

Primary Care Guidelines for the Management of Vitamin D Deficiency in Adults

April 2017

Table of Contents:

Purpose and Scope 1

Sources of vitamin D..... 1

Groups at risk of Vitamin D deficiency 2

Symptoms of Vitamin D deficiency..... 3

Testing for Vitamin D deficiency..... 3

Recommended Investigations 4

Classification of vitamin D status..... 4

Indications for specialist referral 5

Treatment of vitamin D deficiency 5

Calcium and Vitamin D 6

Product Selection and Dosing..... 7

Management of Vitamin D deficiency/Insufficiency in Pregnant & Breastfeeding Women..... 8

Monitoring requirements during vitamin D treatment..... 9

Vitamin D toxicity 10

Contraindications to vitamin D supplementation 10

Cautions and drug interactions 10

Appendix 1:..... 11

Appendix 2: Licensed Vitamin D (Colecalciferol) Preparations Available for Adults (August 2015) and their suitability in certain diets..... 12

Appendix 3:..... 13

Appendix 4..... 14

References..... 15

Purpose and Scope

This guideline is intended to support primary care and secondary care (Croydon Health Services, CUH) clinicians with the prevention, identification and management of Vitamin D deficiency within the general adult (≥ 18 years) population.

This guideline relates only to the management of vitamin D deficiency to promote optimal bone health and **does not** address the use of vitamin D for other potential indications such as auto-immune disease, cancer, mental health problems and cardiovascular disease.

This guideline does not address the management of vitamin D deficiency in children or patients with severe or end-stage chronic kidney disease (CKD 4-5), severe liver disease, malabsorption syndromes, unexplained bone pain, unusual fractures and other evidence of metabolic bone disorders. Specialist advice should be sought for the management of such patients.

Whilst this guideline outlines general strategies for the management of women who are pregnant, clinicians are advised to seek specialist advice (obstetrician/endocrinologist) prior to treating Vitamin D deficiency in this group.

Sources of vitamin D

The sources of vitamin D are diet and sunlight exposure, with sunlight being a major source in most people. Approximately 80-90% of human vitamin D supply is manufactured in skin under the stimulus of solar ultraviolet B (UVB) light, the other 10-20% comes from the diet.

A. Sunlight (this section should be read in conjunction with [NICE guidelines 34: Sunlight exposure risks and benefits](#)).

Environmental and personal factors greatly affect vitamin D production in the skin, making it difficult to recommend a one-size-fits-all level of exposure for the general population.

In the UK, sunlight is strongest between 11am and 3pm between March/early April and the end of September. Between 11am and 3pm most people can make sufficient vitamin D by going out for short periods and leaving areas of skin uncovered, such as forearms, hands or lower legs. Longer periods may be needed for those with darker skin.

Before 11am and after 3pm it takes longer to synthesis sufficient vitamin D, however the risk of sunburn is less.

Exposure to sunlight through windows is insufficient because glass blocks UVB light which required for vitamin D synthesis.

In the UK, from October to March, there is no ambient UVB sunlight of appropriate wavelength to generate skin synthesis of vitamin D. During, this time the population relies on both body stores from sun exposure in the summer and dietary sources to maintain vitamin D status.

B. Diet

Vitamin D2 is found in foods of non-animal origin (particularly mushrooms) and vitamin D3 in foods such as fatty fish, fish liver oil and egg yolk.

Food sources which contain greater than 200 units (5 μ g) per portion of vitamin D include:

- 2 teaspoons of cod liver oil, 70g sardines,
- 100g tinned salmon, pilchards or tuna,
- 110g of cooked mackerel or herring and 130g cooked kipper.

Small amounts of vitamin D are provided by egg yolk, red meat and fortified foods, such as formula milks for infants and toddlers (plain cow's milk is not fortified in the UK), some breakfast cereals, fat spreads (margarine) and some yogurts.

Consumption of food sources alone, in the absence of skin synthesis, will not provide optimal vitamin D status.

C. Supplements

Following the review by the Scientific Advisory Committee on Nutrition (SACN) on the evidence of vitamin D and health, Public Health England (PHE) have advised that to protect bone and muscle health, everyone needs vitamin D equivalent to an average daily intake of 400 units (10 µg)

In the UK, during spring and summer, the majority of the population get will get enough vitamin D through sunlight on the skin and a healthy balanced diet, however during autumn and winter; everyone will need to rely on dietary sources of vitamin D. Since it is difficult for people to meet the of 400 units (10 µg) recommendation from consuming foods naturally containing or fortified with vitamin D, **PHE advise that everyone should consider taking a daily supplement containing 400 units (10 µg) of vitamin D during the autumn and winter months (i.e. between October to March).**

Those groups at high risk of vitamin D deficiency (see Table 1) should consider taking a daily supplement containing 400 units (10 µg) of vitamin D throughout the year.

General Lifestyle Advice

Appropriate lifestyle advice which encourages, 'enjoying the sun safely whilst taking care not to burn' (please note: exposure to sunlight through windows is insufficient because glass blocks UVB light), adequate dietary intake and daily vitamin D supplementation where necessary, should be provided to all patients.

NHS Choices provides up to date advice on [vitamin D](#) and [sunlight](#).

Groups at risk of Vitamin D deficiency

The Department of Health recommends vitamin D supplementation in certain high risk adult groups in order to prevent Vitamin D deficiency, as per Table 1.

Table 1: Department of Health Recommendations on Vitamin D supplementation in the UK (Adults)

Groups at risk of vitamin D deficiency
All pregnant and breastfeeding women *
People aged 65 years and over (particularly those living in institutions or who are not regularly exposed to sunlight)
People who are not exposed to much sun (e.g. housebound individuals and those who cover their skin for cultural reasons)
People with pigmented skin (includes people of African, African-Caribbean and South Asian family origin)
Recommendation: Promote self-care - advise over the counter (OTC) supplements containing 400 units (10 mcg) per day

**Pregnant /breastfeeding women may be eligible to obtain vitamins free of charge as part of the Healthy Start Scheme. Further information on the eligibility criteria can be found at www.healthystart.nhs.uk.*

Pregnant or breastfeeding women who are not eligible for Healthy Start, can purchase Healthy Start vitamins from community pharmacies or be advised to buy an over the counter multivitamin preparation with similar vitamin and mineral composition to the Healthy Start vitamins, which are available at most pharmacies and larger supermarkets (see Appendix 3 – Table 2).

