Gloucestershire Hospitals NHS Foundation Trust

TREATMENT OF VITAMIN D DEFICIENCY

1. INTRODUCTION / RATIONALE

- Guideline for treating vitamin D deficiency in adults with eGFR >30 and low or normal serum calcium.
- This guideline represents the views of the Gloucestershire Hospitals NHS Foundation Trust Osteoporosis Guidelines Group. They were arrived at after consideration of the available evidence and the development of consensus.
- The guideline aims to ensure equity and best practice within the context of resources currently available to the NHS locally.
- This guideline does not override the responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient in consultation with the patient and/or carer.
- This guideline provides recommendations on the treatment of established vitamin D deficiency in adults with eGFR >30 and low or normal serum calcium.
- This guideline is not for the general public with regards to maintaining good bone health and does not address the management of Vitamin D deficiency in childhood or adolescents or in pregnancy.
- For recommendations on vitamin D supplementation please see Department of Health guidance.
- For recommendations on treating vitamin D deficiency in patients with severe or end-stage CKD (stages 4 or 5) please see NICE guidance.

2. DEFINITIONS

Word/Term	Descriptor
Colecalciferol	Vitamin D3
Ergocalciferol	Vitamin D2

3. ROLES AND RESPONSIBILITIES

Post/Group	Details
Osteoporosis Guidelines Group	Responsible for ensuring guidelines remain up to date with clinical evidence/national consensus
Prescribers	Responsible for following this guideline

4. PREVENTION OF VITAMIN D DEFICIENCY

Vitamin D deficiency is common and associated with many diseases.

Vitamin D 'insufficiency' occurs in >50% of the adult UK population. The incidence is much higher in the elderly and occurs in >90% of care home residents.

The Scientific Advisory Committee on Nutrition (SACN) recommends a reference nutrient intake of 400 IU (10µg) of daily Vitamin D throughout the year, for adults of all ages in the general UK population.

The NICE Vitamin D Clinical Knowledge Summary (revised Jan 2022) details the following adult groups at higher risk of Vitamin D deficiency. Those:

- over 65 years old
- who have low or no exposure to the sun, e.g. who cover their skin for religious/cultural reasons, who are housebound or confined indoors for long periods
- with darker skin pigmentation. e.g. of African, African-Caribbean, or South Asian origin
- with malabsorption disorders, or following weight loss surgery
- with severe liver or stage 4 or 5 chronic kidney disease
- taking certain drugs that increase the risk of Vitamin D deficiency e.g. anti-epileptics and oral glucocorticoids
- who are pregnant or breastfeeding
- with obesity

It is recommended that those over 65 years old or in one of these higher risk groups take a daily supplement containing 400 IU (10µg) of Vitamin D.

NOTE: supplements are widely available as over-the-counter (OTC) preparations and SHOULD NOT be prescribed to the general population for the **prevention** of Vitamin D deficiency.

In the context of Osteoporosis and other specific bone conditions higher levels, specifically 800 up to 2000 IU daily, may be appropriate and in this situation can be purchased OTC or prescribed if deemed appropriate.

5. ASSESSING VITAMIN D STATUS

Vitamin D status is most reliably determined by assay of serum 25-hydroxyvitamin D (25-OHD).

Interpretation of serum 25-OHD concentration:

<25nmmol/l - Deficient
25-50nmmol/l - Inadequate in some people
>50nmmol/l - Sufficient for almost the whole population

6. DIETARY ADVICE

Diet is generally a poor source of vitamin D.

7. SUN ADVICE

Sun exposure is the main source of vitamin D, but excessive sun exposure is the main cause of skin cancer, including melanoma, the fastest rising type of cancer in the UK. Enjoying the sun safely, while taking care not to burn, can help to provide the benefits of vitamin D without unduly raising the risk of skin cancer.

It is impractical to offer a 'one-size-fits-all' recommendation for the amount of sun exposure that people need to make sufficient vitamin D, as this varies according to a number of environmental, physical and personal factors.

