyroid function tests, erythrocyte sedimentation rate (ESR) (myeloma), serum testosterone in men less than 60 years, parathyroid hormone (PTH).

Referral to secondary care
• Patients with a contraindication to vitamin D; hypercalcaemia and metastatic calcification
• Patients with renal impairment (stage 4 Chronic Kidney Disease (CKD) or eGFR less than 30ml/minute), renal stones or severe hypercalciuria
• Primary hyperparathyroidism
• Symptomatic after completion of high dose treatment
**Treatment**

Colecalciferol (vitamin D3) is considered the preferred form of vitamin D for treatment.

The National Osteoporosis Society recommends a regimen equivalent to approximately 300,000 IU to replenish stores in deficiency. Bolus doses are not advised as they may be ineffective and increase fracture risk.

As a fat soluble vitamin, oral vitamin D products should be taken with food to improve absorption. Avoid taking at the same time as orlistat as this reduces absorption.

**Adverse effects:** Whilst on treatment patients should be advised of signs of hypercalcaemia such as nausea, thirst, constipation, polyuria and confusion.

**Monitoring:** Adjusted serum calcium should be checked 1 month after completing treatment regimen in case primary hyperparathyroidism has been unmasked. Routine monitoring of serum 25OHD after treatment is generally unnecessary but may be appropriate if patients continue to be symptomatic or malabsorption or poor compliance with medication is suspected.

<table>
<thead>
<tr>
<th>Serum 25OHD concentration</th>
<th>Vitamin D status</th>
<th>Product (see table below on preparations for licensing, supplier and allergy information)</th>
<th>Treatment dose and frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 nmol/l</td>
<td>Deficient</td>
<td>Hux D3 20,000 IU capsules&lt;br&gt;Alternatives are Pro D3 20,000 IU capsules, Dekristol 20,000 IU capsules</td>
<td>Colecalciferol 60,000 IU (3 capsules) once weekly for 5 weeks then maintenance</td>
</tr>
<tr>
<td>30-50 nmol/l</td>
<td>Insufficient</td>
<td>Desunin 800 IU tablets (contains sucrose)&lt;br&gt;Alternative: Fultium 800 IU capsules (contains arachis oil)</td>
<td>Colecalciferol 1,600 IU (2 tablets) daily for 12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients not exempt from prescriptions charges: nutritional supplements are available to purchase over-the-counter from pharmacies or health food stores</td>
<td>Colecalciferol 2,000 IU daily for 10 weeks</td>
</tr>
<tr>
<td>&gt;50 nmol/l</td>
<td>Sufficient</td>
<td>None required</td>
<td>None required</td>
</tr>
</tbody>
</table>

**Maintenance**

| Maintenance | At high risk*<br>*including CMO recommendation | Adcal-D3 caplet (750mg calcium carbonate/5mcg (200 IU))<br>colecalciferol)*<br>(*or suitable equivalent. Avoid in patients with adequate calcium intake or at risk of hypercalcaemia) OR<br>Desunin 800IU tablets | Calcium 750mg + colecaltiferol 200 IU<br>2 caplets twice a day<br>OR<br>Colecalciferol 800 IU (1 tablet) daily<br>Patients not exempt from prescriptions charges: nutritional supplements are available to purchase over-the-counter from pharmacies or health food stores | Colecalciferol 1,000 IU daily |

*All patients should be given lifestyle advice about safe sun exposure and diet in order to achieve adequate amounts of vitamin D.*
<table>
<thead>
<tr>
<th>Preparations, manufacturers, and distributors</th>
<th>Actual product cost (Drug Tariff, BNF list price or from the manufacturer)</th>
<th>Expiry period once product opened</th>
<th>Handling or other auxiliary costs</th>
<th>Licensing status</th>
<th>Risk Category</th>
<th>Allergy and/or dietary restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desunin (colecalciferol) tablets 800 IU (30 tablets) Available via normal wholesaler routes</td>
<td>£3.60</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Product has UK marketing authorisation.</td>
<td><strong>Category A</strong> Suitable for all groups of patients.</td>
<td>Colecalciferol is derived from healthy live sheep’s wool fat – may be acceptable to vegetarians.</td>
</tr>
<tr>
<td>Fultium D3 (colecalciferol) capsules 800 IU (30 capsules) Available from Jenson Pharmaceuticals Services Ltd. via normal wholesaler routes</td>
<td>£3.60</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Product has UK marketing authorisation.</td>
<td><strong>Category A</strong> Suitable for all groups of patients.</td>
<td>Contains gelatine and arachis (peanut/groundnut) oil. Gelatine is halal and kosher compliant.</td>
</tr>
<tr>
<td>Hux D3 (colecalciferol) capsules 20 000 IU (20 tablets) Available via normal wholesaler routes</td>
<td>£3.49</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Does not have UK marketing authorisation. Marketed as a nutritional supplement.</td>
<td><strong>Category D</strong> Use cautiously in high risk patient groups.</td>
<td>Contains Halal certified gelatine.</td>
</tr>
<tr>
<td>ProD3 (colecalciferol) capsules 20 000 IU (30 capsules) Available from AAH Pharmaceuticals, tel. 0844 561 8899</td>
<td>£23.99</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Does not have UK marketing authorisation. Marketed as a nutritional supplement.</td>
<td><strong>Category D</strong> Use cautiously in high risk patient groups.</td>
<td>Colecalciferol is derived from sheep’s wool fat – however the company has confirmed suitability for vegetarians.</td>
</tr>
<tr>
<td>Dekristol (colecalciferol) capsules 20 000 IU (50 capsules) Available from Pharmarama, tel. 0208 238 6770; IDIS world medicines, tel. 01932 824 100; Martindale Pharmaceuticals, tel. 0800 028 7933; UL medicines, tel. 01923 204 333</td>
<td>Pharmarama £10.40; IDIS £23.20; Martindale £18.45; UL medicines £10.99</td>
<td>Not applicable</td>
<td>Pharmarama orders &lt;£30 incur £6.50 handling fee; Martindale orders &lt;£75 incur £14.45 handling fee; UL medicines standard handling fee £9.99</td>
<td>Does not have UK marketing authorisation. Manufactured and licensed by MIBE Pharmaceuticals, Germany.</td>
<td><strong>Category B</strong> Suitable for all groups of patients.</td>
<td>Contains gelatine and groundnut oil.</td>
</tr>
<tr>
<td>Adcal-D3 (calcium carbonate 750mg and colecalciferol 200 IU) caplets (112 caplets) Available via normal wholesaler routes</td>
<td>£3.65</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Product has UK marketing authorisation.</td>
<td><strong>Category A</strong> Suitable for all groups of patients.</td>
<td>Does not contain gelatine or soya. Suitable for vegetarians but not vegans.</td>
</tr>
</tbody>
</table>