Other risk factors for Vitamin D deficiency

- Malabsorption conditions (Crohn's disease, coeliac disease, short bowel syndrome, cystic fibrosis)
- Vegan or strict vegetarian diet
- Obesity (possible reduced availability of vitamin D due to sequestration in body fat)
- Chronic liver or renal disease
- Medications that can increase metabolism or reduce absorption of vitamin D (e.g. carbamazepine, phenytoin, primidone, barbiturates, oral glucocorticoids (i.e. for 3 months or longer), rifampicin, colestyramine, colestipol, orlistat and antiretrovirals. There are some thoughts that aromatase inhibitors may have a bone modifying effect that is linked to vitamin D levels

Symptoms of Vitamin D deficiency

Symptoms of vitamin D deficiency are vague and it can be difficult to ascertain whether a low vitamin D is causal or a surrogate marker. **Symptoms that could be attributed to vitamin D deficiency (especially if patients are in high risk groups) include:**

- Insidious onset of widespread or localised bone pain and tenderness (especially lower back and hip pain, but may include rib, thigh or foot pain)
- Proximal muscle weakness i.e. quadriceps and glutei. This may cause difficulty rising from a chair and/or a waddling gait
- Swelling, tenderness and redness at pseudo-fracture sites
- Fragility fractures, typically femoral neck, scapula, pubic rami, ribs or vertebrae
- Non-specific myalgia especially with a raised Creatine Kinase (CK)

Testing for Vitamin D deficiency

Routine vitamin D testing is not recommended to screen the normal population for deficiency. Vitamin D testing should be prioritised to those where the outcome will alter clinical management

Testing vitamin D levels in patients at high risk of vitamin D deficiency is NOT recommended unless they show symptoms of deficiency. Efforts should be focused on giving appropriate lifestyle advice and encouraging daily supplementation of vitamin D (see page 2 and the CCG's position statement on the prescribing of Vitamin D supplementation in Adults).

Vitamin D testing should be considered in the following:

- **Patients with disease where outcomes that may be improved with vitamin D treatment**
 - Confirmed osteomalacia
 - Osteoporosis and fragility fractures - testing is unnecessary where oral bisphosphonates with vitamin D supplementation (\pm calcium) have been prescribed as recommended by [NICE](#). Testing may be appropriate for patients that sustain a fragility fracture despite adhering to treatment or where fracture healing is delayed.
- **Patients with symptoms that could be attributed to vitamin D deficiency (especially if patients are in high risk groups)**
 - see "Symptoms of Vitamin D deficiency" above
 - Other causes for symptoms should be excluded, for example myeloma, rheumatoid arthritis, polymyalgia rheumatic and hypothyroidism.
- **Patients where correction rapid correction of Vitamin D is required prior to specific treatment**
 - i.e. patients starting on a potent anti-resorptive agents e.g. IV Bisphosphonate/Teriparatide/Denosumab. It would be expected that this group of patients would be managed by secondary care.

Recommended Investigations

Initial blood tests: Serum 25OHD, calcium (if hypercalcaemia present do not undertake vitamin D treatment until parathyroid hormone (PTH) status is known), phosphate, alkaline phosphatase (ALP), U&Es

Additional blood tests:

Renal function (to exclude renal failure), liver function tests (to exclude hepatic failure), full blood count (anaemia may be present if malabsorption), thyroid function tests, erythrocyte sedimentation rate (myeloma), serum testosterone in men less than 60 years, parathyroid hormone (PTH)(Vitamin D deficiency can lead to secondary hyperparathyroidism. A high PTH is common in renal disease - there is no indication for measuring vitamin D levels in chronic kidney disease patients, unless the patient is at risk of deficiency).

Classification of vitamin D status

Table 2 outlines the classification of vitamin D status and recommended management strategies. These are broadly in line with National Osteoporosis Society Vitamin D and Bone Health Guidelines 2013.

Table 2: Classification of vitamin D status and management strategies

Serum 25OHD concentration	Vitamin D status	Management
<30 nmol/L	Deficient	<p>Lifestyle advice plus:</p> <p>High-dose vitamin D followed by <u>over the counter (OTC)</u> long term maintenance vitamin D supplementation and lifestyle advice</p>
30-50 nmol/L	Insufficient	<p>Lifestyle advice plus:</p> <p>If in one of the following cohorts:</p> <ul style="list-style-type: none"> • Fragility fractures, documented osteoporosis or high fracture risk • Treatment with anti-resorptive medication of the bone • Symptoms suggestive of vitamin D deficiency • Increased risk of developing vitamin D deficiency because of reduced exposure to sunlight, religious/cultural dress code, pigmented skin, etc. • Raised parathyroid hormone • Medication with oral glucocorticoids (>3 months) • Conditions associated with malabsorption <p>Treat with high-dose vitamin D followed by <u>over the counter (OTC)</u> long term maintenance vitamin D supplementation</p> <p>For ALL other patients: <u>over the counter (OTC)</u> long term maintenance vitamin D supplementation.</p>
<p>>50 nmol/L*</p> <p>(Optimal vitamin D levels > 75 nmol/L)</p>	Sufficient	<p>For the general population reassurance and lifestyle advice</p> <p><i>Note: Patients with established bone disease e.g. previous osteoporotic fractures should maintain a vitamin D level ≥75nmol/L</i></p>

*NB: Vitamin D toxicity is known to occur at 25OHD values above 375nmol/L

Indications for specialist referral

- Patients with contraindications to vitamin D supplementation: severe renal impairment (CKD stage 4 or eGFR < 30ml/min/1.73m²), hypercalcaemia or metastatic calcification, primary hyperparathyroidism, renal stones, severe hypercalciuria and nephrocalcinosis.
- Patients developing hypercalcaemia following supplementation
- Patients with malabsorption conditions
- Patients with liver disease, sarcoidosis or tuberculosis
- Pregnant women with vitamin D deficiency (see pregnant and breast feeding women section)
- **Specialist advice should be sought for patients taking antiepileptic drugs or aromatase inhibitors**

Treatment of vitamin D deficiency

Prescribing considerations

Key aims for treating vitamin D deficiency are to ensure correction of vitamin D deficiency (serum 25OHD ideally >50nmol/L), reverse the clinical consequences of vitamin D deficiency in a timely manner and to avoid toxicity.

