
Clinical Guideline

Replacement of low Vitamin D in Adults, including in chronic kidney disease, pregnancy and breastfeeding

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REPLACEMENT OF LOW VITAMIN D IN ADULTS, INCLUDING IN PREGNANCY AND BREAST FEEDING

GSTT/KCH; Departments of Ageing & Health, Clinical Chemistry, Rheumatology, Renal Medicine, Women's Health, Pharmacy.

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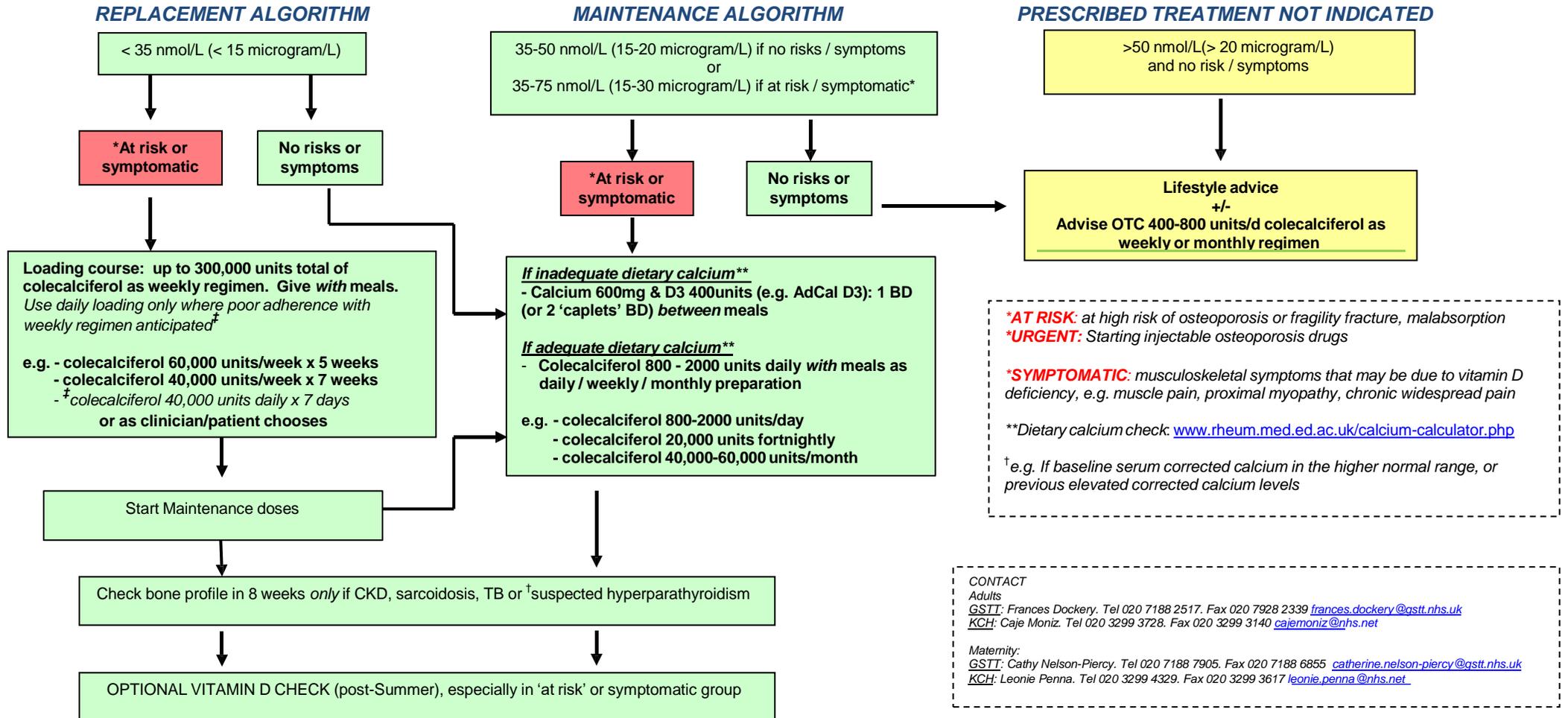
GSTT laboratory reports in nmol/L.
KCH laboratory reports in microgram/L
2.5 X microgram/L = nmol/L

NB – Contraindicated: hypercalcaemia, **CKD 3b-5 (see separate guidance).** **Caution:** history of renal stones, sarcoidosis (seek specialist advice)

CKD = chronic kidney disease

Routine vitamin D testing may be unnecessary in the following: They can be presumed in need of supplementation and given at least 800 units/d unless severe deficiency suspected (then check level).