The time required to make sufficient vitamin D is typically short and less than the amount of time needed for skin to redden and burn. Regularly going outside for a matter of minutes around the middle of the day without sunscreen should be enough. When it comes to sun exposure, little and often is best, and the more skin that is exposed, the greater the chance of making sufficient vitamin D before burning. However, people should get to know their own skin to understand how long they can spend outside before risking sunburn under different conditions.

8. WHO SHOULD BE TESTED FOR VITAMIN D DEFICIENCY?

Routine testing for Vitamin D deficiency is NOT necessary.

Vitamin D measurement is indicated for the following:

- **Patients with bone diseases that may be improved with Vitamin D replacement e.g. Osteomalacia, Osteoporosis, Paget's**
- **Before commencing potent anti-resorptive therapy (e.g. Zoledronic acid, Denosumab, Teriparatide, Romosozumab)**
- **Patients with musculoskeletal symptoms that might be attributable to Vitamin D deficiency (e.g. myopathy or chronic widespread pain with other features of osteomalacia)**
- **Patients with melanoma (NICE NG14)**

There is NO NEED to routinely test for vitamin D deficiency in the following groups:

- **Asymptomatic individuals at higher risk of Vitamin D deficiency – these patients should be commenced on Vitamin D supplementation**
- **Osteoporosis or fragility fracture where a decision has been made to prescribe an oral bisphosphonate; in this situation a Vitamin D preparation (with or without Calcium) should be routinely co-prescribed**
- **Asymptomatic healthy individuals**

9. IF TESTED: WHO WILL BENEFIT FROM TREATMENT?

In those who fulfil the criteria for testing (see above): the results should be acted on as follows:

- **Serum 25(OH)D <25nmol/L: treatment recommended**

- **Serum 25(OH)D 25-50nmol/L: treatment is recommended in patients with the following:**

    - **fragility fracture, documented osteoporosis or high fracture risk**
    - **treatment with anti-resorptive medication for bone disease**
    - **symptoms suggestive of Vitamin D deficiency**
    - **increased risk of developing Vitamin D deficiency in the future because of reduced sun exposure, religious/cultural dress code, dark skin etc**
    - **raised PTH**
    - **on anti-epileptic drugs or oral glucocorticoids**
    - **medical conditions causing or leading to risk of malabsorption**

- **Serum 25(OH)D >50nmol/: provide reassurance, give advice on maintaining adequate Vitamin D levels through safe sun exposure, diet and OTC supplement use.**

10. REPLACEMENT OF CONFIRMED VITAMIN D DEFICIENCY

Oral dosing with Colecalciferol (D3) has been shown to be the preferred method, aiming to replace approximately 600,000 IU per annum.

10.1 Ergocalciferol (D2 [plant]):

Inconsistent data regarding persistence and bioactivity and so not recommended unless animal source of vitamin D is unacceptable (see vegan section below).

10.2 Intramuscular Vitamin D:

This has an unpredictable and slow systemic uptake. It is only recommended for patients with small bowel resections, who are unable to take or non-compliant with oral therapy.

11. CALCIUM SUPPLEMENTATION

The use of calcium supplements is generally associated with poor concordance and persistence. Some evidence has suggested there may be an increased risk of adverse cardiovascular outcomes associated with calcium supplementation, although more recent studies have reassuringly not shown this effect. There is an increased risk of renal stones in those taking calcium supplements.

For the above reasons it is recommended that an adequate intake of calcium (>700mg daily) should be achieved preferably through dietary intake. But if this is not possible then given as a combined preparation with Vitamin D. Various on-line 'Calcium calculators' can be used to assist patients and clinicians.

NOTE: combined Calcium/Vitamin D preparations should not be used as sources of Vitamin D for any higher dose Vitamin D loading regimens (detailed in the following pages), given the resulting high dosing of calcium.