The National Osteoporosis Society Vitamin D and Bone Health Guidelines 2013 **recommend a regimen equivalent to approximately 300,000 units total cumulative dose to replenish stores in deficiency.**

Oral vitamin D is the preparation of choice. Whilst intramuscular administration results in 100% adherence, it has an unpredictable bioavailability, slower onset of action and is associated with the additional administration burden in comparison to oral preparations. Yearly high dose vitamin D is ineffective and may cause increased risk of fracture.

Prescribing of intramuscular vitamin D preparations should remain with the specialist, as this is usually reserved for those patients with compliance issues or malabsorption conditions.

As a fat soluble vitamin, oral vitamin D preparations should preferably be taken with a meal, to aid absorption.

Colecalciferol (vitamin D3) is considered the preferred form of vitamin D for treatment, as it has been reported to raise vitamin D levels more effectively than ergocalciferol (vitamin D2) and has a longer duration of action. A colecalciferol preparation should be prescribed unless this is unacceptable to the patient.

Colecalciferol (vitamin D3) is commercially synthesised from an animal source such as lanolin/wool fat from sheeps wool. If the animal is not harmed in the manufacture of the raw vitamin D3, the product could be considered suitable for vegetarians. It is advised that the source of vitamin D3 be discussed with vegans in order for them to make an informed choice as to whether this is acceptable to them or not.

Ergocalciferol (vitamin D2) is derived from a common plant steroid, and could be used at equivalent doses (in a gelatine free product) for vegans who do not find it acceptable to take colecalciferol containing products.

The choice of preparation should be discussed with patients who have various dietary requirements (e.g. halal, kosher, vegan or vegetarian, soya allergies), so that they can make an informed decision.

As there are now many licensed preparations of colecalciferol available for high dose (and maintenance vitamin D supplementation, if appropriate) which can be prescribed to meet the needs of various dietary requirements e.g. vegetarian, allergies (See Appendix 2 – Table 1). **It is therefore, expected that prescribing of unlicensed preparations, will only be undertaken in exceptional circumstances to meet the**

specific needs of an individual. If in doubt on the suitability of a preparation, contact the Medicines Optimisation Team for further advice.

Licensed preparations should be prescribed by BRAND, where possible to avoid potential risk of unlicensed preparations or preparations that do not meet the dietary requirements of specific patients being dispensed.

It is recommended that where high dose vitamin D is prescribed, this is prescribed as an acute prescription in order to avoid inadvertent repeated prescribing.

Alfacalcidol and calcitriol should not be used for the routine treatment of primary vitamin D deficiency, as unlike vitamin D, they carry a higher risk of toxicity and require long term monitoring.

Calcium and Vitamin D

Combined calcium and vitamin D preparations should not be used for the treatment of vitamin D deficiency as the high dose of vitamin D required will result in excess calcium being consumed.

Supplemental calcium is **NOT** required for most patients.

Where it is appropriate the relevance of adequate dietary calcium intake should be promoted to patients and consideration should be given to the patient's dietary intake of calcium, possibly by using "calcium calculators" e.g. <http://www.rheum.med.ed.ac.uk/calcium-calculator.php>

If patients with osteoporosis/those being treated for prevention of fragility fractures (e.g. post-menopausal women, those on bisphosphonate therapy) are found not to be reliably or regularly consuming at least 700mg of calcium per day, combined calcium and vitamin D supplements should be prescribed. This prescribing is supported by the CCG.

Anti-fracture studies in patients with osteoporosis being treated with bisphosphonates show that combined calcium and vitamin D supplementation is associated with an improvement in mortality, which is not observed with vitamin D supplementation alone. The evidence based doses are 1g per day of calcium and around 800 IU vitamin D.

A Cochrane review and meta-analysis suggested that frail older people confined to institutions may sustain fewer hip fractures if given vitamin D with calcium, but vitamin D alone is unlikely to prevent fracture.

Where combined calcium and vitamin D supplements are required these should be prescribed as combination product containing calcium 500mg or 600mg & colecalciferol 400 units twice a day. Calcium supplements are best absorbed from the intestine in smaller amounts (500-600mg or less), hence twice daily dosing.

Chewable calcium supplements may be unpalatable for many patients, resulting in poor compliance. A cost effective alternative may be to consider prescribing a caplet combination product containing calcium 750mg & colecalciferol 200 units at a dose of two caplets twice daily or prescribing a vitamin D supplement alone and providing advice on increasing dietary calcium intake.

