Vitamin D Guidelines

Version Control Table

<table>
<thead>
<tr>
<th>Version number and issue number</th>
<th>Date</th>
<th>Author</th>
<th>Reason for Change</th>
<th>Description of Changes Made</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version 1.0</td>
<td>August 2016</td>
<td>S Collins</td>
<td>New document</td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>December 2016</td>
<td>G Ells</td>
<td>APC requirement</td>
<td>various</td>
</tr>
</tbody>
</table>

Consultation Table

This document has been developed in consultation with the groups and/or individuals in this table:

<table>
<thead>
<tr>
<th>Name of Individual or group</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Lolin</td>
<td>Consultant in Chemical Pathology &amp; Metabolic Medical</td>
<td>May 2016</td>
</tr>
<tr>
<td></td>
<td>Biochemistry</td>
<td></td>
</tr>
<tr>
<td>Dr Muhi-Iddin</td>
<td>Consultant Paediatrician</td>
<td>May 2016</td>
</tr>
<tr>
<td>Mr Mucci</td>
<td>Consultant Physician</td>
<td>May 2016</td>
</tr>
<tr>
<td>Richard Partington</td>
<td>Medicines Management Adviser</td>
<td>May 2016/ Jan 2017</td>
</tr>
</tbody>
</table>
## Contents

1. Introduction ............................................................................................................. 3
2. Rationale .................................................................................................................. 3
3. Scope ....................................................................................................................... 3
4. Sources of vitamin D and daily requirements ......................................................... 3
5. Definitions ............................................................................................................... 4
6. Implications of vitamin D deficiency ....................................................................... 4
7. Risk factors for vitamin D deficiency$^2,7$ ............................................................... 4
8. Prevention of Vitamin D deficiency in at risk groups ............................................. 4
9. Measurement of Vitamin D ..................................................................................... 5
10. Accountabilities .................................................................................................... 5
11. Maintenance, treatment and monitoring ............................................................... 6
    11.1 Treatment of vitamin D deficiency (<25nmol/L) ............................................. 6
    11.2 Treatment of probable deficiency ................................................................. 6
    11.3 Treatment of Vitamin D insufficiency (25-50 nmol/L) .................................. 6
    11.4 Maintenance following treatment for vitamin D deficiency ......................... 7
    11.5 Products .......................................................................................................... 7
12. Special Considerations ........................................................................................ 8
    12.1 Cautions and precautions regarding vitamin D products ............................ 8
    12.2 Swallowing difficulties .................................................................................. 8
    12.3 Dietary culture and beliefs ............................................................................. 8
    12.4 Vitamin D toxicity .......................................................................................... 8
13. Chronic Kidney Disease ...................................................................................... 9
14. Treatment and Maintenance in children ............................................................ 10
15. Treatment of Vitamin D deficiency in Adults ..................................................... 11
16. References .......................................................................................................... 12
1. Introduction
Vitamin D is a fat soluble pro-hormone. In the UK, about 50% of the population is thought to have inadequate serum vitamin D levels, particularly by spring, and about 16% to have severe deficiency. Lack of sun exposure and to a lesser extent lifestyle and diet are the main reasons. About 80% of our vitamin D comes from the action of sun ultra violet light (UV) on the skin and the rest from a healthy diet.

2. Rationale
Since the resurgence of interest in vitamin D in the last 20 years or so there has been an increase in testing and supplementation/treatment protocols with not always sufficient rationale behind them. This guideline is to provide support to clinicians for optimum treatment of vitamin D deficiency and monitoring in adults and children.

3. Scope
These guidelines are applicable to patients within East Sussex Health Economy and aim to provide advice for consistent management of patients across primary and secondary care.

4. Sources of vitamin D and daily requirements
Dietary sources:
- Oily fish (salmon, sardines, mackerel). A tablespoon of cod liver oil provides about 1300IU
- Egg yolk 20 IU
- Fortified fat spreads 320 IU/100 g
- Fortified breakfast cereals 80-320 IU/100g
- White mushrooms up to 2700 IU/60g
- Infant formula milk 40-100 IU/100kcal

* Supermarket white mushrooms are often UV radiated to increase the whiteness thereby also increasing Vit D synthesis

Safe Sun Exposure
For vitamin D synthesis two or three exposures (of the face and arms without sunscreen and not behind glass) of 20 to 30 minutes between 10am and 3pm each week should provide adequate amounts of vitamin D for most individuals. However this may not be sufficient for some groups who require increased exposure time or frequency to get the same level of vitamin D synthesis, for example those with heavily pigmented skin and the elderly. Studies have consistently shown that vitamin D can be efficiently and sufficiently produced at doses of UV below those which cause sunburn.

