Clinical Guideline for testing and replacement of Vitamin D

MAIN POINTS:

Only request vitamin D blood levels in high risk/symptomatic patients (Table 1)

Suggest lifestyle/dietary advice and standard OTC supplementation for asymptomatic patients with low vitamin D levels (25OHD level). Monitoring vitamin D levels is not required. As per the NHS England Over the Counter Medicines Prescribing Guidance patients should be advised to buy maintenance doses of Vitamin D https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-consutlation-report-of-findings.pdf

When to request vitamin D tests

At present, there is insufficient evidence base for routine testing of vitamin D in patients with non-specific complaints (e.g. chronic fatigue or low mood).

The conditions where vitamin D levels may be clinically useful include:

Table 1

1	Established metabolic bone disease (e.g. primary post-menopausal osteoporosis, osteoporosis secondary to other medical conditions and/or drugs, primary hyperparathyroidism [PHPT])
2	Suspected osteomalacia: raised Alkaline Phosphatase, low normal or low serum calcium, muscle and bone pain, skeletal abnormalities.
3	Medical conditions predisposing to vitamin D deficiency (e.g. PHPT, coeliac disease, Asian pregnant women)
4	Patients receiving highly potent anti-resorptive agents (e.g. intravenous bisphosphates or denosumab) or when a DEXA scan indicates the need to check vitamin D status.
5	Proximal muscle weakness and musculoskeletal disorders.

Replacing vitamin D

The decision to replace vitamin D should be tailored according to clinical need. Not every patient with low vitamin D levels needs high dose replacement.

Incidental findings: A significant proportion of people in the general population, and a larger percentage of hospital in-patients, will have low vitamin D levels. **NICE guidance recommends 10mcg vitamin D /day for all UK adults irrespective of testing vitamin D levels at least during the autumn and winter months.** As per the NHS England Over the Counter Medicines Prescribing Guidance patients should be advised to buy maintenance doses of Vitamin D https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-consutlation-report-of-findings.pdf

1. Before replacing, please ensure that vitamin D level is recent (within 3 months). Repeat test especially if lower levels were in winter.

2. Marginally low 25OHD levels may resolve in spring/summer. Note that the probability of low vitamin D recurring in autumn/winter is high. As per the NHS England Over the Counter Medicines Prescribing Guidance patients should be advised to buy maintenance doses of Vitamin D https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-consutlation-report-of-findings.pdf

Recommendations

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

- Where correction of vitamin D deficiency is less urgent and when co-prescribing vitamin D supplements with an oral anti-resorptive agent, maintenance therapy may be started without the use of loading doses.

ALLERGY WARNING

Please note some brands of colecalciferol contain peanut oil and is contraindicated in patients with allergy to peanut and soya oil.

Prescribers and pharmacist should check food allergy before supply is made.

Note this guidance does not apply to those with CKD 4 or 5 in whom vitamin D replacement (where indicated) should be guided by secondary care.

Replacement regime for vitamin D deficiency where clinically relevant (See table 1)

Table 2. Starting doses according to pre-treatment Vitamin D (25OHD level)

Pre-treatment 25OHD level	Regime
<25 nmol/L and symptomatic	• Colecalciferol - Total loading dose of approximately 300,000 units given either as weekly or daily split doses: 50,000 units once a week for 6 weeks (300,000 units) OR 4000 units daily for 10 weeks (280,000 units). • Maintenance : 800 units to 1600 units daily (occasionally up to 4,000 units daily), for high risk/symptomatic patients. • For patients with swallowing difficulties who are unable to take oral tablets, use InVita D3 50,000 units oral solution weekly for 6 weeks, followed by maintenance therapy of 25,000 units per month, for high risk/symptomatic patients. • Consider rpt vitamin D **no sooner than 3 months** after start of treatment. (refer to flow chart). • If rapid correction is desired (e.g. for patients who are on, or planned for, treatment with potent anti-resorptive drugs (e.g. Zoledronate or Denosumab) Refer to the specific guidance – Prescribing framework for Denosumab
25-50 nmol/L and symptomatic	• Treat with colecalciferol 800 units to 1600 units daily. Use standard vitamin D (± calcium) preparations for 8 weeks. As per the NHS England Over the Counter Medicines Prescribing Guidance patients should be advised to buy maintenance doses of Vitamin D https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-consutlation-report-of-findings.pdf • For patients with swallowing difficulties who are unable to take oral tablets, use InVita D3 25,000 units oral solution monthly for 2 months. • For **high risk/symptomatic patients** – If risks / symptoms persist, repeat test after 3 months - for levels less than 50 nmol/L consider reasons (compliance) and continue treatment. Repeat again in 3-6 months if **symptoms persist** and consider other causes. • If rapid correction is desired (e.g. for patients who are on, or planned for, treatment with potent anti-resorptive drugs (e.g. Zoledronate or Denosumab) Refer to the specific guidance – Prescribing framework for Denosumab