Product Selection and Dosing

Table 3: Preferred products and doses of licensed colecalciferol preparations for management of vitamin D deficiency and insufficiency in Adults (excluding pregnant and breast feeding woman)

Vitamin status 25OHD level (nmol/L)	Licensed Product	Dose and Frequency
Deficient <30 nmol/L	Preferred 1st line option:	
	Plenachol 40,000 units ¹ or Plenachol 20,000 units capsules	40,000 units (1 x 40,000 units or 2 x 20,000 units capsules) weekly for 7 weeks followed by maintenance vitamin D
	2nd line option: Reserve for patients unable to swallow capsules or requiring a preparation that is Halal or Kosher Certified	
	Stexerol-D3 25,000 units tablets (Tablets can be swallowed whole or crushed)	50,000 units weekly for 6 weeks followed by maintenance vitamin D supplementation
	3rd line option: Reserve for patients unable to swallow capsules or crush tablets	
	Thorens 25,000 units/2.5ml oral solution	50,000 units weekly for 6 weeks followed by maintenance vitamin D supplementation
	Daily dose preparations: Prescribe <u>ONLY</u> for patients who are unable to comply with weekly dosing	
	Fultium-D3 3,200 units capsules	3,200 units daily for 12 weeks followed by maintenance vitamin D supplementation
	Stexerol-D3 1,000 units tablets (Tablets can be swallowed whole or crushed)	4,000 units daily for 10 weeks followed by maintenance vitamin D supplementation
Insufficient 30-50 nmol/L	Treat as for deficiency if one of the following present:	
	<ul style="list-style-type: none"> • Fragility fractures, documented osteoporosis or high fracture risk • Treatment with anti-resorptive medication of the bone • 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, pigmented skin, etc. • Raised parathyroid hormone • Medication with antiepileptic drugs or oral glucocorticoids (>3 months) 	
	ALL other patients: promote self-care-advise OTC vitamin D supplements to provide 800 – 2000 units daily (see page 13).	
Maintenance Therapy	After a treatment course with vitamin D, the following is recommended:	
	1. Lifestyle and dietary advice:	
	<ul style="list-style-type: none"> • Between March/early April to end of September short daily periods of sun exposure of skin (forearms, hands or lower legs) without sunscreen (10-15 minutes for most) • Dietary - vitamin D can be acquired from oily fish, eggs and meat, margarine, soya products, dairy products. 	
	2. Maintenance Therapy: (See CCG position statement on the prescribing of Vitamin D Supplements in Adults)	
	Croydon CCG recommends maintenance therapy is purchased over the counter (OTC) in the first instance.*	
	*Prescriptions for maintenance therapy should only be considered for patients who have undergone two or more previous treatment courses and other special groups (patients who have medical conditions which may pre-dispose them to inadequate vitamin D levels and where clinical assessment of the patient indicates that continuous treatment is justified e.g. conditions resulting in intestinal malabsorption e.g. Crohn's disease).	
	Should it be necessary to prescribe maintenance therapy, the following options are recommended	
	Preferred 1st line option:	
	Plenachol 40,000 units or Plenachol 20,000 units capsules	40,000units (1 x 40,000 units or 2 x 20,000 units capsules)once a month
	2nd line option:	
	Reserve for patients unable to swallow capsules or requiring a preparation that is Halal /Kosher Certified	
	Stexerol-D3 25,000 units tablets	25,000 - 50,000 ² units once a month
	3rd line option: Reserve for patients unable to swallow capsules or crush tablets	
Thorens 25,000 units/2.5ml oral solution	25,000 - 50,000 ² units once a month	
Daily dose preparations: Prescribe <u>ONLY</u> for patients where monthly dosing may cause confusion or in patients who may have compliance aids		
Preferred 1st line option:		
Stexerol-D3 1,000 units tablets	1,000 units daily	
2nd line option		
Fultium-D3 800 units caps or Desunin 800 units tabs	800 – 1,600 units daily	
3rd line option: Reserve for patients unable to swallow capsules or crush tablets		
Thorens 10,000 units/ml oral drops	800 units (4 drops) – 1,600 units (8 drops) daily	
Is Calcium required? Supplemental calcium is not required for most patients. Calcium may be indicated in those with osteoporosis/ those being treated for prevention of fragility fractures e.g. post-menopausal women, those on bisphosphonate therapy: If inadequate dietary calcium prescribe; Calcium 500mg or 600mg PLUS colecalciferol 400 units twice a day (as a combination preparation).		

¹NOTE: Local experience is to avoid use of higher physiological doses by prescribing as the 20,000 unit capsules and splitting the dose over two days, however once weekly dosing may be preferable to aid adherence. The 20,000 unit capsule is slightly smaller, so may be more acceptable for people who have difficulty swallowing capsules.

²Higher dose to be prescribed for high risk patients groups outlined on table above under 'Insufficient –prescribe and treat as for deficiency'

Management of Vitamin D deficiency/Insufficiency in Pregnant & Breastfeeding Women

All pregnant and breastfeeding women are recommended to receive routine supplementation of 400 units (10mcg) of vitamin D per day (see page 2).

Pregnant women (only if deficient)

Primary care clinicians are advised to seek specialist advice (e.g. obstetrician/endocrinologist) when treating vitamin D deficiency in patients who are pregnant.

It is not possible to make rigorously evidence-based recommendations regarding maternal vitamin D supplementation during pregnancy. **Information in this section has been based on UKMI Q&A 329.3: Which oral vitamin D dosing regimens correct deficiency in pregnancy? June 2016**

During pregnancy, maternal vitamin D deficiency could lead to deficiency in the infant, resulting in rickets and other skeletal abnormalities.

Vitamin D use in human pregnancy is not associated with an increased risk of congenital malformation, although data is insufficient to confirm there is unequivocally no risk.

A regimen equivalent to approximately 150,000 units or 300,000 units should be used to replenish stores in deficiency. Bolus injections or oral doses above 10,000 IU per day should not be used, as theoretically, adverse effects are more likely to occur.

Correction of vitamin D deficiency in pregnancy should start in the 2nd or 3rd trimester, because of the lack of safety or outcome data in 1st trimester and because of the majority of skeletal growth and development is thought to occur in the second or third trimester.

There are preparations of colecalciferol (vitamin D3) which are licensed for use in vitamin D deficiency in pregnancy. These licensed preparations enable a dosing regimen of 2,000 units to 4,000 units per day.

Rapid correction of vitamin D deficiency might be appropriate for pregnant patients with severe vitamin D deficiency (serum 25OHD level <15nmol/L). Primary care clinicians should refer the patient to a specialist for management.

Once deficiency has been addressed and treatment moves onto maintenance, a dose consistent with that of the general population is appropriate.

