Prescribing Guidance for the Management of Vitamin D Deficiency

Purpose of Guidance:
- Advice on the diagnosis and management of vitamin D deficiency / insufficiency.
- To define the balance between patient lifestyles, self-management and medical treatment.
- To outline the most cost-effective treatments for NHS prescribing.

Background:
Vitamin D (Calciferol) is a fat soluble nutrient that is important for bone formation in all age groups. It maintains neuromuscular function and various other cellular processes including the immune system and insulin production. Severe deficiency can result in rickets (among children) and osteomalacia (among children and adults). Over 90% of our vitamin D requirement is obtained by the action of UVB sunlight on the skin, which occurs between April and September in the UK. Small amounts of vitamin D are also obtained in the diet from oily fish (sardines, salmon, herring, mackerel, fresh tuna), red meat, liver, egg yolks, mushrooms, fortified breakfast cereals, margarine and infant formula milks. Vitamin D deficiency is increasingly prevalent in the UK population. National surveys suggest that around a fifth of adults and 8 to 24% of children may have low vitamin D status.1

Risk Factors for Vitamin D Deficiency:
Vitamin D deficiency develops when there is inadequate exposure to sunlight or a lack of Vitamin D in the diet and usually takes a long time to develop due to the slow release of the vitamin from body stores. The specific risk factors that have been linked to vitamin D deficiency are:

<table>
<thead>
<tr>
<th>Reduced Sun Exposure</th>
<th>Poor Dietary Intake</th>
<th>Metabolic Risk</th>
<th>Increased Need</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern latitude (e.g. UK)</td>
<td>Vegetarian or vegan (fish free diet)</td>
<td>Reduced synthesis in elderly ≥ 65 years and those with darker skin</td>
<td>Pregnant and breastfeeding women (particularly teenagers and young women)</td>
</tr>
<tr>
<td>Season – winter &amp; spring</td>
<td>Malabsorption</td>
<td>Increased breakdown due to drugs (rifampicin, antiretrovirals, anticonvulsants, glucocorticoids)</td>
<td>Infants and children aged under 5</td>
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<tr>
<td>Pigmented skin</td>
<td>Liver Disease</td>
<td></td>
<td>Adolescents</td>
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<tr>
<td>Occlusive garments</td>
<td>Renal Disease</td>
<td></td>
<td>Obesity</td>
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<tr>
<td>Habitual sunscreen use</td>
<td>Short bowel</td>
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<tr>
<td>Immobile or housebound</td>
<td>Breast fed infants</td>
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Note: Patients with risk factors for deficiency but who are asymptomatic do not require any further investigations. Lifestyle and dietary advice should be offered and self-management recommended in the form of appropriate over-the-counter supplements containing 10 micrograms (400 units) per day of vitamin D.
NICE guidance recommends supplementation in the following groups:¹

- All pregnant and breastfeeding women should take a daily supplement containing 10 micrograms (400 units) of vitamin D, to ensure the mother’s requirements for vitamin D are met and to build adequate fetal stores for early infancy. These may be available free of charge for patients eligible for Healthy Start www.healthystart.nhs.uk
- All infants and young children aged 6 months to 3 years are advised to take a daily supplement containing vitamin D in the form of vitamin drops. But infants who are fed infant formula will not need them until they have less than 500 ml of infant formula a day, because these products are fortified with vitamin D. Breastfed infants may need drops containing vitamin D from 1 month of age if their mother has not taken vitamin D supplements throughout pregnancy. (Vitamin D – advice for supplements for at risk groups – letter from the UK Chief Medical Officers’ Department of Health²). Recommended safe intake from birth to 1 year is 8.5-10 micrograms per day and aged 1-4 years is 10 micrograms per day. People aged 65 years and over and people who are not exposed to much sun should also take a daily supplement containing 10 micrograms (400 units) of vitamin D. These can be purchased from pharmacies and supermarkets.