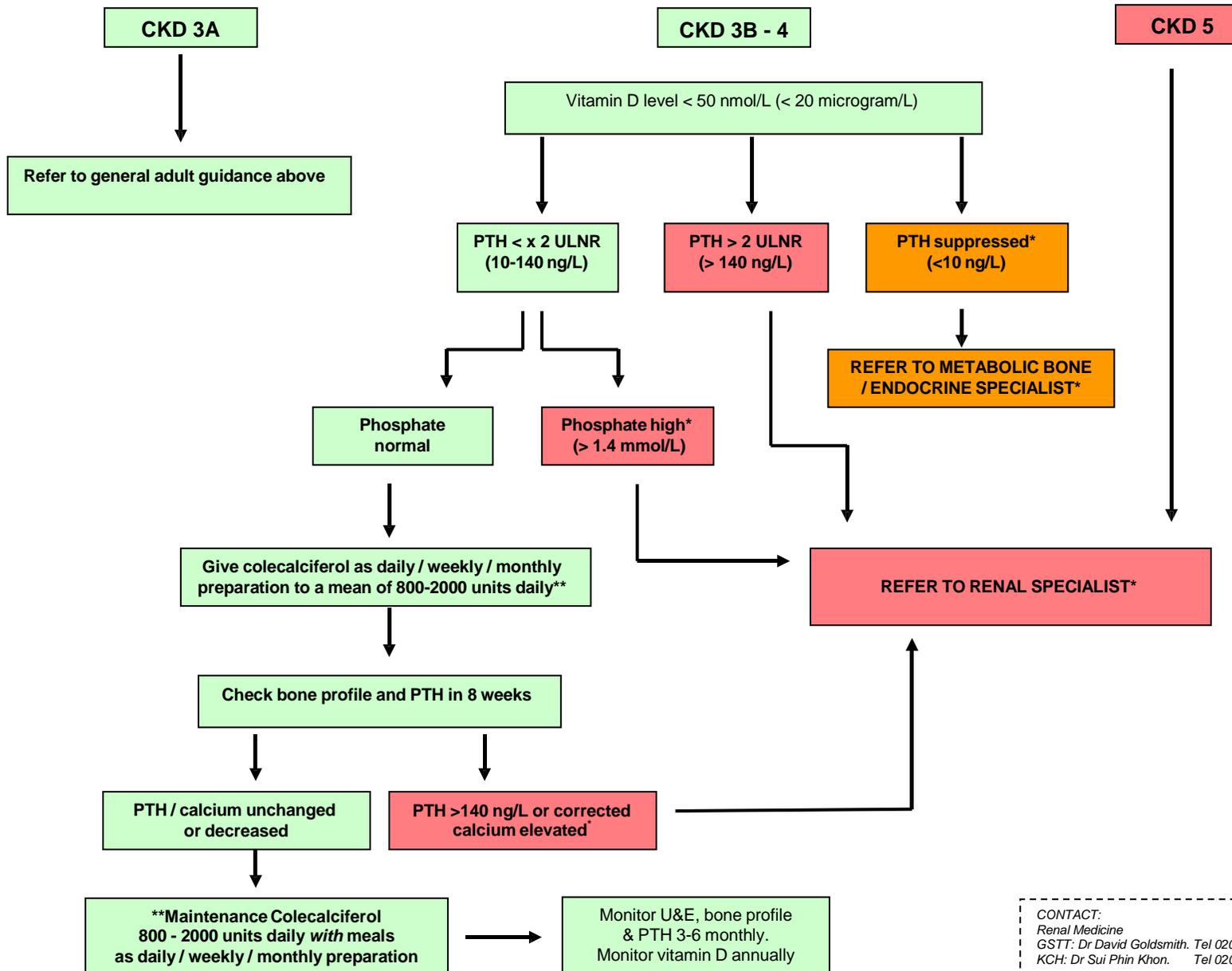
- Starting oral osteoporosis medications
- Frequent fallers
- Liver disease
- Pregnant and breast-feeding women (give a minimum of 400 units/d)
- No sun exposure (e.g. sun-sensitive skin condition, full body clothing, housebound/long-term care residents)
- Drugs impairing vitamin D metabolism (e.g. anticonvulsants, aromatase inhibitors, antiretrovirals)



Replacement Of Low Vitamin D In Adults, Including In Chronic Kidney Disease, Pregnancy And Breast Feeding

*GSTT laboratory reports in nmol/L.
KCH laboratory reports in microgram/L
2.5 X microgram/L= nmol/L*

REPLACEMENT OF LOW VITAMIN D IN ADULTS WITH CKD 3B-5, AND WHO HAVE NORMAL SERUM CALCIUM



***NB - REFER ONLY AFTER CONFIRMED ON REPEAT TESTS**

****Example regimens include:**
- 800-1600 units daily
- 20,000 units weekly/fortnightly
- 40,000-80,000 units monthly

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REPLACEMENT OF LOW VITAMIN D LEVEL IN ADULTS WITH LOW / NORMAL CALCIUM LEVEL

GSTT/KCH: Departments of Ageing & Health, Clinical Chemistry, Rheumatology, Renal Medicine, Women's Health, Pharmacy.