Breastfeeding women

There is a lack of data available with regards to the management of vitamin D deficiency in breast feeding women. The risk of vitamin D deficiency in the breast fed infant should also be a consideration.

It is recommended that preparations of colecalciferol (vitamin D3) which are licensed for use in vitamin D deficiency in breast feeding are prescribed. These licensed preparations enable a dosing regimen of up to 4,000 units per day. Pharmacological doses above 10,000 units daily should be avoided if possible.

Once deficiency has been addressed and treatment moves onto maintenance, a dose consistent with that of the general population would be considered appropriate.

Whilst there is no need to routinely monitor calcium levels in the breastfed infant, it would be recommended the infant be regularly monitored for signs of hypercalcaemia. If high doses of colecalciferol are being used it may be clinically necessary monitor infant's calcium levels.

Table 4: Preferred products and doses of licensed colecalciferol preparations for management of vitamin D deficiency and insufficiency in pregnant (Based on UKMI Q&A 329.3: *Which oral vitamin D dosing regimens correct deficiency in pregnancy?, June 2016*) and breast feeding woman (Adults)

Vitamin D status, 25OHD level (nmol/L)	Product	Dose and Frequency
In pregnant women start correction in 2nd or 3rd trimester because of the lack of safety or outcome data in first trimester, and because the majority of skeletal growth and development is thought to occur in the 2nd or 3rd trimester.		
Deficient <30 nmol/L* *Pregnant women with serum level <15 nmol/L – refer to specialist for management to be undertaken by an obstetrician as rapid correction may be required	Preferred 1st line option:	
	Fultium-D3 3200units capsules	3200 units daily up to 12 weeks followed by maintenance vitamin D supplementation
	2nd line option: Reserve for patients unable to swallow capsules or requiring a preparation that is Halal or Kosher Certified	
	Stexerol-D3 1000 units tablets (Tablets can be swallowed whole or crushed)	2000 - 4,000 units daily for 10 weeks followed by maintenance vitamin D supplementation
	3rd line option: Reserve for patients unable to swallow capsules or crush tablets	
	Thorens 10,000 IU/ml oral drops	2000 units (10 drops) - 4,000 units (20 drops) daily for 10 weeks followed by maintenance vitamin D supplementation
Insufficient 30-50 nmol/L	Promote self-care- advise purchasing OTC vitamin D supplements to provide 800 – 2,000 units daily (see Appendix 3). For those unable to buy OTC preparations prescribe maintenance therapy (see below)	
Maintenance Therapy	<u>Supplemental calcium is NOT required for most patients.</u>	
	Calcium may be indicated in those patients who have an inadequate dietary intake under specialist recommendation.	
	Preferred 1st line option:	
	Fultium-D3 800units capsules	800 – 1600 unit daily
	2nd line option: Reserve for patients unable to swallow capsules or requiring a preparation that is Halal or Kosher Certified	
	Stexerol-D3 1000 units tablets	1000 units daily
	3rd line option: Reserve for patients unable to swallow capsules or crush tablets	
	Thorens 10,000 units/ml oral drops	800 units (4 drops) – 1600 units (8 drops) daily

Monitoring requirements during vitamin D treatment

Routine monitoring of serum 25OHD is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or malabsorption, or where non-compliance with medication is suspected.

Serum 25OHD levels will take 3-6 months to reach steady state after high dose vitamin D therapy. Where indicated, **vitamin D levels should therefore be checked at least 6 months after treatment with high dose vitamin D.**

Patients who do not respond to treatment with high dose vitamin D may be considered for referral to secondary care.

Adjusted serum calcium should be checked 1 month after completing high dose vitamin D treatment or after starting maintenance vitamin D supplementation, **in case hyperparathyroidism has been unmasked or to detect hypercalcaemia.** The presence of hypercalcaemia should lead to cessation of further vitamin D supplementation prior to investigation of the hypercalcaemia.

In patients receiving high dose vitamin D treatment, serum calcium levels should be monitored at one month and month 2 if:

- Risks of hypercalcaemia are higher than average such as in patients with Chronic Kidney Disease (CKD) or those taking thiazide diuretics.
- Patients taking digoxin or other cardiac glycosides – where drug effect may be accentuated with vitamin D
- Any symptoms or signs of hypercalcaemia (anorexia, nausea, thirst, polyuria, vomiting, constipation, confusion)

To avoid maternal (and possibly foetal or neonatal) hypercalcaemia, it is recommended that pregnant women being treated with vitamin D deficiency should have their serum calcium levels checked 1 month after starting treatment and then 3 months later, when steady state vitamin D levels have been achieved. It might also be sensible to check neonatal calcium and vitamin D levels at delivery.

Vitamin D toxicity

Vitamin D toxicity, defined by hypercalcaemia, is known to occur at serum 25OHD levels of above 375nmol/L. However, toxicity is rare and is unlikely to occur with recommended supplemental or therapeutic doses. Research has suggested vitamin doses below 10,000 units/day is not usually associated with toxicity, whereas doses equal to or above 50,000 units/day for several weeks or months are frequently associated with toxicity.

Early symptoms of toxicity will include symptoms of hypercalcaemia, such as thirst, polyuria, constipation, nausea and vomiting and weight loss. Toxicity can lead to renal failure if left untreated, therefore, if toxicity is suspected, vitamin D must be withdrawn and serum calcium and renal function checked urgently. In severe cases patients may require emergency inpatient care with rehydration therapy.

Contraindications to vitamin D supplementation

Vitamin D is contraindicated in patients with severe renal impairment (CKD stage 4 or eGFR <30ml/min/1.73m²), hypercalcaemia or metastatic calcification. Relative contraindications include primary hyperparathyroidism, renal stones, severe hypercalciuria and nephrocalcinosis.