**Signs & Symptoms of Vitamin D Deficiency:**

<table>
<thead>
<tr>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Osteomalacia</td>
<td>- Deformed bones (bow legs or knock knees)</td>
</tr>
<tr>
<td>- Gradual onset &amp; persistent bone pain without preceding mechanical injury (frequently in back or lower limb)</td>
<td>- Poor growth, delayed fontanelle closure</td>
</tr>
<tr>
<td>- Gradual onset &amp; persistent musculoskeletal pain without preceding mechanical injury</td>
<td>- Delayed walking or a waddling gait</td>
</tr>
<tr>
<td>- Waddling gait or change in gait</td>
<td>- Tender or swollen joints, classically the wrists or costochondral junctions</td>
</tr>
<tr>
<td>- Proximal muscle weakness (difficulty with stairs, getting up off the floor or standing after sitting in a low chair)</td>
<td>- Bone pain or tenderness</td>
</tr>
</tbody>
</table>

**Diagnosis of Vitamin D Deficiency:**

NICE Guidance recommends that health care professionals should not routinely test people’s vitamin D status unless:¹

- They have symptoms of deficiency
- They are considered to be at particularly high risk of deficiency (for example, they have very low exposure to sunlight)
- There is a clinical reason to do so (for example, they have osteomalacia, or have had a fall)

The National Osteoporosis Society published a practical clinical guideline in December 2018 to support health professionals provide a uniform approach in the management of vitamin D deficiency.³ The Royal College of Paediatrics and Child Health published a Guide for Vitamin D in Childhood in October 2013⁴ and a Position Statement in March 2018⁵. Both guidelines provide clarity on who should be tested for vitamin D deficiency, how to interpret the results and how to treat deficiency once diagnosed.
Vitamin D deficiency is determined by measuring serum 25-hydroxy vitamin D (25-OHD).

<table>
<thead>
<tr>
<th>Total 25-OHD Level</th>
<th>Status</th>
<th>Recommendation (see flow charts for detail &amp; doses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25 nmol/L</td>
<td>Deficient</td>
<td>High dose initial treatment &amp; long term maintenance</td>
</tr>
<tr>
<td>25.1 – 49.9 nmol/L</td>
<td>Inadequate in some people</td>
<td>Lifestyle advice (+/- long-term maintenance**)</td>
</tr>
<tr>
<td>&gt; 50.0 nmol/L</td>
<td>Sufficient for almost the whole population</td>
<td>Lifestyle advice</td>
</tr>
</tbody>
</table>

**Treatment of patients who are considered to be vitamin D insufficient is not routinely recommended. Lifestyle advice on regular sunlight exposure, dietary sources of vitamin D and use of over the counter supplements are appropriate interventions. Maintenance treatment should only be offered if there is no improvement in vitamin D status after 12 months of appropriate lifestyle measures.

When to Refer:
Consider seeking specialist advice for children or any patient of concern according to clinical judgement. For the following patients a referral is generally the appropriate course of action:

- All children under 1 year of age
- Deficiency due to malabsorption
- Liver disease or abnormal LFTs across the range
- Parathyroid disorders
- Sarcoidosis
- Tuberculosis
- Lymphoma
- Renal disease or renal stones
- Skeletal deformity or short stature
- Unexplained deficiency
- Alopecia
- Cardiac Failure
- Atypical clinical manifestations
- Focal bone pain
- Metastatic cancer
- Unexplained weight loss
- Significant hypocalcaemia
- (adjusted calcium < 2.00 mmol/L)
- Significant hypercalcaemia
- (adjusted calcium > 2.60 mmol/L)
- Failure to respond after 3 months treatment

References:


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Approved at Area Prescribing Committee on 13 Nov 2018; updated July 2019 for review by March 2021
Flowchart for ADULTS – Assessment & Treatment of Vitamin D Deficiency

Clinical Assessment & Identification (Patient ≥ 18 years)
Assessment of patient as per risk factors and signs & symptoms

Arrange for necessary investigations
U&E, LFT, Bone Profile, 25-OH Vitamin D

Can the patient be appropriately managed within primary care?
1. No marked renal impairment (i.e. eGFR ≥ 30 mL/min)
2. Adjusted calcium in range 2.00–2.60 mmol/L
3. Normal LFTs (other than an isolated raised Alk Phos which is not uncommon in Vitamin D deficiency)

No Refer to appropriate speciality

Yes

Management of Vitamin D Deficiency (25-OHD < 25 nmol/L)

Loading Dose
50,000 units Colecalciferol* once weekly for 6 weeks (total dose 300,000 units)

Monitoring
U&E + Bone Profile 4 weeks after completing loading dose (more frequent testing may be appropriate if CKD 3-5)
Vitamin D Level at 3 months and refer to endocrinology if not responding (response cannot be accurately measured before this. Routine regular vitamin D levels is generally unnecessary)

