



March 2016

Treatment of Vitamin D Deficiency and Insufficiency in Adults

The New Therapies Subgroup discussed the above drug at a meeting on the 15th March 2016. The recommendation of this subgroup is as follows:*

The New Therapies Subgroup of the GMMMG considered the treatment of vitamin D Deficiency and Insufficiency.

The group recommends that the vitamin D and bone health clinical guideline for patient management from the National Osteoporosis Society be followed <https://nos.org.uk/for-health-professionals/tools-resources/>

The guideline outlines the proposed thresholds for vitamin D and discusses treatment for Vitamin D deficiency. The group recommends that the choice of vitamin D product should be determined locally and communicated to prescribers.

According to set criteria Vitamin D was deemed to be a medium priority for prescribing.

** This recommendation is valid unless it is has been superseded by a NICE TA or national guidance. The recommendation will only be reviewed when there is substantial new data that may change the initial recommendation. For recommendations that are >24 months old please note that there may be new data available and this should be checked prior to prescribing.*

References available on request.

Summary of the National Osteoporosis Society [NOS] Vitamin D guideline: the key recommendations and additional information for prescribers.¹

Measurement

Measurement of serum 25OHD [25-hydroxy Vitamin D] is the best way of estimating vitamin D status. Serum 25OHD measurement is recommended for:

- **Patients with bone diseases that may be improved with vitamin D treatment e.g. those with osteomalacia or osteoporosis or other bone diseases where correcting vitamin D deficiency before drug treatment is recommended** e.g. when treating Paget's disease with a bisphosphonate. Correction of vitamin D deficiency is also required before starting osteoporosis treatment with a potent antiresorptive agent (zoledronate or denosumab), to avoid the development of hypocalcaemia. However, routine 25OHD testing may be unnecessary in patients with osteoporosis or fragility fracture, where a decision has been made to co-prescribe vitamin D supplementation with an oral antiresorptive treatment
- **Patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency.** Symptoms of vitamin D deficiency are vague and it can be difficult to ascertain whether a low serum 25OHD level is causal or a surrogate marker (e.g. of poor nutrition or a lack of outdoor activity). Nonetheless, if patients are suspected of having symptoms caused by osteomalacia, or have chronic widespread pain, it may be reasonable to measure serum 25OHD as part of their clinical and laboratory evaluation.
- **Routine vitamin D testing may be unnecessary in patients with osteoporosis or fragility fracture, who may be co-prescribed vitamin D supplementation with an oral antiresorptive treatment.**
- **Although vitamin D deficiency is highly prevalent, universal screening of asymptomatic populations is not recommended.**

Thresholds and groups to consider for treatment

The following vitamin D thresholds have been adopted in respect to bone health in Greater Manchester:

- serum 25OHD < 30 nmol/L [12ng/ml] is deficient. Treatment is recommended
- serum 25OHD of 30–50 nmol/L [12–20ng/ml] may be inadequate in some people. Treatment is advised in the following groups:
 - 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.
- serum 25OHD > 50 nmol/L [20ng/ml] is sufficient for almost the whole population. Provide reassurance and give advice on maintaining adequate vitamin D levels through safe sunlight exposure and diet.

The Department of Health has identified certain adult groups at risk of vitamin D deficiency.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/134550/dh_132508.pdf.pdf

Abbreviated DH advice:

Adult groups at risk of vitamin D deficiency:

- all pregnant and breastfeeding women, especially teenagers and young women
- older people, aged 65 years and over

1. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management, April 2013; review date April 2016. This summary produced September 2013, updated February 2016 to take account of licensed Vitamin D preparations.

- people who have low or no exposure to the sun, for example those who cover their skin for cultural reasons, who are housebound or who are confined indoors for long periods
- people who have darker skin, for example people of African, African-Caribbean or South Asian origin, because their bodies are not able to make as much vitamin D.

Recommendations:

- All pregnant and breastfeeding women should take a daily supplement containing 10 µg (400 units) of vitamin D, to ensure the mother's requirements for vitamin D are met and to build adequate foetal stores for early infancy. [Healthy Start Vitamins for pregnant and breastfeeding women should be considered]
- People aged 65 years and over and people who are not exposed to much sun should also take a daily supplement containing 10 µg (400 units) of vitamin D.