- **If asymptomatic or where there has been a need to re-test** and levels are >50 nmol/L then general guidance from NICE is that all patients should take 10mcg/day with **no requirement to monitor levels.** As per the NHS England Over the Counter Medicines Prescribing Guidance patients should be advised to buy maintenance doses of Vitamin D https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-consutlation-report-of-findings.pdf

Monitoring when high dose replacement is used.

1. Monitoring is the responsibility of the prescriber.
2. Where colecalciferol is prescribed by the specialist and it is impracticable for the patient to return to secondary care for phlebotomy, Lab 1A form(s) should be completed by the prescribing specialist in order for phlebotomy to be arranged by GP surgery.
3. Check biochemical profile (BCP), U+E, LFT and calcium before replacement.
4. For high-risk patients (please see table below), BCP should be checked at weeks 1, 4, 8 and 12. The purpose is to avoid hypercalcaemia and acute kidney injury that occur (rarely) in association with vitamin D correction.
5. Routine monitoring of BCP during treatment is not required.
6. Repeat vitamin D levels 3 months after start of treatment
7. If the 25OHD levels are satisfactory (at least 50 nmol/L) maintenance should be with standard Vitamin D preparations 10mcg/day. Monitor **annually** for high risk patients.
8. If the levels remain less than 50nmol/L, adherence should be ascertained and a further replacement regime prescribed as listed above.
9. Vitamin D toxicity is rare. For vitamin D levels (>200 nmol/L) there is potential for hypercalcaemia and renal function /calcium should be checked.

