NICE recommends that health professionals should NOT routinely test people’s vitamin D status unless:
• They are considered to be at particular high risk
• There is a clinical reason such as a metabolic factor
• They show clinical features of deficiency - see appendix 4
  ➢ Test before starting patients on an antiresorptive agent e.g. IV zoledronic acid or denosumab or oral osteoporosis therapy if not going to be co-prescribed vitamin D containing supplements
  ➢ Specialists may test other specific patient groups as deemed clinically necessary
  ➢ See Public Health England advice about winter months

Also arrange:
U+Es, LFTs, Bone profile, and PTH if calcium <2.15 mmol/L or >2.6mmol/L

Measure 25OH vitamin D

30-50 nmol/L
Treat only if one or more of following applies:
• Fragility fracture / osteoporosis / high fracture risk
• Drug treatment for bone disease
• Symptoms suggestive of vitamin D deficiency
• Increased risk of developing vitamin D deficiency e.g. Reduced UV exposure, raised PTH, treatment with anticonvulsants or glucocorticoids, malabsorption

If treatment not required reinforce lifestyle advice

If treatment required, is patient suitable for non-specialist management?
Consider specialist referral if they have any of the following:
eGFR < 30 ml/min/1.73m² Hypercalcaemia Granulomous conditions e.g. sarciodosis, active TB

Patient symptomatic or about to start zoledronate or denosumab?

Yes

Consider loading regimen
(Approximately 300,000 units colecalciferol orally over 6-10 weeks) e.g.
• Colecalciferol 20,000 unit capsules (prescribed by brand) – Take two capsules once a week for 7 weeks or
• Invita D3 25,000 unit/1ml oral solution – Take the contents of two ampoules (50,000 units) by mouth once a week for 6 weeks

Check serum calcium 3-4 weeks after finishing loading regimen of vitamin D. Vitamin D repletion may unmask primary hyperparathyroidism

No

Consider referral to appropriate speciality for advice

Calcium intake sufficient (≥ 700mg per day)?

Yes, intake sufficient
Treat with colecalciferol 800 – 2000 units oral daily (may be purchased OTC) see appendix 1. In extreme cases where a prescription is required, prescribe Stexerol D3 1000 unit tablets – one tablet daily

No, intake insufficient
Consider calcium and vitamin D orally e.g.
Adcal D3 chewable (1500mg calcium carbonate / 400 units colecalciferol) one tablet twice daily.
Add in Stexerol 1000 units daily if Vitamin D was < 12nmol/L prior to treatment

Routine repeat vitamin D testing is not required, but reinforce concordance at routine reviews
Following loading regimen, if still symptomatic at 3 months retest vitamin D and review diagnosis. Patients with malabsorption conditions may require repeat testing. Review of on going treatment will be dependent on the patient's symptoms, risks and lifestyle

Routine replacement / maintenance therapy
(for less urgent replacement and maintenance therapy)

Calcium normal
Initiate maintenance therapy (see routine regimen)

Hypercalcaemia
Check PTH and refer to appropriate clinic.

Vitamin D Guideline: Deficiency and Insufficiency in Adults

Nottinghamshire Area Prescribing Committee
Appendix 1: Vitamin D products available without prescription

Patients should be encouraged to buy supplements unless in extreme circumstances where a prescription may be required

Patients can buy single vitamin D supplements at most pharmacies and supermarkets for less than £3 for a three month supply. Women and children who qualify for the Healthy Start scheme can get free supplements containing the recommended amounts of vitamin D. NHS choices website can provide additional information for patients. Products available over the counter are suitable for replacement/maintenance doses as well as for prophylaxis in winter if required.

Healthy Start vitamins
Healthy Start vitamins (www.healthystart.nhs.uk) for women and children are free of charge for low income families and are available from Sure Start centres and some other health centres. You can also ask your midwife or health visitor for where they are available locally.

Women qualify for free Healthy Start vitamins from the 10th week of pregnancy or if they have a child under four years old, and if she or her family receives:
• Income Support, or
• Income-based Jobseeker’s Allowance, or
• Income-related Employment and Support Allowance, or
• Child Tax Credit (but not Working Tax Credit unless the family is receiving Working Tax Credit run-on only) and has an annual family income of £16,190 or less.