During winter months the body relies on tissue stores and diet.

Recommended daily intake
In the UK, advice regarding the RNI for vitamin D has been reviewed by the Scientific Advisory Committee on Nutrition (SACN). SACN now recommend a RNI for vitamin D of 10mcg/day (400IU/day), throughout the year, for everyone in the general UK population aged 4 years and above. This includes pregnant and lactating women and population groups at increased risk of vitamin D deficiency. Since there is insufficient data to set RNIs for children aged under 4 years safety intakes are now recommended for this age group 8.5-10mcg/340-400IU/day for < 1 years and 400IU/day for 1-4 years.
Since it is difficult to achieve the RNI from natural food sources alone the SACN has recommended that the Government considers strategies to help the UK population consume the recommended intake of Vitamin D. Further information relating to the population as a whole is therefore awaited.

5. Definitions

The term Vitamin D is used for a range of compounds which include;

- colecaciferol (vitamin D3)
- ergocalciferol (vitamin D2) -less active than D3
- calcidiol (25-hydroxy vitamin D -hydroxylation of D2 and D3 in the liver)
- calcitriol (1,25-hydroxy vitamin D -second hydroxylation in the kidney)
- When serum vitamin D level is requested, total 25-hydroxy vitamin D is measured (D2 and D3).

6. Implications of vitamin D deficiency

Vitamin D is essential for good bone health. Deficiency of vitamin D results in rickets in children and osteomalacia in adults. Clinical features of vitamin D deficiency are outlined in the table 1 below.

Table 1.

<table>
<thead>
<tr>
<th>Clinical features of vitamin D Deficiency in adults²,⁷</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insidious onset, widespread or localised bone pain or tenderness without preceding mechanical injury</td>
</tr>
<tr>
<td>Proximal muscle weakness or muscle aches</td>
</tr>
<tr>
<td>Swelling, tenderness and redness at pseudo-fracture sites</td>
</tr>
<tr>
<td>Insufficiency fractures/ fragility fracture</td>
</tr>
</tbody>
</table>

7. Risk factors for vitamin D deficiency²,⁷

The following groups of people are at risk of vitamin D deficiency;

- pregnant/breast feeding women
- infants and young children under 5 years of age
- older people aged over 65 years
- people who are institutionalised or housebound, and those who cover their skin for cultural reasons
- pigmented skin tone

Medical risk factors for deficiency include;

- malabsorption diseases (cystic fibrosis, coeliac disease, Crohn's, gastric/intestinal bypass surgery)
- medications reducing cholesterol absorption and bile sequestrants
- enzyme-inducing medication e.g. anticonvulsants
- obesity (reduces bioavailability of vitamin D)
- glucocorticoids, antiretrovirals
- nephrotic syndrome (increases urinary loss)
- liver failure; chronic kidney disease (CKD)
- inherited enzyme deficiency (low levels of 1,25-dihydroxyvitamin D)
- hyperthyroidism

8. Prevention of Vitamin D deficiency in at risk groups
The Department of Health recommends at risk groups should take vitamin D supplements as outlined in Table 2 below:

Table 2: Department of Health recommendations for preventing vitamin D deficiency in at risk groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Recommended supplementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women</td>
<td>Daily supplement containing 10 micrograms (400 units) of vitamin D to build adequate foetal stores for early infancy</td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>Daily supplement containing 10 micrograms of vitamin D</td>
</tr>
<tr>
<td>Infants and young children</td>
<td>All infants and young children aged 6 months to 5 years should take a daily supplement containing vitamin D in the form of vitamin drops, to help them meet the requirement set for this age group of 7-8.5 micrograms of vitamin D per day.</td>
</tr>
<tr>
<td>People aged 65 years and over</td>
<td>Daily supplement containing 10 micrograms (400IU) of vitamin D</td>
</tr>
<tr>
<td>People who have low or no exposure to the sun</td>
<td>Daily supplement containing 10 micrograms (400IU) of vitamin D</td>
</tr>
</tbody>
</table>

Women and children from families who are eligible for the Government's Healthy Start scheme can get free vitamin supplements which include vitamin D, in the form of tablets for women and drops for children. Further information can be found on the Healthy Start website: [www.healthystart.nhs.uk](http://www.healthystart.nhs.uk)

Information is not provided in this guideline in relation to correction of vitamin D deficiency during pregnancy – consult local specialists for advice.

