Clinical Guideline for the Management of Vitamin D Deficiency and Insufficiency in Adults

Introduction

Vitamin D is essential for musculoskeletal health as it promotes calcium absorption from the bowel, enables mineralisation of newly formed osteoid tissue in bone and plays an important role in muscle function.¹

There are two physiological forms of vitamin D; vitamin D2 (ergocalciferol) and vitamin D3 (colecalciferol) which have similar structures and actions. Colecalciferol is the most abundant in humans and is produced in the skin following exposure to sunlight.¹

Vitamin D is activated by a series of hydroxylation reactions; the first occurs in the liver to produce 25-hydroxyvitamin D (25OHD) and the second occurs in the kidneys producing the biologically active metabolite 1,25-dihydroxy vitamin D (calcitriol).

The main manifestation of vitamin D deficiency is osteomalacia in adults and rickets in children, which are generally associated with a serum 25OHD concentration of less than 30 nmol/L.¹ Less severe vitamin D deficiency, sometimes termed vitamin D insufficiency, may lead to secondary hyperparathyroidism, bone loss, muscle weakness, falls and fragility fractures in older people.¹ There is also currently a growing understanding of the importance of vitamin D in terms of its potential role in the prevention of non-skeletal disorders such as auto-immune disease, cancer, mental health problems and cardiovascular disease.

Purpose and Scope

This document is a local cross-sector guideline broadly based on the National Osteoporosis Society Vitamin D and Bone Health Guidelines 2013¹ and sets out to provide guidance on which patients to test for vitamin D deficiency, how to supplement vitamin D in the case of insufficiency or deficiency, and how to conduct and interpret the necessary monitoring for patients who require supplementation.

This guideline does not address the management of vitamin D deficiency in children or in patients with severe or end-stage chronic kidney disease (CKD Stages 4–5)
Important points:
- Oral Vitamin D absorption is aided by fat so doses should be taken with food.
- If the patient has an eGFR <30 ml/min/1.73m² (CKD stage 4 or 5) do not use this guideline, refer to a renal specialist for advice

Who should be tested for vitamin D deficiency?

Check Vitamin D status in the following:
- Fragility fracture despite osteoporosis drug treatment
- Fragility fracture at young age (<60 years)
- Patient starting parenteral potent anti-resorptive agent (IV Bisphosphonate/Teriparatide/Denosumab)
- Patients with a significant risk of osteoporosis eg:
  - Corticosteroid use, inflammatory bowel disease, rheumatoid arthritis, COPD, prolonged immobilisation, sickle cell disease, liver disease, anorexia nervosa, diabetes, HIV.
- Malabsorption states (e.g. small bowel resection, coeliac disease, bariatric surgery)
- Pregnancy or breast feeding where severe deficiency is suspected
- Musculoskeletal symptoms that may be attributed to vitamin D deficiency, e.g. muscle weakness, widespread chronic pain.

Routine vitamin D levels may be unnecessary in the following:
These patients can be presumed in need of supplementation and should take 800-2,000 units daily as per maintenance therapy in algorithm below unless severe deficiency suspected (then check level).
- Patients taking antiepileptics or antiretrovirals (these can impair vitamin D metabolism)
- Patients with low sun exposure (e.g. sun sensitive condition, full body clothing)
- Housebound patients and care home residents (in whom calcium intake should be also be considered)
- Frequent fallers
- Black or Asian patients or those with dark skin, as there is a reduced potential for production of vitamin D from sunlight. If symptomatic with fatigue or myalgia check vitamin D status in order identify if the patient has more severe deficiency.

If Alkaline Phosphatase (ALP) is noted as being raised in any patient in the above groups this may indicate more severe osteomalacia, in which case check 25OHD level.

