

Bedfordshire & Luton Guideline for the Management of Simple Vitamin D Deficiency in adults >18 years with eGFR >30ml/min

Version 1: September 2018

This local guideline is intended for all clinicians in Luton and Bedfordshire in the diagnosis and management of patients with vitamin D deficiency ensuring an integrated approach across primary and secondary care. The benefits of Vitamin D include the maintenance of health bones, teeth and muscle function.

Table 1: Causes of vitamin D deficiency

Insufficient exposure to sunlight
 Inadequate dietary and supplemental Vitamin D
 Conditions that impair Vitamin D absorption
 Conditions that impair Vitamin D activation
 Other conditions (chronic kidney disease eGFR>30, coeliac disease, ulcerative colitis, crohn's disease, cystic fibrosis)
 Drugs (antiepileptic drugs, antiretroviral treatment, drugs that reduce fat absorption)

Table 2: Risk factors – People at higher risk of vitamin D deficiency

People with limited sun exposure (people who cover skin for cultural reasons, people who are housebound or in care facilities)
 People with darker skin tones (more light exposure required to produce same amount of vitamin D as people with lighter skin tones due to higher concentration of melanin)
 People aged 65 years and older
 Pregnant women and breastfeeding women
 People who are obese (BMI > 30 or have had a gastric bypass)
 People at increased risk of nutritional deficiency (vegans, people who do not eat fish, generally poor diet)
 Family history of vitamin D deficiency

Table 3: Vitamin D (25[OH]D) testing indicators (based on current BHT and L&D pathology commissioning arrangements)

Low serum adjusted calcium (less than 2.25mmol/l OR less than 2.3mmol/L, if rheumatology request) at higher risk of vitamin D deficiency AND one or more of the following:
 Symptoms of osteomalacia (bone discomfort or pain, impaired physical function, muscle aches and weakness)
 Chronic widespread pain
 If clinically indicated (e.g. person has had a fall, person has bone disease that may improve with vitamin D treatment, features of hypocalcaemia, postmenopausal women with fragility fractures, people at risk/ suffering from osteoporosis e.g. long term use of steroids, people commencing bone active therapies)

Table 4: Vitamin D thresholds (in accordance with NICE CKS)

Vitamin D Deficiency	Serum 25[OH]D less than 30 nmol/L
Vitamin D Insufficiency	Serum 25[OH]D 30-50 nmol/L (In some conditions specialists may choose to treat at higher thresholds)
Vitamin D Sufficient	Serum 25[OH]D greater than 50 nmol/L

Table 5: Lifestyle Advice

Safe sun exposure - A good source of vitamin D can be obtained by short daily periods of sun exposure (about 10 to 15 minutes for most people) without sunscreen. In the UK, the best source of vitamin D is obtained during the middle of the day (11am – 3pm) in the summer months (April until October). Sunbeds are not an effective method of protecting against vitamin D deficiency.

Seasonal variation – It is important to take into account seasonal variation when interpreting vitamin D results

Dietary intake of vitamin D - Vitamin D can be acquired from dietary sources such as oily fish (e.g. salmon, mackerel and sardines) eggs and meat, margarine, supplemented breakfast cereals, infant formula milk, soya products, dairy products powdered milks and fat spreads. Cod liver oil contains high amounts of vitamin D (this contains vitamin A, which in high doses, should be avoided in pregnancy). Please refer to patient information leaflet from British Dietetic Association (BDA) on Vitamin D dietary requirements <https://www.bda.uk.com/foodfacts/VitaminD.pdf>

Dietary intake of calcium - Rich sources of calcium include dairy foods (milk, cheese, and yoghurts) and tinned sardines with bones. See BDA leaflet on dietary calcium intake <https://www.bda.uk.com/foodfacts/Calcium.pdf>

Adherence to long-term supplementation and SELF-CARE – long term supplementation with vitamin D should be adhered to in order to prevent recurrence of deficiency and to maintain bone health. For those who have received treatment for deficiency, maintenance is usually lifelong. In this guideline we promote **SELF-CARE** for patients on maintenance 400 IU or 800 IU daily. There are a wide-ranging array of affordable nutritional supplements available to all adults in the UK that can be purchased from Pharmacies, Health Food shops and Supermarkets.