9. Measurement of Vitamin D

Routine testing of Vitamin D is not encouraged. Vitamin D deficiency should be considered and checked where patients have:

- one or more risk factor for vitamin D deficiency

AND

- clinical features of vitamin D deficiency

AND

- other causes for symptoms have been excluded

All patients should be provided advice on sun exposure and dietary sources of vitamin D.

Table 3: Serum 25-hydroxyvitamin D concentrations, health and disease

<table>
<thead>
<tr>
<th>25-hydroxyvitamin D concentration</th>
<th>Vitamin D status</th>
<th>Manifestation</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25nmol/L</td>
<td>Deficient</td>
<td>Rickets, osteomalacia</td>
<td>Treat with high dose vitamin D (see section 11.1)</td>
</tr>
<tr>
<td>25-50 nmol/L</td>
<td>Insufficient</td>
<td>Associated with risk of disease</td>
<td>See section 11.3</td>
</tr>
</tbody>
</table>

Although it is thought that levels >50 nmol/L may be sufficient for most people, the optimal levels are thought to be >75 nmol/L.

10. Accountabilities

Prescribers must ensure that levels are only checked in patients with one or more risk factors for vitamin D deficiency AND with clinical features of deficiency. If required, vitamin D should be prescribed according to the regimes outlined in these guidelines. Pharmacists should advise the prescribers, when necessary, on the dose, formulation and the frequency of the treatment. Nurses must ensure that the correct medicine with the right dose and frequency is administered to the patient.
11. Maintenance, treatment and monitoring

11.1 Treatment of vitamin D deficiency (<25nmol/L)

Patients identified as being deficient in vitamin D should be treated in accordance with table 4 below.

Table 4: Treatment of vitamin D deficiency in adults

<table>
<thead>
<tr>
<th>Age</th>
<th>Regimens options</th>
<th>Initial/loading treatment</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;18 years</td>
<td>Daily regimen</td>
<td>(Target for replacement ~300,000 units)</td>
<td>• Check serum calcium 1 month after starting treatment to allow detection of subclinical primary hyperparathyroidism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fultium D3 3,200 units capsule: 1 capsule daily for 13 weeks then follow maintenance advice</td>
<td>• Routine monitoring of vitamin D levels 13 weeks after starting treatment is not needed but may be appropriate in patients who are still symptomatic, have malabsorption or where poor concordance is suspected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Fultium contains gelatin consider using drops).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daily regimen for patients with swallowing difficulties</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fultium D3 drops 2,740 units/ml : 1.2ml (3,288 units) daily for up to 13 weeks then follow maintenance advice</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(manufacturers have no data to support enteral tube administration)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stat dose of ergocalciferol Injection is to ONLY be given if non-compliant or NBM (as less effective than daily regimens)</td>
<td>300,000 units once or twice within a year One 300,000 units of ergocalciferol IM injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>High dose 7 day regimen (prescribed and supplied by secondary care)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fultium D3 20,000 units capsule x 2 (40,000 units) daily for 7 days and then follow maintenance advice. Secondary care use where 7 day course will be prescribed and supplied</td>
<td></td>
</tr>
</tbody>
</table>

Clinicians should prescribe colecaciferol preparation by brand name as prescribing generically may result in expensive specials being supplied.

11.2 Treatment of probable deficiency

Patients with the following conditions should be regarded as having probable deficiency and treated in accordance with table 5 below:

- Parathyroid disease
- Thyroid disease
- Severe malabsorption

Table 5. Treatment of probable deficiency in high risk patients

<table>
<thead>
<tr>
<th>Regimens options</th>
<th>Maintenance treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily regimen</td>
<td>Fultium D3 800 unit capsules or 2740 units/ml drops Desunin 800 unit tablets Dose: 800 – 2,000 units daily</td>
</tr>
</tbody>
</table>

11.3 Treatment of Vitamin D insufficiency (25-50 nmol/L)

There is no good evidence to demonstrate that treating vitamin D insufficiency leads to improved clinical outcomes. Therefore it is recommended that patients are given lifestyle advice and are advised to purchase OTC colecaciferol at a dose of 800 to 2,000 units daily.
### 11.4 Maintenance following treatment for vitamin D deficiency

Colecalciferol at a dose of 800 to 2,000 units daily may be required once deficiency has been corrected for those patients who are still considered at risk. In some cases this may be lifelong therapy. Patients who were previously prescribed Adcal D3 or equivalent can continue treatment with this preparation where appropriate. Calcium replete patients should be advised to purchase appropriate vitamin D supplements over the counter (OTC). Lifestyle advice should also be provided.