Women who are under 18 and pregnant also qualify, even if they do not get any of the above benefits or tax credits.

Some Sure Start centres will also sell them to other customers (at minimal charge), but not all have the facility to take money.

There are two different Health Start products:
• Healthy Start women’s vitamin tablets. The daily dose of one tablet contains: 400 units of vitamin D3 per tablet (as well as 70 micrograms of vitamin C and 400 micrograms of folic acid)

• Healthy Start children’s vitamin drops. The daily dose of five drops contains: 300 units of vitamin D3 (as well as 233 micrograms of vitamin A and 20 milligrams of vitamin C)

For those people in whom healthy start vitamins are not suitable, a range of vitamin D3 supplements are available for purchase from various manufacturers, some examples of which are included in Table 1 below.

Appendix 2: Patient information about vitamin D and lifestyle advice

A variety of patient information leaflets are available including:
Public Health England: Vitamin D – All you need to know
NHS Choices Vitamin D PIL
National Osteoporosis Society: Healthy bones:
Royal National Orthopaedic Hospital: FAQs about Vitamin D in childhood
Royal College Obstetrics and Gynaecologists: Healthy eating and vitamin supplements in pregnancy
BDA food fact sheet on Vitamin D
Appendix 3: Recommended Vitamin D preparations for prescribing (when treating in accordance with Nottinghamshire vitamin D guideline)

Table 1: Recommended vitamin D preparations (To be taken with food).
Further information on available products is available here

<table>
<thead>
<tr>
<th>Oral Vitamin D preparation</th>
<th>Licensing status</th>
<th>Availability</th>
<th>Cost</th>
<th>Allergy / dietary info</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colecalciferol 20,000 unit capsules</td>
<td>Licensed UK products (e.g. Fultium D3, Aviticol, Plenachol)</td>
<td>POM - normal wholesalers</td>
<td>£17.04 for 15 £29.00 for 30 capsules</td>
<td>Check individual products Gelatin in Aviticol and Fultium D3 suitable for kosher and halal. No Gelatin in Plenachol. Aviticol, Plenachol and Fultium D3 are arachis oil free.</td>
</tr>
<tr>
<td>Invita D3 25,000 units/ 1ml oral solution. Formulation is a 1ml single dose “snap and squeeze” ampoule</td>
<td>Licensed UK product (replaces Pro D3 and Dekristol capsules)</td>
<td>POM - normal wholesalers</td>
<td>£4.45 for 3 ampoules</td>
<td>Does not contain peanut oil or soya. Olive oil based liquid. Suitable for vegetarians</td>
</tr>
</tbody>
</table>

Comes as a “Snap and squeeze” ampoule (see below). Patients should be advised to take Invita D3 at mealtimes – If preferred, the contents can be emptied onto a spoon and taken orally or mixed with a little cold or lukewarm food immediately before use. See SPC for further information

- [1] Stexerol-D3® 1000 units colecalciferol tablets | Licensed UK product | POM - normal wholesalers | £2.96 for 30 tablets | Does not contain gelatin, peanut oil or soya. Colecalciferol is derived from healthy live sheep’s wool fat – may be acceptable to vegetarians |
- [2] Fultium D3® 800 unit colecalciferol capsules (30 caps) N.B. doses over 4 capsules a day are off-label | Licensed UK product | POM - normal wholesalers | £3.60 for 30 capsules | Contains glycerol and gelatin. The gelatin used in the capsule shell is certified to Halal and kosher standards (see website) |
- [3] Desunin® 800 unit colecalciferol tablets (30 tabs) N.B. doses over 5 tablets a day are off-label | Licensed UK product | POM - normal wholesalers | £3.60 for 30 tablets | Does not contain gelatin, peanut oil or soya. Colecalciferol is derived from healthy live sheep’s wool fat – may be acceptable to vegetarians |

NOT RECOMMENDED: Named patient ‘specials’ of vitamin D (unlicensed) for adults in primary care should NOT be routinely prescribed.