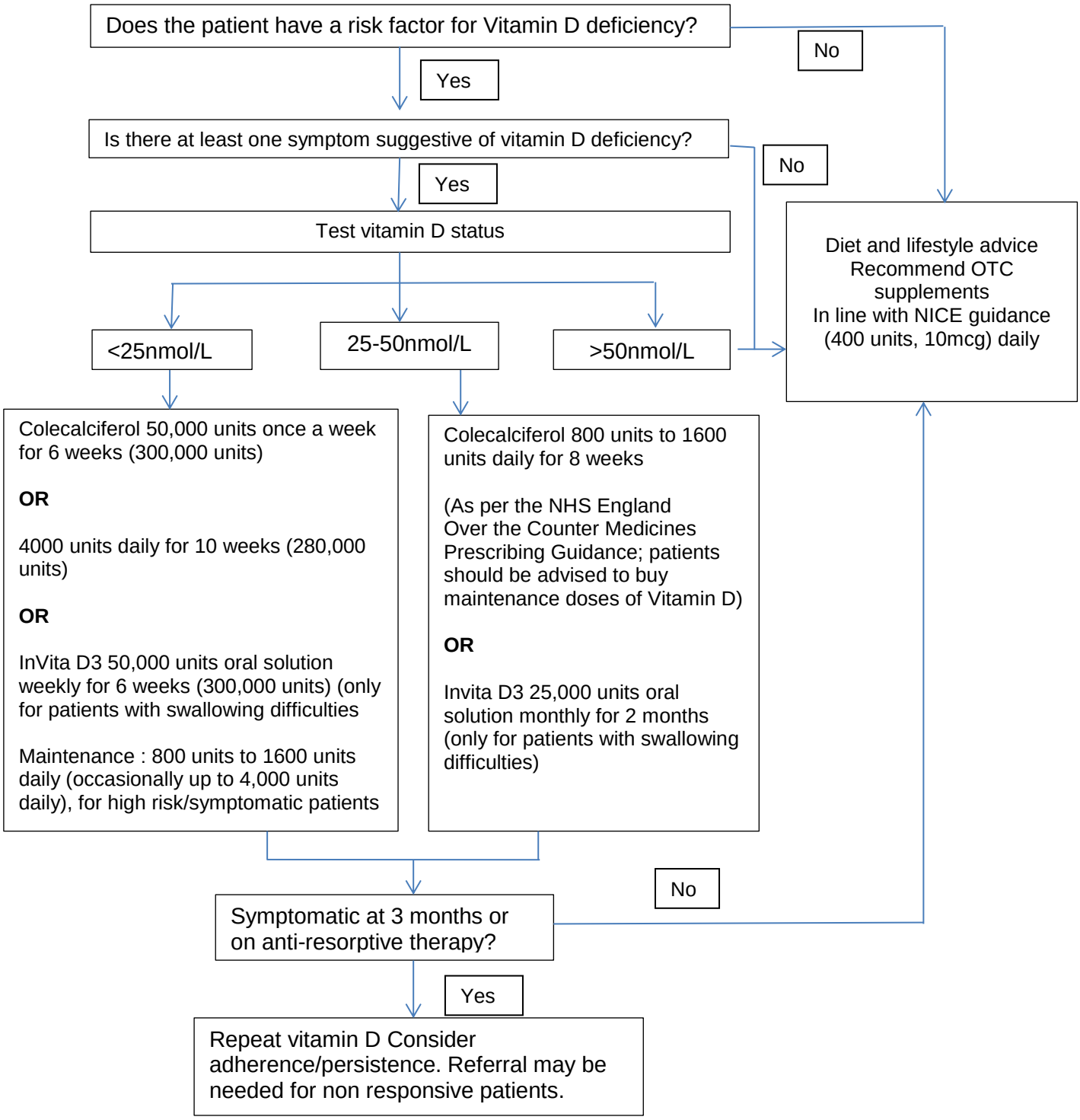
Patient category	Notes
Known primary hyperparathyroidism (PHPT) • Patients with known PHPT with associated vitamin D deficiency. • Vitamin D deficiency coexists with, is exacerbated by, and itself exacerbates adenomatous PHPT. • Correction may be desirable (a) to avoid post-operative hypocalcaemia and (b) to minimise skeletal complications of PHPT.	• Monitoring is mandatory. • Treatment should be initiated by secondary care specialist. • Monitor BCP at weeks 1, 4, 8 and 12. • Consider starting at a lower dose than indicated for correction (800 units per day).
Possible/masked PHPT More common in older women. Suspect if: • Calcium high normal (2.5 – 2.6 mmol/L) **or** • Previous high calcium (>2.6 mmol/L) – check prior results, **or** • Low phosphate with high normal (≥2.5 mmol/L, high calcium)	• Monitor BCP at weeks 1, 4, 8 and 12. • Consider starting at a lower dose than indicated for correction (800 units per day).
Kidney disease/renal impairment • CKD Stage 3B – eGFR 30-45ml/min/1.73m^2 • Chronic volume depletion – e.g. long-term diuretic therapy • Structural renal disease	• Monitor BCP at weeks 1, 4, 8 and 12.

Caution

Activated vitamin D: Some patients, esp. those known to secondary care services, may be taking activated vitamin D in the form of calcitriol or alfacalcidol. The present guidelines do not apply to those patients. Low 25OHD levels in those patients should not be corrected except with advice from the relevant secondary care specialist.

Renal disease: This guidance does not apply to patients with chronic kidney disease who have estimated GFR 30/ml/min/1.73m^2 or worse (e.g. CKD Stage 4 or worse).

Flowchart summarising the treatment algorithm for correction and prevention of vitamin D insufficiency or deficiency (not for use in patients on potent antiresorptives e.g denosumab & zolendronate – see table 2) **(for rapid correction doses see page 3)**



APPROVAL PROCESS

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