### Products

- **Fultium D3 capsules/drops**[^12]
  - Available as: 800 unit capsules, 3,200 unit capsules, 20,000 unit capsules, 2,740 units/ml (3 drops = 200 units).
  - Licensed POM medicine.
  - Licensed for the treatment of vitamin D deficiency in adults and during pregnancy and breast-feeding.
  - Additional information: excipients include gelatine, glycerol and maize oil.

- **Desunin tablets**[^13]
  - Available as: 800 unit and 4,000 unit tablets
  - Licensed for the prevention and treatment of vitamin D deficiency in adults and adolescents.
  - Additional Information: Tablets can be swallowed whole or crushed. Gelatin free, does not contain peanut oil.

- **Ergocalciferol IM injection**
  - Use of the IM injection is only recommended when there are concerns regarding oral absorption (e.g. extensive bowel resection). The usual dose is 300,000 units given as a single dose and repeated if necessary after 3-4 months depending upon the clinical response and requirements. If the injection is used, close monitoring of serum calcium, phosphate and renal function is needed to avoid hypercalcaemia.

- **Alfacalcidol**
  - Available as: Capsules 250 nanograms, 500 nanograms, 1 micrograms
  - Oral drops 2 microgram in 1ml

[^12]: Fultium D3 capsules/drops
[^13]: Desunin tablets
12. Special Considerations

This section consists of contraindications, swallowing difficulties, and dietary cultures and beliefs.

12.1 Cautions and precautions regarding vitamin D products

The information provided below does not replace the necessity to refer to the summary of product characteristics and patient information leaflet provided by the manufacturer.

Contraindications include\textsuperscript{10,12,13}:
- Hypersensitivity to vitamin D or any of the excipients in the product
- Hypervitaminosis D
- Nephrolithiasis
- Diseases or conditions resulting in hypercalcaemia and/or hypercalciuria
- Severe renal impairment
- Metastatic calcification

Drug interactions\textsuperscript{12,13}
- Concomitant treatment with phenytoin or barbiturates can decrease the effect of vitamin D because of metabolic activation.
- Concomitant use of glucocorticoids can decrease the effect of vitamin D.
- The effects of digitals and other cardiac glycosides may be accentuated with the oral administration of calcium combined with vitamin D.
- Thiazide diuretics reduce the urinary excretion of calcium. Concurrent use with thiazide diuretics should therefore be reviewed.
- Simultaneous treatment with ion exchange resins such as cholestyramine may reduce the gastrointestinal absorption of vitamin D.
- Patients should avoid taking vitamin D at the same time of day as orlistat as this reduces absorption.

12.2 Swallowing difficulties

Patients who are unable to swallow tablets have an unsafe swallow with liquids can benefit from ergocalciferol 300,000 units IM injection. This vitamin D is less potent than oral colecalciferol.

12.3 Dietary culture and beliefs

Colecalciferol is synthesized commercially from a precursor obtained from an animal source such as wool fat. Wool fat derived products are unacceptable to vegans and would only be approved by the Vegetarian Society if the origin is sheep’s wool that had been pressed and not derived from slaughter.

For more information regarding dietary belief or clinical advice please contact Medicines Information at ESHT.

12.4 Vitamin D toxicity

Vitamin D toxicity is rarely seen however if toxicity is suspected, vitamin D should be withdrawn and serum calcium and renal function checked urgently. Early signs of toxicity include symptoms of hypercalcaemia such as thirst, polyuria and constipation\textsuperscript{5,10}.
13. Chronic Kidney Disease
Patients with chronic kidney disease (CKD) may also suffer from renal bone disease (osteodystrophy). In these patients it is important to control PTH and phosphate levels for bone health as over-suppression of PTH may lead to a dynamic bone disease. In renally impaired patients it is important to measure the PTH level as well as the vitamin D level.

13.1.1. Vitamin D treatment
Alfacalcidol and calcitriol are the activated form of vitamin D and should be supplied to those with advanced CKD. However, it is important to note that there are some extra-renal conversions of 25-hydroxyvitamin D to its active form so treatment with colecalficeral is sometimes considered to be appropriate according to specialist advice.

13.1.2. Alfacalcidol
Alfacalcidol is indicated in conditions where there is chronic severe liver disease (impaired 25 OH hydroxylation), chronic kidney disease *(impairred hydroxylation of 25OH to 1,25 OH vitamin D)* or deficient PTH secretion (impairred hydroxylation of 25 to 1,25 OH vitamin D)

- Renal osteodystrophy
- Primary hypoparathyroidism
- Neonatal hypocalcaemia
- Pseudo-deficiency (D-dependent) rickets and osteomalacia
- Hypophosphataemic vitamin D resistant rickets and osteomalacia

alfacalcidol is generally recommended when egfr < 30mL/min/1.73m².