Intramuscular Injection:
Please note that injection of Ergocalciferol is not routinely encouraged due to variable absorption and slower onset of repletion. Therefore it should only be used if a patient cannot take an oral preparation.
Dose for osteomalacia treatment: 300,000 units of ergocalciferol given by intramuscular injection once only or give a second dose 3 months later
There is a licensed UK injection of ergocalciferol but its not always available. This is gelatin free. Ergocalciferol, 7.5 mg (300 000 Units)/mL in oil. Injection for intramuscular use only. 1-mL amp = £9.35, 2-mL amp = £10.84.

Alfacalcidol/Calcitriol (Specialist initiation only)
Alfacalcidol and Calcitriol have no routine place in the management of primary vitamin D deficiency and should be reserved for use in renal disease, liver disease and primary hypoparathyroidism.

Additional reference sources
Is there a calcium and vitamin D preparation which is suitable for a vegetarian or vegan?
Is there a suitable vitamin d product for a patient with a peanut or soya allergy?
Appendix 4: Risk factors, features and treatment of insufficiency and deficiency

Table 1: Risk factors for vitamin D deficiency

<table>
<thead>
<tr>
<th>Inadequate UVB light exposure</th>
<th>Inadequate dietary intake or absorption</th>
<th>Metabolic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigmented skin (non-white ethnicity)</td>
<td>Vegetarian (or other fish-free diet)</td>
<td>Older people aged 65 years and over (reduced synthesis in the skin)</td>
</tr>
<tr>
<td>Lack of sunlight exposure or atmospheric pollution</td>
<td>Malabsorption (e.g. coeliac disease, Crohn’s disease etc)</td>
<td>Drug interactions e.g. rifampicin, anticonvulsants (carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone and valproate), isoniazid, cholestyramine, sucralfate, glucocorticoids, highly active antiretroviral treatment (HAART)</td>
</tr>
<tr>
<td>Skin concealing garments or routine use of sun protection factor 15 or above</td>
<td>Short bowel</td>
<td></td>
</tr>
<tr>
<td>Northern latitude</td>
<td>Cholestatic liver disease, jaundice</td>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>Housebound or indoor living (e.g. care homes)</td>
<td></td>
<td>Chronic renal disease</td>
</tr>
<tr>
<td>Seasonal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical features of vitamin D deficiency and Osteomalacia

- Gradual onset and persistent bone pain without preceding mechanical injury (frequently in back, ribs or lower limbs)
- Frailty fracture
- Proximal muscle weakness (difficulty with stairs, getting up off the floor or standing after sitting in a low chair, waddling gait) or muscle pain
- Carpopedal spasm, tetany, seizures or irritability due to hypocalcaemia and requiring urgent treatment
- Osteopenia on plain radiograph
- Low bone density on dual energy x ray absorptiometry scan (does not equate to osteoporosis)

Treatment of insufficiency and deficiency

Treatment of insufficiency is advised in patients with the following:

- fragility fracture, documented osteoporosis or high fracture risk
- treatment with antiresorptive medication 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 PTH
- medication with antiepileptic drugs or oral glucocorticoids
- conditions associated with malabsorption.

Good sources of vitamin D (advice from NHS choices)

- From about late March/early April to the end of September, most people should be able to get all the vitamin D they need from sunlight. The body creates vitamin D from direct sunlight on the skin when outdoors. Between October and early March we don't get enough vitamin D from sunlight. Read more about vitamin D and sunlight.
- Vitamin D is also found in a small number of foods Including oily fish (salmon, sardines, herring, mackerel and fresh tuna), red meat, liver, egg yolks, fortified foods – such as most fat spreads and some breakfast cereals. Another source of vitamin D is dietary supplements.
- In the UK, cows’ milk is generally not a good source of vitamin D because it isn’t fortified, as it is in some other countries.
Appendix 5: Maintenance doses for at risk patients