Cautions and drug interactions

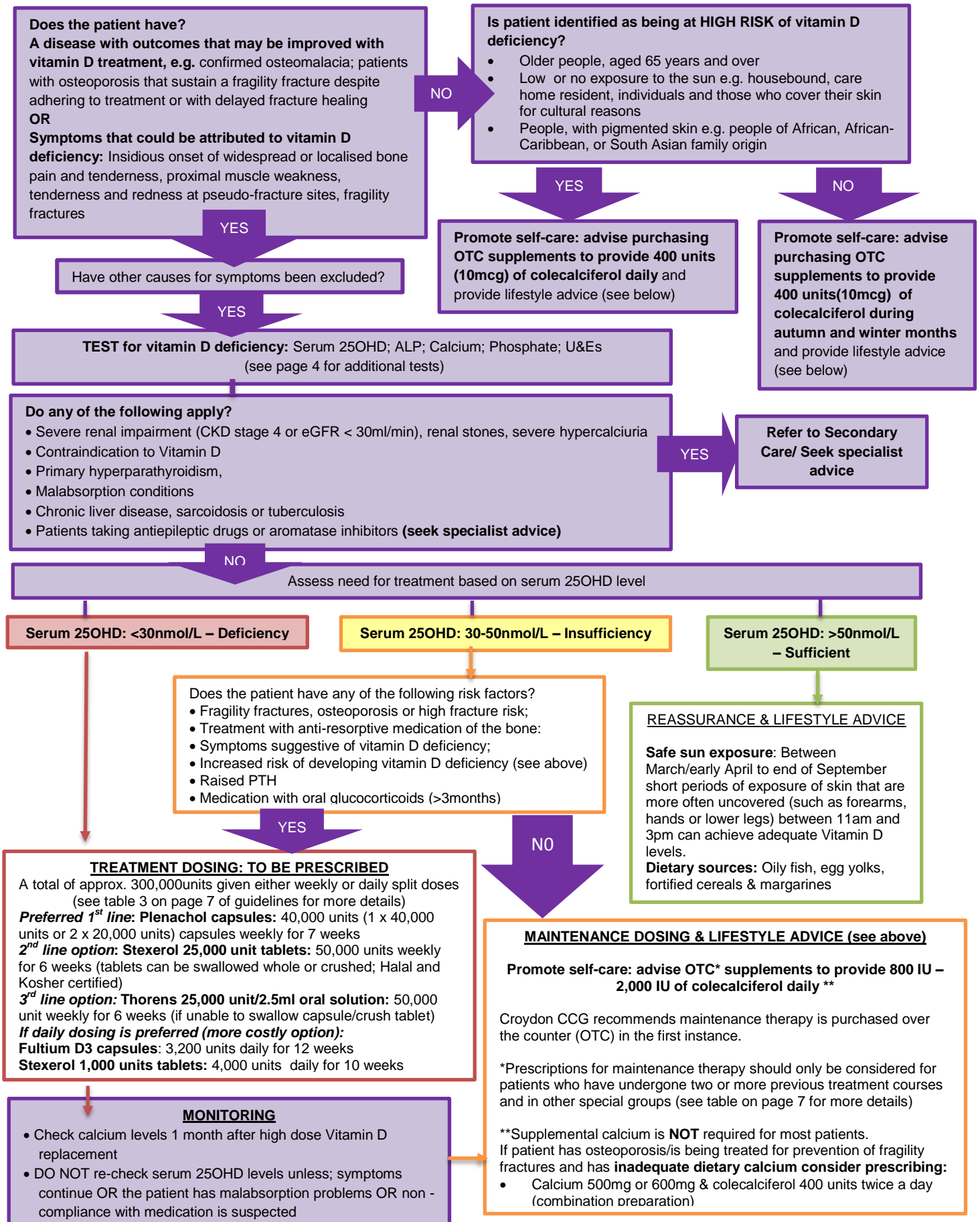
This list is not exhaustive. Please refer to individual product Summary of Characteristics accessible via: <http://www.medicines.org.uk/emc/search> for further details.

- Effects of digoxin and other cardiac glycosides may be accentuated by vitamin D
- Risk of hypercalcaemia is increased in patients taking thiazide diuretics
- Concomitant treatment with carbamazepine, phenytoin, barbiturates, primidone, corticosteroids and some antiretroviral activation can decrease effect of vitamin D

Appendix 1:

Flowchart: Investigation and Treatment of Vitamin D deficiency and insufficiency for Adults (excluding pregnant and breastfeeding women).

Please refer to full guidelines for further details. 400 units of colecalciferol is equivalent to 10mcg of colecalciferol



Appendix 2: Licensed Vitamin D (Colecalciferol) Preparations Available for Adults (August 2015) and their suitability in certain diets