Optimal vitamin D levels are unclear but studies suggest that levels $\geq 75\text{nmol/L}$ ($>30\text{ ng/L}$) are associated with better bone and general health as PTH is optimally suppressed at this level. Longer term outcomes of achieving and maintaining these levels in the general population are unclear and levels of over 50nmol/L are likely to be adequate for most people. There is no consensus on best regimen to achieve these levels; the following guidance is drawn from best available evidence as well as expert opinion.

Levels are seasonal so a majority in the UK will have low levels post-Winter.

- Older skin +/- pigmented skin may produce less vitamin D with sun.
- 10 mins of midday summer sun (no sun block) generates approx 3,000 units vitamin D (must be balanced against skin cancer risk from sun exposure).
- Diet is a poor source of vitamin D (at most, 20%).

1) WHO SHOULD HAVE VITAMIN D LEVELS CHECKED:

- Levels should only be checked post-Summer unless house-bound or skin never exposed to sunshine – then check level at any time.
- The following can be presumed deficient in vitamin D and routine lab testing is not necessary. They should be given maintenance treatment of a minimum of 800 units. However if severe deficiency suspected (see below) check levels and follow algorithm (as may need loading course in addition).
 - New oral osteoporosis meds, where co-prescribed vitamin D is standard.
 - Low sun exposure (e.g. sun-sensitive skin condition, full body clothing, housebound/ long-term care/care home residents). Older age and dark skin as they have reduced production of vitamin D from sunlight.
 - Frequent fallers.
 - Pregnant and breast-feeding women should receive at least 400 units/d with combined multivitamins, unless at higher risk (see page 5 below).
 - Taking drugs which may impair vitamin D metabolism: anticonvulsants, aromatase inhibitors, antiretrovirals.

• Check vitamin D levels in the following:

- Fragility fracture despite adequate osteoporosis drug treatment.
- Fragility fracture at young age (<60 yrs).
- Starting iv bisphosphonate / Teriparatide / Denosumab.
- Risk of osteoporosis: steroid use, inflammatory bowel disease, rheumatoid arthritis, COPD, prolonged immobilization, sickle cell disease, liver disease, anorexia nervosa, diabetes, HIV.
- Malabsorption (e.g. coeliac disease, small bowel resection).
- Pregnancy/breast-feeding where severe deficiency is suspected.
- Musculoskeletal symptoms that may be attributed to vitamin D deficiency e.g. muscle weakness, widespread chronic pain.

CHECKING VITAMIN D / BONE BIOCHEMISTRY

- Ensure serum (corrected) calcium available (2.15-2.55mmol/L).
 - If low Ca, check Vitamin D, PTH; consider referral to Endocrine/Bone clinic.
 - If calcium $>2.6\text{mmol/L}$ (on repeat sample) check PTH +/- 24hr urinary calcium, stop calcium supplements, refer to Endocrine/Bone clinic.
- BONE BIOCHEMISTRY ASSESSMENT
 - Bone profile (Ca, PO₄, albumin, Alk Phos) – serum tube / clotted blood
 - 25OHD – serum tube /clotted blood
 - PTH (if hypercalcemia / CKD/suspected hyperPTH) – EDTA tube, straight to lab.
 - Urinary Ca/Creat ratio (only if high PTH / renal stones) morning sample
 - 24hr urinary Ca (only if high PTH / renal stones)
 - Bone turnover markers: CTX, P1NP (specialist use) – serum /clotted blood

2) REPLACING VITAMIN D:

- Colecalciferol (D3) is superior to Ergocalciferol (D2) in optimising levels.
- Intramuscular vitamin D2 (IM D3 is not available in UK presently):
 - Unpredictable and slow systemic uptake.
 - Recommend where small bowel resection / malabsorption.