Note: The limited availability of licensed products necessitates the use of nutritional supplements, imported or unlicensed products.
INVESTIGATION AND TREATMENT OF VITAMIN D DEFICIENCY IN ADULTS IN PRIMARY CARE

Is the patient at high risk?
- Pregnancy and breastfeeding
- Older people, aged 65 years and over
- Low exposure to sun, e.g. routine covering of skin, housebound
- Darker skin, e.g. African, African-Caribbean or South Asian origin
- Conditions resulting in intestinal malabsorption, e.g. coeliac, Crohn’s
- Liver or renal disease
- Vegan or vegetarian diet
- Medications: anticonvulsants, cholestyramine, rifampicin, glucocorticoids, antiretrovirals

Is the patient symptomatic?
- Bone, joint and muscle pain or tenderness, muscle weakness, waddling gait
- Chronic widespread pain

Have other causes for symptoms been excluded?
- e.g. myeloma, rheumatoid arthritis, polymyalgia rheumatica, hypothyroidism.

Assessment of vitamin D status required: 25(OH)D
Calcium, phosphate, ALP also required. Consider U+Es, LFTs, FBC, PTH.

Deficiency <30 nmol/L
- HuxD3 (colecalciferol 20,000 IU): 3 capsules (60,000 IU) once a week for 5 weeks
- Alternatives: ProD3 20,000 IU or Dekristol 20,000 IU capsules

Insufficiency 30-50 nmol/L
- Desunin (colecalciferol 800 IU): Take 2 tablets (1,600 IU) daily for 12 weeks
- Alternatives: Fultium 800 IU capsules or purchase nutritional supplement OTC

Sufficient >50 nmol/L
Lifestyle advice

Lifestyle advice and maintenance therapy

Check calcium 1 month after high dose treatment. A vitamin D level after treatment is unnecessary but may be checked if patient is still symptomatic or malabsorption or poor compliance is suspected.

Maintenance therapy for patients at high risk
- Calcium carbonate 750mg & colecalciferol 200unit (5mcg) caplet (e.g. Adcal-D3 or equivalent): Take 2 caplets twice a day OR
- Desunin (colecalciferol 800 IU): Take 1 tablet daily (if patients have adequate dietary calcium intake or are at risk of hypercalcaemia)

Nutritional supplements purchased over-the-counter (OTC) are also suitable: colecalciferol 1,000 IU daily

EXCLUSIONS:
- Hypercalcaemia
- Metastatic calcification
- Renal stones
- Severe hypercalciuria
- Stage 4 CKD or eGFR < 30m/minute
- Primary hyperparathyroidism

Refer to appropriate specialist in secondary care. Depending on outcome vitamin D treatment may still be required; of which the first treatment course should be prescribed and provided by secondary care before transferring patient with care plan back to primary care.

Lifestyle Advice
Safe sun exposure: From May to September, two or three exposures of 20 to 30 minutes each week between 10am and 3pm to achieve adequate levels. In the UK, from October to April sun exposure is not adequate for synthesis of vitamin D and the body relies on tissue stores.

Dietary sources: oily fish, egg yolks, fortified cereals & margarines.
References:

- Q&A 82.2 What dose of vitamin D should be prescribed for the treatment of vitamin D deficiency? Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals. Date prepared: 8th January 2013. Available at: www.evidence.nhs.uk.
- Q&A 387.2 Which vitamin D preparations are suitable for a vegetarian or vegan diet? Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals. Date prepared: 18th March 2013. Available at: www.evidence.nhs.uk.
- Pearce SHS, Cheetham TD. Diagnosis and management of vitamin D. BMJ 2010; 340: 142-147.