Name and Form	Price Unit/Pack size	Price for Adult treatment course (approx. 300,000 units as per licensed dose)	Suitability				Preparations contains			
			Halal	Kosher	Vegetarian	Vegan	Soya	Nut	Gelatine	Lactose
Colecalciferol 200 units										
Fultium-D3 2740 unit/ml oral drops Dose: Please check SPC for the dose recommendations	£10.70 / 25ml	£42.80	Not halal certified	Not kosher certified	✓	See notes	×	×	×	×
Thorens 10,000 unit/ml oral drops Dose: Please check SPC for the dose recommendations	£5.85 / 10ml	£17.55	See notes	See notes	✓	See notes	×	×	×	×
Colecalciferol 800 units										
Aviticol 800 unit capsules Dose: Please check SPC for the dose recommendations	£3.60 / 30 capsules	£42.00	×	×	×	×	×	×	✓	×
Desunin 800 unit tablets Dose: Please check SPC for the dose recommendations	£3.60 / 30 tablets or £10.17 / 90 tablets	£38.55 - £42.00	×	✓	✓	See notes	×	×	×	×
Fultium-D3 800 unit capsules Dose: Please check SPC for the dose recommendations	£3.60 / 30 capsules or £10.80 / 90 capsules	£40.32	See notes	See notes	×	×	See notes	See notes	✓	×
Colecalciferol 1,000 units										
Aviticol 1,000 unit capsules Dose: Please check SPC for the dose recommendations	£3.16 / 30 capsules	£29.49	×	×	×	×	×	×	✓	×
Stexerol-D3 1,000 unit tablets Dose: Please check SPC for the dose recommendations	£2.95 / 28 tablets	£31.60	✓	✓	✓	See notes	×	×	×	×
Colecalciferol 3,000 units										
Colecalciferol 3,000 unit/ml oral solution (Thame) Dose: Please check SPC for the dose recommendations	£119.70 / 100ml	£119.70	×	×	✓	×	✓	✓	×	×
Colecalciferol 3,200 units										
Fultium-D3 3,200 unit capsules Dose: Please check SPC for the dose recommendations	£13.32 / 30 tablets	£37.30	See notes	See notes	×	×	×	×	✓	×
Colecalciferol 20,000 units										
Aviticol 20,000 unit capsules Dose: Please check SPC for the dose recommendations	£29.00 / 30 capsules	£13.53	×	×	×	×	×	×	✓	×
Fultium-D3 20,000 unit capsules Dose: Please check SPC for the dose recommendations	£17.04 / 15 capsules or £29.00 / 30 capsules	£13.53 - £15.90	See notes	See notes	×	×	See notes	See notes	✓	×
Plenachol 20,000 unit capsules Dose: Please check SPC for the dose recommendations	£9.00 / 10 capsules	£12.60	See notes	See notes	✓	See notes	×	×	×	×
Colecalciferol 25,000 units										
InVita D3 25,000 unit dose vials SF oral solution Dose: Please check SPC for the dose recommendations	£4.45 / 3 x 1ml	£17.80	Not halal certified	Not kosher certified	✓	See notes	×	×	×	×
Thorens 25,000 unit/2.5ml oral solution Dose: Please check SPC for the dose recommendations	£1.55 / 2.5ml	£18.60	See notes	See notes	✓	See notes	×	×	×	×
Stexerol-D3 25,000 unit tablets Dose: Please check SPC for the dose recommendations	£17.00 / 12 tablets	£17.00	✓	✓	✓	See notes	×	×	×	×
Colecalciferol 40,000 units										
Plenachol 40,000 unit capsules Dose: Please check SPC for the dose recommendations	£15.00 / 10 capsules	£10.50	See notes	See notes	✓	See notes	×	×	×	×



Preferred first line option in treatment of deficiency



2nd line option in treatment of deficiency



3rd line option in treatment of deficiency

Appendix 3:

Additional Notes on Products For Patients Who Have Specific Dietary Requirements

Desunin® (800 unit tablets)
The manufacturers have confirmed that the finished product has no excipients originating from an animal source. The source of colecalciferol (vitamin D3) is synthetically produced in a process that includes wool grease/lanolin from healthy live sheep. The company has confirmed the product is suitable for vegetarians.
Fultium-D3® (Oral drops, 800 & 20,000 unit capsules)
Drops: The drops do not contain gelatine and the manufacturer has advised the drops are suitable for vegetarians. The active ingredient is derived from sheep wool.
Capsules: Fultium-D3 800 unit capsules previously contained nuts and soya but are now reformulated with maize oil. Previous batches may still be in circulation so patients should consult their pharmacist when receiving them. The gelatine used in 800 unit and 20 000 unit capsules are derived from beef bone and hide. Only the gelatine in the capsule is halal and kosher certified. The remaining constituents of the product have not been halal/kosher certified.
Plenachol® (20,000 & 40,000 unit capsules)
Only the capsule in Plenachol is halal and kosher certified. The company has confirmed that Plenachol is suitable for vegetarians. The formulation base for Plenachol comprises only synthetic constituents/constituents derived from plant sources. The vitamin D3 itself is derived from lanolin (oil extract from the wool of live sheep).
Aviticol® (20 000 unit capsules)
The gelatine used to manufacture the capsule is of bovine and porcine origin. The Aviticol capsules are not halal or kosher certified.
Thorens® (25 000 unit oral solution & 10,000 unit oral drops)
Thorens oral solution contains colecalciferol and refined olive oil. The colecalciferol is derived from cholesterol from wool grease (lanolin). Thorens is considered to be suitable for vegetarian patients but is not considered suitable for vegan patients. The colecalciferol in Thorens is halal and kosher-certified. The olive oil excipient has not been certified as halal or kosher.
InVita D3® (25 000 unit oral solution)
InVita D3 is gluten-free, alcohol-free, yeast-free and is olive oil based. It does not use any ingredients from slaughtered animals and does not contain gelatine or porcine sourced materials. The vitamin D3 is sourced from lanolin from sheep's wool.
Stexerol-D3® (25,000 unit & 1,000 unit) tablets
The manufacturers have confirmed that the finished product is Halal and Kosher certified. The tablets are gelatine-free. The company has confirmed that Stexerol-D3 is suitable for vegetarians and soya-free and nut-free.
Other
The choice of product should be discussed with patients who have halal, kosher, vegan or vegetarian requirements, so that they may make an informed decision.

Appendix 4

Table 1: Examples of OTC (Over the Counter) Vitamin D preparations available for adults

Brand	Strength	Approximate price	Source	Suitability
Boots Pharmaceuticals® Vitamin D3	1000 units (25mcg) tablets	90 tablets £4.99	Available for purchase only from Boots or www.boots.com	Suitable for vegetarians but not vegans
Holland and Barrett® Fast Acting Liquid Vitamin D3	1000 units (25mcg)/10 drops	59mls £13.99	Available for purchase only from Holland and Barrett or www.hollandandbarrett.com	Suitable for vegetarians but not vegans
BioLife® Vitamin D3 chewable tablets	1000 units (25mcg) tablets	90 chewable tablets £9.98	Available for purchase only from www.lifestylenaturalhealth.co.uk	Suitable for vegetarians but not vegans
Nature's Remedy® Vitamin D3	1000 units (25mcg) tablets and capsules	200 tablets/ capsules £11.99	Available for purchase only from www.naturesremedy.co.uk	Suitable for vegetarians but not vegans
Superdrug® Vitamin D3	500 units (12.5mcg) tablets	90 tablets £2.15	Available for purchase only from Superdrug or www.superdrug.com	Suitable for vegetarians but not vegans
Tesco® Vitamin D3	1000 units (25mcg) tablets	90 tablets £3.50	Available for purchase only from Tesco or www.tesco.com	Suitable for vegetarians but not vegans
Valupak® Vitamin D3	1000 units (25mcg) tablets	60 tablets £0.99	Available from pharmacies	Suitable for vegetarians but not vegans