- Hydroxylated vitamin D (1- α calcidol / calcitriol / 1,25OHD):
 - Only to be used in chronic kidney disease severe enough to impair hydroxylation to 1,25OHD (*specialist use only*).
 - Be aware that vitamin D assay (25OHD) does not capture 1-25OHD levels for those on this supplement.
- Oral D3 absorption is aided by fat in diet so should be taken *with* meals.
- High-dose oral vitamin D courses of 300,000 units in deficiency states are safe and effective but single large bolus doses are linked with higher falls and fracture risk in older women; give over weeks instead.
- Toxicity is rare until levels are > 250 nmol/L (100 microgram/L).
- People outside of risk groups in section 1 above, who either have a level checked or enquire re this, should be given lifestyle advice +/- advised to buy OTC supplements of 400-1000 units Colecalciferol daily.
- Pregnant and breast-feeding women should routinely receive a minimum of 400 units colecalciferol daily without the need to check levels, unless severe deficiency suspected (see maternity section page 5 below).
- Patients with sarcoidosis, and those with TB to a lesser extent, may be at risk of hypercalcaemia on vitamin D repletion due to increased conversion to 1,25OHD in granulomatous tissue. This is rare however, and many are vitamin D deficient. They are usually under the care of specialists already.
- It is not necessary to check serum calcium level post-vitamin D supplementation except in sarcoidosis, TB or where primary hyperparathyroidism is suspected (unmasked by vitamin D repletion).
- It is not necessary to recheck vitamin D levels post-supplementation except where malabsorption, poor adherence suspected or need to maintain higher serum levels (e.g. osteoporosis). Levels post-supplementation take months to plateau so do not repeat for 3-6 months.
- Ensure subsequent vitamin D levels are processed in the same laboratory as baseline sample, as assays vary between labs.

CALCIUM SUPPLEMENTATION:

- Replacement of vitamin D is usually combined with calcium. Combined calcium/vitamin D supplements contain 500-600g calcium and 400units vitamin D per tablet, maximum is 2 daily due to the calcium content.
- 800 units vitamin D daily from combined tablets may be insufficient to replete very low levels; they should receive loading doses prior.
- Side-effects of calcium include constipation, abdominal pain. Poor adherence may compromise benefits of osteoporosis treatments.
- Supplementing those with high dietary calcium intake may increase risk of renal stones and possibly, cardiovascular risk though unproven.
- Combined Calcium/Vitamin D supplements should be taken in split doses (bd) instead of od, as calcium absorption reaches a peak and is impaired by a number of foods, so take *2 hours before/after meals*.
- DIETARY CALCIUM – Consider deficient if low intake of dairy products and fish (see web link to Calcium Calculator below or use chart below).

www.rheum.med.ed.ac.uk/calcium-calculator.php

RECOMMENDED DAILY INTAKE	
Adults	700mg
Osteoporosis	1.2g
Malabsorption	1.2g
Breastfeeding	1.2g
<i>1 PORTION</i>	<i>Calcium (mg)</i>
Tea/coffee with milk (full fat = skimmed)	45
*Milk shake / café latte / glass of milk (200mls)	250
Soya milk (non-calcium-enriched) (200mls)	25
Ice cream (2 scoops)	100
Yoghurt (125g pot)	100
[†] Bread, per slice	30
Cheddar cheese (40g portion)	300
Cottage cheese	50
Cheese omelette	470
Pizza/moussaka/lasagne/macaroni cheese	225
Green vegetables	40
Sardines/pilchards	350
White fish	50
Eggs	37
Oranges	75
Chocolate bars	110

4) IN CHRONIC KIDNEY DISEASE

Chronic kidney disease patients may have renal bone disease (osteodystrophy). Controlling high phosphate and PTH levels is important for bone health in this setting, but over-suppression of PTH should be avoided as may precipitate adynamic bone disease. In advanced CKD activated vitamin D (1- α calcidol) is generally needed however there remains some extra-renal conversion of 25OHD to its activated form so treatment with colecalciferol may also be appropriate. Patients on the combination will generally be under specialist care however as their bone biochemistry needs closer monitoring.

- Check PTH levels with vitamin D in *all* cases of CKD.
- **CKD stage 3A** – As per guidance above.
- **CKD stage 5** – Refer to renal specialist.
- **CKD stage 3B-4:**
 - *If low vitamin D is accompanied by normal plasma phosphate, but raised PTH (< 2 times upper limit of normal lab range (ULNR)), give colecalciferol alone, 800-2000 units/day as daily, weekly or monthly preparation.*
 - Recheck PTH and bone profile 8 weeks post-vitamin D repletion; recheck Vitamin D level annually post-Summer.
 - *If PTH > 2 x ULNR or PO4 high, seek advice from renal specialist as may require phosphate binders and 1- α calcidol with closer monitoring of bone and renal biochemistry. Ensure abnormality confirmed on repeat samples before referring.*
 - Vitamin D assay (25OHD) does not capture 1-25OHD levels, for those patients taking this supplement (alfacalcidol).
 - Avoid calcium supplementation in CKD, choosing colecalciferol alone instead.