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Check serum Vitamin D (25[OH]D) level (See table 3 - vitamin D testing indicators)

For differential diagnosis, consider additional investigations where clinically appropriate, e.g.: Bone profile, renal, liver, thyroid function test, parathyroid hormone levels, full blood count, malabsorption screen, rheumatoid and other autoimmune screening, inflammatory markers (see table 7 – differential diagnosis)

< 30 nmol/L - Vitamin D deficiency

Refer to specialist team if the patient has eGFR<30mmol/L, history of renal stones, hypercalcaemia, sarcoidosis, liver disease, TB, lymphoma, metastatic cancer, parathyroid disorders atypical biochemistry, pregnancy. If patient has none of the above conditions and no contraindications, treat for vitamin D deficiency

Treatment of Vitamin D deficiency

Prescribe **Plenachol**[®] capsules, 40,000 IU weekly for 7 weeks* (first line choice) OR prescribe **Invita D3**[®] oral solution, 50,000 IU weekly for 6 weeks* (first line choice) (see table 6 for alternate treatment choices)

Total treatment dose of 280,000 - 300,000 units

Give lifestyle advice (see table 5)

*in certain cases, specialists may opt for accelerated regimens

30-50 nmol/L - Vitamin D insufficiency

Treatment is advised 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 exposure to sunlight, religious/cultural dress code, dark skin, etc., raised parathyroid hormone (PTH), medication with antiepileptic drugs or oral glucocorticoids or drugs known to cause vitamin D deficiency like colestyramine, conditions associated with malabsorption.

Treatment of Vitamin D insufficiency

Give lifestyle advice (see table 5)

Recommend colecalciferol 2,000 IU daily for 12 weeks via **SELF-CARE** (OTC supplements) **OR** prescribe POM licensed products: **Plenachol**[®] 20,000 IU 2-3 times a month for 12 weeks or **Desunin**[®] 1600 IU daily for 12 weeks

> 50nmol/L - Vitamin D sufficient

Prevention of Vitamin D deficiency

All adults living in the UK including people at higher risk of vitamin D deficiency (table 2) should take vitamin D (colecalciferol) 400 IU supplement daily (**SELF-CARE**) throughout the year (table 6). Pregnant and breastfeeding women eligible for the NHS Healthy Start scheme can obtain free Healthy Start vitamin tablets (wheat, fish, egg, salt, colour, flavour, gluten & preservative free, suitable for vegetarians). Give lifestyle advice (see table 5). If musculoskeletal symptoms persist, consider alternate diagnosis.

If plasma level indicates hypocalcaemia OR dietary calcium intake less than 700mg daily AND failed/ unable or unwilling to increase dietary calcium – consider use of a calcium supplement (1.2g elemental calcium daily). Calcium/vitamin D combinations should NOT be used as sources of vitamin D for deficiency/insufficiency regimens. If patient already on calcium supplement refer to specialist team.

If plasma level indicates hypercalcaemia – stop calcium supplements if prescribed, assess hydration state and consider admission if appropriate. Refer to specialist team.

If levels normal – stop calcium supplement if patient currently taking

Check adjusted serum calcium 1 month after starting treatment (to detect subclinical primary hyperparathyroidism)

Calculate dietary calcium intake <http://www.cgem.ed.ac.uk/research/rheumatological/calcium-calculator> - if dietary intake less than 700mg, advise dietary measures – please refer to BDA factsheet on increasing dietary intake of calcium <https://www.bda.uk.com/foodfacts/Calcium.pdf>

Following treatment course, commence maintenance regime: colecalciferol 800 IU daily via SELF-CARE

Routine monitoring, re-testing and treatment failure: Routine monitoring of vitamin D (25[OH] D) levels is not recommended by NICE and re-testing is generally not necessary. Vitamin D (25[OH]D) testing may be clinically appropriate after 3-6 months for patients who have received high dose vitamin D deficiency treatment, with symptomatic vitamin D deficiency or malabsorption and where poor compliance with medication is suspected. Adjusted serum calcium levels post treatment are commissioned and can be used as a pre-indicator (in addition to previous criteria stated) of vitamin D re-testing. If serum vitamin D 25[OH]D levels are less than 50nmol/L, refer to specialist team. If serum vitamin D 25[OH]D levels are more than 50nmol/L, continue on maintenance dose of 800 IU daily. Vitamin D testing is not recommended for vegan patients on ergocalciferol (D₂).