How to treat

Oral vitamin D3 is the treatment of choice in vitamin D deficiency.

Where rapid correction of vitamin D deficiency is required, such as in patients with symptomatic disease or about to start treatment with a potent antiresorptive agent (zoledronate or denosumab), the recommended treatment regimen is based on fixed loading doses followed by regular maintenance therapy:

Loading doses [reminder: usually only required where rapid correction is necessary]

- a loading regimen to provide a total of approximately 300,000 units vitamin D, given either as separate weekly or daily doses over 6 to 10 weeks : The exact regimen will depend on local preference and local availability of vitamin D preparations but could include:
 - 20,000 units capsules, two given weekly for 7 weeks (280,000 units)
 - 800 units capsules, five a day given for 10 weeks (280,000 units).

The following preparations have a marketing authorisation for treatment of Vitamin D deficiency:

Aviticol 20 000 IU capsules[®], two each week for 7 weeks [280,000 units]

Desunin 800 IU Tablets[®], five daily - would have to be taken for 10 weeks [280,000 units]

Fultium-D3 20,000IU capsules[®], two each week for 7 weeks [280,000 units]

Fultium-D3 3,200IU capsules[®], one daily for up to 12 weeks [268,800 units]

Fultium-D3 800IU capsules[®], one to four daily for up to 12 weeks [4 daily for 12 weeks delivers 268,800 units]

InVita D3 25,000 IU oral solution[®], two ampoules a week for 6-8 weeks [300,000-400,000 units]

InVita D3 50,000 IU oral solution[®], one ampoule a week for 6-8 weeks [300,000-400,000 units]

Plenachol 20 000 IU Capsules[®], two each week for 7 weeks [280,000 units]

Plenachol 40 000 IU Capsules[®], one each week for 7 weeks [280,000 units]

Stexerol-D3 25,000 IU Tablets[®], two each week for 6 weeks [300,000 units]

Stexerol-D3 1,000 IU Tablets[®], three or four daily for 10-12 weeks [210,000-336,000 units]

THORENS 25 000 I.U. /2.5 ml oral solution[®], two each week for 6-8 weeks [300,000-400,000 units]

Maintenance

- Maintenance therapy comprising vitamin D in doses equivalent to 800–2000 units daily (occasionally up to 4,000 units daily), given either daily or intermittently at higher doses.
A number of preparations have a marketing authorisation for Vitamin D maintenance therapy: those containing 800-3200 units are given daily; those containing 20,000-25,000 units are given at a dose of one to three once a month; consult SPCs for details.

Notes:

- In line with the GMMMG Formulary recommendation, only licensed products should be used
- Supplements should be taken with food to aid absorption.
- Calcium/vitamin D combinations should not be used as sources of vitamin D for the loading regimens, given the resulting high dosing of calcium.

Where correction of vitamin D deficiency is less urgent and when co-prescribing vitamin D supplements with an oral antiresorptive agent, maintenance therapy may be started without the use of loading doses. Routine monitoring of serum 25OHD is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption and where poor compliance with medication is suspected. Should re-measurement of vitamin D levels be considered appropriate, this should be performed a minimum of 3 months after treatment has commenced and preferably not until 6 months have passed.

Adjusted serum calcium should be checked 1 month after completing the loading regimen or after starting vitamin D supplementation in case primary hyperparathyroidism has been unmasked

The following treatments and strategies are NOT recommended:

- Single dose loading strategies e.g. *Stosstherapie* regimen
- Annual depot vitamin D therapy either by intramuscular injection or orally
- Use of activated vitamin D preparations (calcitriol and alfacalcidol).

Changes from 2013 version:

- Term *IU* changed to *unit* throughout except names of products are written exactly as per their SPCs
- Removed reference to 50,000 units capsules – no product known with a UK Marketing authorisation
- Incorporation of products with a marketing authorisation to treat deficiency and comment about maintenance doses

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