5) IN PREGNANCY / BREAST FEEDING

Maternal hypovitaminosis D is linked with higher risk of pre-eclampsia, increased caesarean section rates, low birth weight, neonatal hypocalcaemia and tetany. It may also be linked to impaired foetal skeletal growth and impaired foetal lung development but definite evidence for this is lacking.

Routine supplementation for all pregnant women is advised. Ideal doses are unclear however, with different national and international expert groups recommending between 400-1000 as a minimum. Doses of 400 units daily are recommended by UK Dept. of Health but this dose is insufficient to maintain levels \geq 30nmol/, where levels are checked.

- All pregnant and lactating women should receive a minimum of 400 units daily of colecalciferol as a multivitamin preparation (e.g. healthy start/pregnacare which contain 400 units colecalciferol).
- Those at risk of severe deficiency (as per general adult guidance above – no sun exposure, dark skin, skin fully covered etc. and consider in obese women), should have higher maintenance doses of up to 2000 units daily.
- Breast-feeding mothers need up to 2000 units daily if infant is not also receiving a vitamin D supplement.
- Check vitamin D levels only where severe, symptomatic deficiency is suspected, then follow adult guidance on repletion and maintenance.
- Consider adding calcium supplements in those with dietary deficiency, and especially in those who are at risk of pre-eclampsia.

6) NON-ADHERENCE TO ORAL MAINTENANCE D3 REGMIEN

Review reason for non-adherence and review the need for maintenance

- Try *whole tablets to swallow* – “*AdcalD3 caplets*” OR soluble Ca/vit D preparation e.g. *Calceos or AdcalD3 Dissolve*
- OR consider 40,000-60,000 units / month oral colecalciferol
- OR consider Intra-muscular D2 - 300,000 units ergocalciferol 6-monthly

Single vitamin D preparations with a marketing authorisation (refer to SPC for full product details)								
Generic / Form	Brand	Licensed Dosage / Administration	Product considered suitable for Halal / Kosher	Preparation contains			Availability	
				Soya	Nut	Gelatin	Hospital	Community
Colecalciferol High Strength 20,000 units	Plenachol Capsules (Gelatin free)	Deficiency: 40,000 units once a week (with meals) for 7 weeks Maintenance: 40,000 – 60,000 units once a month (with meals) Prevention: 20,000 units once a month (with meals)	✓	✗	✗	✗	✓	✓
Colecalciferol Low Strength	Fultium capsules (Contains gelatin) Available as 800 or 3,200 unit capsules	Deficiency: 800 – 3,200 units each day (with meals) for up to 12 weeks Maintenance: 800 – 1,600 units each day (with meals) Prevention: 800 units each day (with meals)	✓	✗	✗	✓	✓	✓
	Desunin 800 unit tablets (Gelatin free)	800 units each day (with meals), depending on vitamin D levels, dose can be increased to 4000 units each day (with meals).	✓	✗	✗	✗	✓	✓
Ergocalciferol IM Injection 300,000 units in 1mL	Focus Pharmaceuticals (UK)	Deficiency: 300,000 units as a single dose, repeat 6-monthly	✓	✗	✗	✗	✓	✓
Colecalciferol oral solution 25,000 in 1 ml	Invita D3 Consilient Health Ltd (UK)	Deficiency: 50000 IU once a week (with meals) for 6-8 weeks Maintenance: 25000 IU once a month (with meals) Prevention: 25000 IU once a month (with meals)	✓	✗	✗	✗	✓	✓
Combined vitamin D & calcium preparations with a marketing authorisation (refer to SPC for full product details)								
Colecalciferol & Calcium Carbonate	Chewable Tablets (Adcal-D3/Calceos)	Maintenance: 1 tablet twice a day (sucked or chewed) 2 hours before or after meals	✗	✓	✓	✓	✓	✓
	Caplets (Adcal-D3)	Maintenance: 2 tablets twice a day (swallowed whole) 2 hours before or after meals	✗	✗	✓	✓	✓	✓
	Effervescent Tablets (Adcal-D3 dissolve)	Maintenance: 1 tablet twice a day in a glass of water 2 hours before or after meals	✗	✓	✗	✗	✓	✓
Vitamin D nutritional supplements available to purchase from community pharmacies								
For patients in whom <i>prescribed</i> vitamin D is not required, advise them to discuss with community pharmacist re- over the counter supplements. Various products, formulations and strengths are available.								

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