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Table 6: Treatment Options - based on current usage, contracted price and licensing at the time the guideline was developed
Vitamin D₃ (coleciferol) is the current recommended treatment of choice over vitamin D₃ (ergocalciferol)

Product	Vitamin D (coleciferol) - 400 IU colecalciferol is equivalent to 10 microgram – BRAND prescribing recommended <i>Please refer to summary of product characteristics (SPC) / or contact the supplement company for further information on the listed products</i>										Vitamin D (coleciferol) + calcium carbonate – VITAMIN D MAINTENANCE ONLY		
	MAINTENANCE (800IU or 400IU) – please note SELF-CARE is first line, if SELF-CARE has failed or clinically inappropriate, CCG prior-approval will be required for the prescribing of current cost-effective POMs – see column below ↓												
SELF-CARE?	NO			YES - OPTIONAL - licensed POM can be offered to patients first line (clinician discretion/patient preference)			YES – SELF CARE IS FIRST LINE In exceptional circumstances, where self-care has failed/ inappropriate – see below:				NO		
Legal status	POM			POM			POM – CCG PRIOR APPROVAL REQUIRED				P		
Regimen	Vitamin D Deficiency			Vitamin D insufficiency			Vitamin D maintenance following treatment (if SELF-CARE fails/ clinically inappropriate)			Prevention of Vitamin D deficiency	Calcium treatment (1-1.2g) and vitamin D maintenance 800IU (can be prescribed generically in secondary care)		
Treatment line	1 st line	1 st line	2 nd line	1 st line	1 st line	2 nd line	2 nd line	2 nd line	2 nd line	2 nd line	1 st line	1 st line	1 st line
Brand name, strength formulation	Plenachol® 20,000 IU, 40,000 IU capsules	InVita D3® 50,000 IU oral solution	Desunin® 4000 IU tablets	Plenachol® 20,000 IU capsules	Desunin® 800 IU tablets	Fultium® 800 IU tablets, 2740 IU/ml oral drops	Plenachol® 20,000 IU capsules	Desunin® 800 IU tablets	Fultium® 2740 IU/ml oral drops	InVita D3® 2,400IU/ml oral drops	Theical D3® chewable tablets (1g Ca/880 IU)	Accrete® chewable tablets (600mg Ca/ 400 IU)	Calfovit D3® sachets (1.2g Ca/ 800 IU)
Licensed dosing	40,000 IU weekly for 7 weeks	50,000 IU weekly for 6 weeks	4000 IU OD for 10 weeks	20,000 IU fortnightly	1600 IU OD	1600 IU OD (24 drops OD)	20,000 IU every 4 weeks	800 IU OD	12 drops OD (800 IU OD)	6 drops OD (400 IU OD)	1 OD	1 BD	1 OD
Pregnancy & breastfeeding	✓ 20,000 IU ✗ 40,000 IU	✓ 25,000 IU ✗ 50,000 IU	✓	✓ 20,000 IU	✓	✓ up to 4000 IU daily	✓ 20,000 IU	✓	✓ up to 4000 IU daily	✓ licensed for pregnant & BF women only	✓	✓	✗
Peanut Oil free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓
Soya free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓
Vegetarian	✓	✓	✓	✓	✓	✗	✓	✓	✗	✓	✓	✗	✗
Alcohol free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Yeast free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Gluten free	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Halal	✓ certified	✓	✓	✓ certified	✓	✓ certified	✓ certified	✓	✓ certified	✓	✓	✗	✗
Kosher	✓ certified	✓	✓	✓ certified	✓	✓ certified	✓ certified	✓	✓ certified	✓	✗	✗	✗
Vegan	The products listed above are NOT suitable for vegans – ergocalciferol (D ₂) oral supplements (unlicensed) are suitable for vegans and can be accessed OTC (SELF-CARE) Please refer to UKMI Which vitamin D preparations are suitable for a vegetarian or vegan diet? Ergocalciferol injection is NOT recommended.												