Maintenance Dose
Consider maintenance therapy 4 weeks after completing the loading dose 800–2000 units colecalciferol* once daily OR 25,000 units colecalciferol* once monthly

Monitoring
U&E + Bone Profile annually
Vitamin D Level annually

*Colecalciferol (Vitamin D3) is preferred unless there is a clear rationale for prescribing an alternative. Ergocalciferol (Vitamin D2) is less widely available and can be highly costly. Alfacalcidol is not appropriate for Vitamin D replenishment unless recommended by a renal specialist due to the risk of hypercalcaemia.

Note: 400 units is equivalent to 10 micrograms of colecalciferol (vitamin D)

Management of Vitamin D Insufficiency (25-OHD 25.0–49.9 nmol/L)

Routine prescribing is not necessary.
Lifestyle advice should be offered on regular sunlight exposure, dietary sources of vitamin D e.g. oily fish (sardines, salmon, herring, mackerel, fresh tuna), red meat, liver, egg yolks, mushrooms, fortified breakfast cereals, margarine and use of over the counter supplements providing at least 800 units Colecalciferol daily.
Blood levels should be repeated after 12 months.
If there is no improvement in vitamin D status despite appropriate lifestyle modifications then consider recommending a colecalciferol supplement as per maintenance doses detailed above.

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Flowchart for **CHILDREN**—Assessment & Treatment of Vitamin D Deficiency

**Clinical Assessment & Identification (Patient aged 16 years and under)**
Assessment of patient as per risk factors and signs & symptoms
Is secondary care referral appropriate based upon symptoms?

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**Arrange necessary investigations:**
U&E, LFT, Bone Profile, PTH, 25-OH Vitamin D

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**Blood results**
Investigations indicate deficiency or insufficiency
Is secondary care referral indicated?

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**Treatment of Vitamin D Deficiency (25-OH Vitamin D < 25.0 nmol/L)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Colecalciferol* Loading Dose</th>
<th>Preferred Formulary Brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 6 months</td>
<td>1,000 – 3,000 units daily for 4 - 8 weeks</td>
<td>See Appendix 1 for approved formulary products. Always prescribe by brand and in appropriate quantities.</td>
</tr>
<tr>
<td>6 months – 12 years</td>
<td>6,000 units daily for 4 - 8 weeks</td>
<td></td>
</tr>
<tr>
<td>12 – 16 years</td>
<td>10,000 units daily for 4 - 8 weeks</td>
<td></td>
</tr>
</tbody>
</table>

**Monitoring**
U&E + Bone Profile 4 weeks after completing loading dose
Vitamin D Level at 3 months and refer to paediatrics if not responding (response cannot be accurately measured before this. Routine repeat vitamin D levels is generally unnecessary)

**Age**
**Maintenance Dose**
**Preferred Formulary Brands**

<table>
<thead>
<tr>
<th>Under 1 month</th>
<th>300 – 400 units Vitamin D daily</th>
<th>Available as over the counter supplements. A prescription is not generally necessary. Maintenance or preventative vitamin D supplementation should be over the counter unless the patient has a long term or chronic condition, or has undergone surgery that results in malabsorption or the patient meets the general exceptions to the NHS England guidance. Continuing need for a prescription should be reviewed on a regular basis. See Appendix 1 for approved formulary products.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month - 16 years</td>
<td>400 – 1000 units Vitamin D daily</td>
<td></td>
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</table>

**Note:** Consider referral to secondary care at any stage if new symptoms cause parental or professional concern

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*Colecalciferol (Vitamin D3) is preferred unless there is a clear rationale for prescribing an alternative. Note: 400 units is equivalent to 10 micrograms of colecalciferol (vitamin D)

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**Management of Vitamin D Insufficiency (25-OHD 25.1 – 49.9 nmol/L)**

Routine prescribing is not necessary.
Lifestyle advice should be offered on regular sunlight exposure and dietary sources of vitamin D e.g. oily fish (sardines, salmon, herring, mackerel, fresh tuna), red meat, liver, egg yolks, mushrooms, fortified breakfast cereals, margarine and infant formula milks.
A range of products are available over the counter including Abidec and Dalivit Drops. Eligible families will have access to Healthy Start Vitamins free of charge in children under the age of 5. If a prescription is appropriate then prescribe as per maintenance doses above.