<table>
<thead>
<tr>
<th>People at risk of vitamin D deficiency</th>
<th>Daily oral supplement advised</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pregnant* and breastfeeding women</td>
<td>400 units daily†</td>
</tr>
<tr>
<td>People aged 65 and over</td>
<td>400 units daily</td>
</tr>
<tr>
<td>People who are not exposed to much sun; for example, those who cover their skin for cultural reasons, are housebound or who stay indoors for long periods (e.g. care home residents) **</td>
<td>400 units daily</td>
</tr>
</tbody>
</table>

* REMEMBER – pregnant women should avoid taking multivitamins containing vitamin A (retinol) due to the teratogenic risk of vitamin A
† High risk women (women with increased skin pigmentation, reduced exposure to sunlight, or those who are socially excluded or obese) may be advised to take at least 1000 units (25 micrograms) daily (in line with RCOG guidelines 2014)
** Evidence from a recent Cochrane Review suggests that calcium and vitamin D supplements, particularly in high risk patients (postmenopausal women and older men in care homes), result in a small reduction in hip fracture risk. There is evidence that vitamin D alone is unlikely to prevent hip fractures in these patients.

N.B. Vitamin D (colecalciferol, cholecalciferol, ergocalciferol) content may be expressed in units. 10 micrograms is equivalent to 400 units.

Public Health England suggest that during autumn and winter when there is limited sun exposure, everyone will need to rely on dietary sources of vitamin D. Since it is difficult for people to meet the 10 microgram recommendation from consuming foods naturally containing or fortified with vitamin D, people should consider taking a daily supplement containing 10 micrograms (400 units) of vitamin D in autumn and winter. Patients should be advised to purchase over the counter, suitable preparations are available in pharmacies and supermarkets for <£5 for a three month supply.

Appendix 6: Options for patients with swallowing difficulties

The following are the most appropriate cost effective alternatives for patients who have swallowing difficulties. Please refer to table 1 for further information on these medications.

Loading regimen:
- Invita D3 25,000 unit/1ml oral solution – Take the contents of two ampoules (50,000 units) by mouth once a week for 6 weeks

Maintenance:
- Fultium D3 drops – 12 drops (800 units) orally once daily. Pack size: 25 ml of oral solution (1020 Drops; 85 days treatment/pack)
- Invita D3 25,000 unit/1ml oral solution – One ampoule by mouth once a month
Authors:
• Nottingham Osteoporosis Group - PJ Prinsloo, Aamer Ali, Ira Pande, Tahir Masud, Kamal Chokkalingham, Namal Weerasuriya, Opinder Sahota, Hrushikesh Divyateja
• James Sutton, Interface and Formulary Pharmacist.
• Updated October 2016 by Laura Catt, Prescribing Interface Advisor
• Updated May 2017 by Nick Sherwood, Interface and Formulary Pharmacist

References:
• Vitamin D: increasing supplement use among at-risk groups NICE guidelines 2014, https://www.nice.org.uk/guidance/ph56
• Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management April 2013 https://www.nos.org.uk/document.doc?id=1352
• UKMI Medicines Q&As:
  • Is there a suitable vitamin D product for a patient with a peanut or soya allergy? here
  • Which vitamin D preparations are suitable for a vegetarian or vegan diet? here
• East and South East England Specialist Pharmacy Services: Vitamin D deficiency and insufficiency: using appropriate available products. August 2014. Available here
• Summary of Product Characteristics available at www.medicines.org.uk/emc
• BNF Sept 2017 available at www.bnf.org
• Drug Tariff May 2017 available at http://www.drugtariff.nhsbsa.nhs.uk/
• Pearce SHS, Cheetham TD. Diagnosis and management of vitamin D. BMJ 2010; 340: 142-147.
• Primary vitamin D deficiency in adults. DTB 2006; 44: 25-29.
• Public Health England: PHE is advising that 10 micrograms of vitamin D are needed daily to help keep healthy bones, teeth and muscles. July 2016. Available here
• Vitamin D an essential nutrient for all… but who is at risk of Vitamin D deficiency? Information for healthcare professionals, Llwdraeth Cymru, 2014, link here

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