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Dietary, allergen and licensing information for other vitamin D products:

The East and South East England Specialist Pharmacy Services document [Vitamin D deficiency and Insufficiency: using appropriate available products](#) has a comprehensive (but not exhaustive) list of available vitamin D products, including unlicensed products.

For people with peanut or soya allergy, see the UK Medicines Information (UKMi) document [Is there a suitable vitamin D product for a patient with a peanut or soya allergy?](#), available on the NICE Evidence website (www.evidence.nhs.uk), for information on suitable peanut and soya-free vitamin D preparations.

For people on a vegetarian or vegan diet and for people with halal or kosher requirements, see the UKMi document [Which vitamin D preparations are suitable for a vegetarian or vegan diet?](#) for vegan preparations (ergocalciferol, D₃)

Table 7: Differential diagnosis		
Apart from vitamin D deficiency there are many alternative causes of widespread pain (e.g. fibromyalgia, polymyositis, or dermatomyositis) or proximal muscle weakness. The table below lists the various biochemical tests and alternate diseases including those where caution is required when considering vitamin D treatment. The tests listed are a general guide, any additional tests required are at the clinician's discretion (as per clinical diagnostic pathway).		
Test	Indicates alternative disease	Detects caution needed before giving vitamin D
FBC	Infection, e.g. glandular fever. Myeloma. Eosinophilia-myalgia syndrome	
RFT	Hypo/hyperkalaemia, Addison's / Cushing's disease	Increased risk of hypercalcaemia / calculi
LFT	Paget's Disease of Bone, myeloma, alcoholism, sarcoidosis	Sarcoidosis
CRP, ESR	Inflammatory myopathy or arthritis, e.g. polymyalgia, rheumatoid	Sarcoidosis
TFT	Hypo/Hyperthyroidism	
FBG	Diabetes mellitus	
Ca++, PTH	Hypo/Hyperparathyroidism*, cancer, sarcoidosis	Hyperparathyroidism*, Sarcoidosis
PO4--	Hypo/Hyperparathyroidism*, malabsorption	Hyperparathyroidism*
CK	Myopathy	
Malabsorption	Cystic fibrosis	
Review medication		Thiazide, digoxin

*Hyperparathyroidism may be secondary to vitamin D deficiency.

Vitamin D Toxicity

Treatment of deficiency can on rare occasions result in vitamin D toxicity. Symptoms similar to hypercalcaemia may present in such circumstances: Nausea and vomiting, Diarrhoea, Constipation, Anorexia and weight loss, Lethargy, Polyuria and thirst, Sweating, Headache, Vertigo, Raised concentrations of calcium and phosphate in plasma and urine.

Table 8: Vitamin D drug interactions <small>(please refer to SPC/BNF/ medicines information/ pharmacist for further advice)</small>	
Antiepileptic drugs (phenytoin/barbiturates)	Can increase the metabolism of vitamin D, leading to a reduction in the effects of vitamin D
Cardiac glycosides	Excessive dosing of vitamin D can induce hypercalcaemia
Corticosteroids	May increase vitamin D metabolism and elimination
Ion exchange resins (colestyramine) laxatives (paraffin oil)	May reduce the gastrointestinal absorption of vitamin D
miconazole	the effects of vitamin D are possibly reduced by miconazole
orlistat	May prevent the absorption of vitamin D, even in people also taking multivitamins, take vitamin D at least 2 hours after orlistat.
Thiazide diuretics (bendroflumethiazide)	May reduce the urinary excretion of calcium (↑ risk of hypercalcaemia)

Further Information - if you have any queries in relation to this guideline please contact Dona Wingfield, Assistant Head, Medicines Optimisation or another member of the Bedfordshire CCG Medicines Management Team via bedcgg.bedsmeds@nhs.net.

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