12. VITAMIN D PREPARATIONS OF CHOICE

		Suitable for vegetarians	Suitable in peanut/soya allergy
INJECTION	**Colecalciferol** (300,000 units/1ml) injection	Yes	Check product info
ORAL	<u>High dose</u> **Hux-D3®** (Colecalciferol 20,000 unit) capsules	Yes	Yes
	<u>Low dose</u> **Stexerol-D3®** (Colecalciferol 1,000 unit) tablets	Yes	Yes

12.1 Miscellaneous (if above preparations not suitable):

Vegan preparations:
Colecalciferol is derived from sheep wool and therefore not suitable for vegans. Ergocalciferol is derived from yeast and is therefore suitable for vegans, provided it is not encapsulated in animal gelatine.

		Suitable for vegetarians	Suitable in peanut/soya allergy
ORAL	**Calcium & Ergocalciferol** (Calcium 97mg/Ergocalciferol 400units) tablets	Yes	Check product info
	Uvestrol D (Ergocalciferol 30,000units/20ml) liquid – available from Clinigen	Yes	Yes

Preparations for patients with swallowing difficulties:

		Suitable for vegetarians	Suitable in peanut/soya allergy
ORAL	**Hux-D3** (Colecalciferol 20,000 unit) capsules The capsule contents may be squeezed out or the capsule may be chewed by patients with swallowing difficulty	Yes	Yes
	InVita D3 (Colecalciferol 25,000 units/1ml) oral solution	Yes	Yes
	Stexerol-D3 (Colecalciferol 1,000 unit) tablets The tablets can be crushed (unlicensed)	Yes	Yes

13. PRESCRIBING ADVICE – CORRECTION OF CONFIRMED VITAMIN D DEFICIENCY

There are 2 potential regimens to correct proven vitamin D deficiency:

1. **Maintenance therapy** – where correction of Vitamin D deficiency is less urgent, or when co-prescribing supplements with an oral anti-resorptive agent, maintenance therapy can be started without the use of loading doses. This is suitable for the majority of people with confirmed Vitamin D deficiency.

STEXEROL 1000 to 2000 units PO OD.

2. **Higher dose loading** over 7 weeks (**followed by maintenance therapy**) - where more rapid correction is needed e.g. in symptomatic disease or prior to commencing treatment with a potent anti-resorptive agent (e.g. Denosumab, Zoledronic acid, Teriparatide or Romosozumab).

HUX-D3 40,000 units PO ONCE WEEKLY for 7 weeks.

Maintenance therapy should then be started 4 weeks after the loading course is completed.

SUMMARY GUIDANCE:

Vitamin D measurement indicated for the following:

- Patients with diseases that may be improved with Vitamin D treatment e.g. Osteomalacia, Osteoporosis, Paget's
- Before starting potent anti-resorptive therapy (e.g. Zoledronic acid, Denosumab, Teriparatide, Romosozumab)
- Patients with symptoms that might be attributable to Vitamin D deficiency (e.g. myopathy or chronic widespread pain)
- Patients with melanoma (NICE NG14)

25(OH) Vitamin D (nmol/L)

>50

Maintain Vitamin D through safe sun exposure, diet and OTC supplement use

25-50

If one or more of the following applies:

- fragility fracture/ osteoporosis/high fracture risk
- treatment with anti-resorptive medication
- symptoms suggestive of Vitamin D deficiency
- raised PTH
- taking antiepileptic drugs or oral glucocorticoids
- malabsorption
- increased risk of developing Vitamin D deficiency e.g. –
    - reduced sun exposure
    - religious/cultural dress code
    - dark skin

Treat

<25

Treat

MAINTENANCE therapy (in most circumstances):

Stexerol-D3 1,000 to 2,000 units PO OD

HIGHER DOSE loading (where rapid correction needed):

HUX-D3 40,000 units PO ONCE WEEKLY for 7 weeks

MAINTENANCE therapy should then be started 4 weeks after the loading course is completed

Check serum calcium levels one month after starting Vitamin D loading or maintenance therapy in case primary hyperparathyroidism has been unmasked