Pregnant and mothers for 1 year post-partum (including breastfeeding mothers)
- Pregnant and mothers for 1 year post-partum (including breastfeeding mothers) should routinely receive a minimum of 400 units colecalciferol daily without the need to check levels¹ (e.g. Healthy Start multivitamins contain 400 units colecalciferol; these are non-prescribable but are available free of charge through community pharmacies and children’s centres)
- This guideline recommends Desunin® or Fultium® 800 unit regimens specifically in the algorithm below for pregnant patients with 25OHD levels displaying deficiency if tested.²
- Correction of deficiency should start in the second or third trimester of pregnancy because of the lack of safety or outcome data in first trimester, and because the majority of skeletal growth and development is thought to occur in the 2nd or 3rd trimester.²
- To avoid maternal (and possibly foetal or neonatal) hypercalcaemia, it is suggested that pregnant women being treated for vitamin D deficiency should have their serum calcium levels checked a month after starting treatment and then three months later, when steady state vitamin D levels have been achieved.²
- Rapid correction of deficiency might be appropriate for pregnant patients with severe deficiency <15nmol/l. Contact a specialist endocrinologist for advice.
Algorithm for Vitamin D replacement and maintenance therapy
(see important points above for consideration in pregnant patients)

Serum 25OHD

<30nmol/L (<12microgram/L)
Deficient
Loading course
Short term use only - prescribe on acute; do not put on repeat list
See specifics of licensed products in table below

Either:
Colecaciferol 40,000 units (2 x 20,000 or 1 x 40,000 unit caps) once each week for 7 weeks
Regimen not recommended for pregnant patients
Or:
Colecaciferol 3,200 unit capsules
1 daily for 12 weeks - Option for pregnant patients
Or:
Colecaciferol 800 unit tablets
5 daily for 10 weeks - Option for pregnant patients
For patients with swallowing difficulties use:
Colecaciferol 25,000 unit dose vials
2 vials (50,000 units) once each week for 6-8 weeks
Regimen not recommended for pregnant patients

Start maintenance therapy

30-50nmol/L (12-20microgram/L)
Insufficient
Maintenance therapy
See specifics of licensed products in table below

Recommend over the counter (OTC) preparations
Vitamin D (ideally colecaciferol) 800 – 2,000 units daily.
If prescribed Vitamin D treatment appropriate instead of OTC:
Colecaciferol 800 unit tabs or caps 1 each day
If inadequate dietary calcium prescribe instead:
Calcium 500mg or 600mg & colecaciferol 400 units twice a day (combination preparation)

>50nmol/L (>20microgram/L)
Sufficient
Replacement not necessary

Offer lifestyle advice
If patients are concerned they cannot follow the lifestyle advice they can purchase an OTC Vitamin D preparation 400 – 1,000 units daily if they wish.

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a 25OHD is the best indicator of vitamin D levels in body stores than the other compounds within the vitamin D metabolism pathway.
b LGT report 25OHD in nmol/L, but some centres report in microgram/L
c Avoid using multivitamin/nutrient preparations. Achieving the correct vitamin D dose might give inappropriate amounts of other nutrients e.g. Cod Liver Oil use might result in vitamin A toxicity.
d Sun exposure is the main source of vitamin D, however this should be balanced with the risks of excessive exposure. 10-15 minutes each day is enough for most lighter-skinned people. Dietary sources of vitamin D include oily fish, red meat, egg yolks, fortified cereals and fortified low fat spreads.
e The recommended intake of calcium is 700mg/day, and 1.2g/day in malabsorption states, osteoporosis and breastfeeding. The following web calculator can be used to assess calcium intake http://www.cgem.ed.ac.uk/research/rheumatological/calcium-calculator. Patients are likely to require additional calcium supplementation if they have a low intake of dairy products and fish.
Licensed colecalciferol products available (Feb 2015):