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**APPENDIX 1 – Preferred Formulary Brands:**

**Note:** Colecalciferol (Vitamin D3) should be used unless there is clear, evidenced rationale for prescribing an alternative. Ergocalciferol (Vitamin D2) is less widely available and can be highly costly as the majority of formulations are unlicensed specials. Alfacalcidol is not appropriate for Vitamin D replenishment unless the patient is under the care of a renal specialist due to the risk of hypercalcaemia.

<table>
<thead>
<tr>
<th>Product</th>
<th>Brand</th>
<th>Prices (Nov 2018)</th>
<th>Availability</th>
<th>Licensing Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colecalciferol 50,000 unit Capsules</td>
<td>InVita D3 50,000 unit Capsules (contains Halal and Kosher compliant gelatine)</td>
<td>£9.90 for 6 (6 week adult course)</td>
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<tr>
<td>Colecalciferol 50,000 units/1ml</td>
<td>InVita D3 50,000 units/1ml sugar free oral solution</td>
<td>£12.50 for 6 (6 week adult course)</td>
<td></td>
<td></td>
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<tr>
<td>Colecalciferol 25,000 unit Capsules</td>
<td>InVita D3 25,000 unit Capsules (contains Halal and Kosher compliant gelatine)</td>
<td>£15.80 for 12 (6 week adult course)</td>
<td>Available from major wholesalers.</td>
<td>Licensed in the UK.</td>
</tr>
<tr>
<td>Colecalciferol 25,000 units/1ml</td>
<td>InVita D3 25,000 units/1ml sugar free oral solution</td>
<td>£17.80 for 12 (6 week adult course)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colecalciferol 25,000 unit Tablets</td>
<td>Stexerol-D3 25,000 unit Tablets (gelatine, peanut &amp; soya oil free. Halal and Kosher certified)</td>
<td>£17.00 for 12 (6 week adult course)</td>
<td></td>
<td></td>
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<tr>
<td>Colecalciferol 10,000 unit/mL Liquid</td>
<td>Thorens 10,000 unit/mL Liquid (alcohol, gluten, lactose and nut free. Halal and Kosher certified) Has a taste of olive oil. Can be taken undiluted or mixed with a small amount of cold or lukewarm food immediately prior to use.</td>
<td>£5.85 for 10ml £17.55 for 30ml £35.10 for 60ml</td>
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<tr>
<td>Colecalciferol 800 unit Capsules</td>
<td>NHS England has identified that colecalciferol 800 unit capsules should not be routinely prescribed in primary care. Patients should be advised that items may be purchased over-the-counter for maintenance or preventative therapy but they are not available at NHS expense other than to treat deficiency e.g. ColeKal-D3.</td>
<td></td>
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<tr>
<td>Colecalciferol 1000 unit Tablets</td>
<td>NHS England has identified that colecalciferol 1000 unit tablets should not be routinely prescribed in primary care. Patients should be advised that items may be purchased over-the-counter for maintenance or preventative therapy but they are not available at NHS expense other than to treat deficiency e.g. Vitabiotics Ultra Vitamin D3 tablets.</td>
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<tr>
<td>Colecalciferol 800 unit Capsules</td>
<td>InVita D3 800 unit capsules (contains Halal and Kosher compliant gelatine)</td>
<td>£2.68 for 30</td>
<td>Available from major wholesalers.</td>
<td>Licensed in the UK.</td>
</tr>
<tr>
<td>Colecalciferol 800 unit Capsules</td>
<td>Fultium D3 800 unit capsules (contains Halal and Kosher compliant gelatine)</td>
<td>£3.60 for 30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colecalciferol 800 unit Tablets</td>
<td>Desunin 800 unit tablets (gelatine, peanut &amp; soya oil free)</td>
<td>£3.60 for 30</td>
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<tr>
<td>Products for Young Children</td>
<td>Abidec Drops (licensed from birth) 0.6mls contains 400 units Ergocalciferol (contains peanut oil)</td>
<td>£3.13 for 50ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Products for Young Children</td>
<td>Dalivit Drops (licensed from 6 weeks) 14 drops contain 400 units Ergocalciferol (peanut &amp; soya oil free) Contains a higher dose of Vit A which may not be suitable for neonates)</td>
<td>£6.50 for 25ml</td>
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