Dosing and monitoring:
The initial starting dose is 1 micrograms daily for adults. Elderly patients should be started on a lower dose of 0.5 micrograms daily. The dose should be adjusted to avoid hypercalcaemia. The usual maintenance dose is 0.25-1 micrograms per day. There is no benefit in measuring vitamin D in such patients since the treatment is with 1,25 vitamin D which is not detected with assays for Vitamin D.

Initiation should be following renal/endocrinology/metabolic specialist advice. Patients receiving alfacalcidol should have their plasma calcium and phosphate levels checked regularly. Blood tests should be taken 1 month after starting, then every 3-6 months depending on CKD stage.

If hypercalcaemia occurs, alfacalcidol should be stopped until plasma calcium returns to normal (approximately 1 week) then restarted at half the previous dose.
14. Treatment and Maintenance in children

DH recommendations\textsuperscript{8} are that:

- All infants and young children aged 6 months to 5 years should take a daily supplement containing vitamin D in the form of vitamin drops, to help them meet the requirement set for this age group of 7-8.5 micrograms of vitamin D per day.
- Those infants who are fed infant formula will not need vitamin drops until they are receiving less than 500ml of infant formula a day, as these products are fortified with vitamin D.
- Breastfed infants may need to receive drops containing vitamin D from one month of age if their mother has not taken vitamin D supplements throughout pregnancy.

Suitable vitamin drops can be purchased over the counter. Children from families who are eligible for the Government's Healthy Start scheme can get free vitamin supplements which include vitamin D, in the form of drops for children\textsuperscript{8}.

Further information can be found on the Healthy Start website: \url{www.healthystart.nhs.uk}

All children identified as being vitamin D deficient or insufficient should be referred to secondary care for further investigation and treatment.

For the full ESHT vitamin D treatment and monitoring guideline please refer to the following link:
\url{http://eshealthcare/guideline/1179.pdf} (N3 connection required)
15. Treatment of Vitamin D deficiency in Adults

**Risk factors for Vitamin D Deficiency**
- Pigmented skin, lack of sun exposure, institutionalised, elderly (65+), vegetarian/vegan
- Malabsorption – cystic fibrosis, IBD, short bowel syndrome, cholestatic liver disease, obesity.
- Metabolic risk – liver/renal disease, use of anticonvulsants, rifampicin, cholestyramine, glucocorticoids, HAART regimes

**Symptoms for Vitamin D Deficiency**
- Insidious onset, widespread or localised bone pain or tenderness without preceding mechanical injury
- Proximal muscle weakness or muscle aches
- Swelling, tenderness and redness at pseudo-fracture sites
- Insufficiency fractures/ fragility fracture

**Test 25-hydroxyvitamin D (25[OH]D) status**
Check PTH, Bone, liver, renal profile

**Vitamin D deficiency (<25nmol/L)**
- Prescribe a course of Vitamin D
  - An overall loading dose of 300,000 units is recommended
  - Fulltium D3 3,200 units: 1 capsule daily for 13 weeks
  - Fulltium D3 Drops 2,740 units/ml: 1.2ml daily for 13 weeks (no data on enteral tube administration)
- High dose regime
  - Fulltium D3 20,000 2 capsules daily for 7 days (prescribe and supply through secondary care only)
  - Check calcium after 1 month on treatment

**Vitamin D insufficiency (25-50 nmol/L)**
- Lifestyle advice + Purchase Vit D 800-2000 units per day

**Levels adequate for most people (>50nmol/L)**
- Lifestyle advice + Purchase Vit D 400-800 units per day

**Maintenance Therapy**
For those with documented vitamin D deficiency where the underlying cause cannot be rectified, ongoing maintenance therapy is advisable along with lifestyle advice.

**Self-purchase:** patients should be advised to take 800-2000 units daily

**Lifestyle Advice**

**Dietary sources**
- Eat more oily fish, cod liver oil & other fish oils
- Eat egg yolks, fortified cereal & margarine

**Safe sun exposure**
In the UK, 2 or 3 short sunlight exposures per week April – September are sufficient to achieve adequate vitamin D levels. In the winter the body relies on tissue stores and diet.

**Patients with Parathyroid disease, thyroid disease or severe malabsorption where ongoing deficiency is probable:** prescribe vitamin D 800 – 2,000 units daily
16. References


2. Update on Vitamin D, Position Statement by the Scientific Advisory Committee on Nutrition, 2007.