<table>
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<tr>
<th>Product</th>
<th>Suitable in soy or peanut allergy?</th>
<th>Suitable for vegetarians?**</th>
<th>Kosher and Halal considerations***</th>
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<tr>
<td>Desunin tabs 800 units</td>
<td>Yes</td>
<td>Yes</td>
<td>Contains no gelatin or porcine sourced excipients</td>
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<tr>
<td>Fultium-D3 caps 800 units</td>
<td>Yes*</td>
<td>No (contains gelatin)</td>
<td>Gelatin is of bovine origin, no porcine sourced excipients</td>
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<tr>
<td>Fultium-D3 caps 3,200 units</td>
<td>Yes*</td>
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<tr>
<td>Fultium-D3 caps 20,000 units</td>
<td>Yes*</td>
<td>No (contains gelatin)</td>
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<tr>
<td>Plenachol caps 20,000 units</td>
<td>Yes</td>
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<td>Contains no gelatin or porcine sourced excipients</td>
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<tr>
<td>Plenachol caps 40,000 units</td>
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<td>Aviticol caps 20,000 units</td>
<td>Yes</td>
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<td>InVita D3 unit dose vials 25,000 units</td>
<td>Yes</td>
<td>Yes</td>
<td>Contains no gelatin or porcine sourced excipients</td>
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*Fultium-D3 was relaunched in January 2015 as peanut and soy free but previous batches may still be in circulation. If patient is allergic to peanuts or soy pharmacist should check specific pack prior to dispensing.

**Colecalciferol is animal derived (from sheep’s wool in most instances) and therefore unlikely to be acceptable for most vegans. Ergocalciferol (in a gelatin free product) could be used at equivalent doses for vegans but there are no current MHRA licensed pharmaceutical strength ergocalciferol products.

***If specific information on kosher/halal certification is required or requested by the patient contact the manufacturers

Rechecking Vitamin D levels:
- Recheck vitamin D levels (serum 25OHD) in patients who have received a loading course, and were symptomatic at the time of the initial level or had severe deficiency (serum 25OHD < 20 nmol/L)
- Recheck levels at 3 months after the loading course as post-supplementation vitamin D levels can take months to plateau
- Ensure subsequent levels are checked in the same laboratory as the original level, as assays vary between laboratories
- It is not necessary to recheck levels in patients on maintenance vitamin D therapy

Only check calcium and parathyroid hormone (PTH) levels at 1 month after the loading course only patients who:
- Had a raised baseline corrected calcium (Ca\(^{2+}\) > 2.6mmol/L) on initial bone profile.
- The presence of hypercalcaemia should lead to cessation of further vitamin D supplementation prior to investigation of the cause of hypercalcaemia.

Other points of note:
- Colecalciferol is superior to ergocalciferol in optimising levels as ergocalciferol has quicker clearance\(^3\) and lower tissue bioavailability\(^4\). In terms of pharmacological activity colecalciferol and ergocalciferol can be considered interchangeable dose for dose.
- 1-hydroxylated vitamin D (alfacalcidol) should only be used for vitamin D supplementation in CKD where eGFR <30 ml/min/1.73m\(^2\) (specialist use outside the scope of this guideline) as it carries a higher risk of toxicity and requires close monitoring. 25OHD assay does not capture alfacalcidol or calcitriol.
- Loading oral courses (total dose of 300,000 units per course) are safe and effective, but single large parenteral bolus doses are linked with falls and higher fracture risk, and are generally not recommended. Toxicity is rare until levels of 25OHD are >250nmol/L.\(^1\)
- There are numerous vitamin D supplements available; however this guideline recommends specific licensed products when prescribing for product quality assurance.
References
1. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. The National Osteoporosis Society April 2013
7. The Replacement of Low Vitamin D in Adults, including Chronic Kidney Disease, Pregnancy and Breast-feeding. King’s Health Partners and Lambeth and Southwark Clinical Commissioning Groups June 2013.

Associated documents
Nil
## Document Control

<table>
<thead>
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<th>Document Reference:</th>
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</table>
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## Document Version Control

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<tr>
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<td>Martin Bradley</td>
<td>Active</td>
<td>This replaces the LHT document Replacement of Low Vitamin D level in adult patients – version 1.0 and the SLHT document – Vitamin D Deficiency in Adults version 3.0 dated May 2013</td>
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