Table 2: Examples of adult vitamin D nutritional supplements suitable for pregnant women

Product	Strength	Approximate price	Source	Suitability
Healthy Start Vitamins for Pregnant women Vitamin D3	400 units (10mcg) (Also contains vitamin C and folic acid)	56 tablets free of charge where eligible	Available from midwives, health visitors and children's centres. For more info visit www.healthystart.nhs.uk	Suitable for vegetarians but not vegans
PregnaCare® multivitamins and minerals Vitamin D3	400 units (10mcg) (Also contains multiple other constituents)	30 tablets Prices vary from £4-£6	Various supermarkets, chemists and online	Suitable for vegetarians but not vegans
Sanatogen® Mum to Be Multivitamins and minerals Vitamin D3	400 units (10mcg) (Also contains multiple other constituents)	60 tablet Prices from £13	Various supermarkets, chemists and online	Suitable for vegetarians but not vegans

References

1. The National Osteoporosis Society. Vitamin D and Bone Health: A practical clinical guideline for patient management. Available at <https://nos.org.uk/for-health-professionals/tools-resources/#> <Accessed 25.04.2017> (note: may not open in older internet browsers)
2. The National Osteoporosis Society. . Vitamin D and Bone Health: A practical clinical guideline for management in Children and Young People. Available at <https://nos.org.uk/for-health-professionals/tools-resources/#> <Accessed 25.04.2017> (note: may not open in older internet browsers)
3. National Institute for Clinical Excellence. Vitamin D: increasing supplement use among at-risk groups. PH Guidance 56; November 2014. <https://www.nice.org.uk/guidance/ph56?unlid=10358694812017218212926> <Accessed 26.04.2017>
4. British Association of Dermatologists. Skin Cancer; Vitamin D. Available at <http://www.bad.org.uk/for-the-public/skin-cancer/vitamin-d> <Accessed 11.05.2015>
5. Pearce S, Cheetham D et al, Diagnosis and management of vitamin D deficiency. BMJ 2010; 340: b5664
6. Royal College of Paediatric and Child Health. Guide for Vitamin D in Childhood. October 2013.
7. UKMI Q&A 82.2. What dose of vitamin D should be prescribed for the treatment of vitamin D deficiency? Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals, Date prepared 8th January 2013, Available via www.evidence.nhs.uk <Accessed 29.05.2015>
8. Public Health England. Vitamin D Information for Healthcare Professionals; December 2014. Available via <https://www.gov.uk/government/publications/vitamin-d-for-healthcare-professionals-and-the-public> <Accessed 29.05.2015>
9. UKMI Q&A 387.3, Which vitamin D preparations are suitable for a vegetarian or vegan diet? Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals, Date prepared 18th February 2015, Available via www.evidence.nhs.uk <Accessed 29.05.15>
10. Committee on Toxicity. COT Statement on Vitamin D – lay summary. December 2014. Available via <http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2014/cot-statement-on-vitamin-d> <Accessed 26.04.2017>
11. UKMI Q&A 82.3. What dose of vitamin D should be prescribed for the treatment of vitamin D deficiency? Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals, Date prepared 7th April 2015, Available via www.evidence.nhs.uk <Accessed 16.07.2015>
12. NHS South West London Croydon Borough Team. Guideline for the Management of Vitamin D Deficiency in Primary Care. June 2011.
13. UKMI Q&A 329.3. Which oral vitamin D dosing regimens correct deficiency in pregnancy? Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals, Date prepared June 2016, Available via <https://www.sps.nhs.uk/articles/> <Accessed 08.11.2016>
14. Medicines and Healthcare products Regulatory Agency. Drug Safety Update: Antiepileptics Adverse Effects on bone. 1st April 2009. Available via <https://www.gov.uk/drug-safety-update/antiepileptics-adverse-effects-on-bone> <Accessed 26.04.2017>
15. Royal College of Gynaecologists. Vitamin D in Pregnancy; Scientific Impact Paper No.43. June 2014.
16. Bronner F. Mechanisms of intestinal calcium absorption. J Cell Biochem. 1st Feb 2003; 88(2);387-93 PubMed
17. Scottish Intercollegiate Guidelines Network. SIGN 142 -Management of osteoporosis and the prevention of fragility fractures. March 2015. Available via <http://www.sign.ac.uk/pdf/SIGN142.pdf> <Accessed 26.04.2017>
18. NHS National Institute for Health Research. Vitamin D supplementation in pregnancy: a systematic review. Health Technology Assessment; Volume 18; Issue 45. July 2014. Available via http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0004/121765/FullReport-hta18450.pdf <Accessed 18.11.2015>
19. UK Drugs in Lactation Advisory Service. UK Drugs in Lactation Advisory Service Database: Vitamin D – Colecalciferol. Available via <http://www.midlandsmedicines.nhs.uk/apps/ukdilas/resultsBNFcat.asp?SubSectionRef=09.06> <Accessed 18.11.2015>

20. Scientific Advisory Committee on Nutrition. Draft Vitamin D and Health report: Scientific consultation: 22 July to 23 September 2015. September 2015. Available via <https://www.gov.uk/government/consultations/consultation-on-draft-sacn-vitamin-d-and-health-report> <Accessed 18.11.2015>
21. National Institute for Clinical Excellence. Sunlight exposure risks and benefits. NG 34; February 2016.
22. Lambeth CCG. A comparison of licensed Vitamin D preparations for Adults available in the UK. November 2015. Available via <http://www.lambethccg.nhs.uk/news-and-publications/meeting-papers/lambeth-borough-prescribing-committee/Lambeth%20Borough%20Prescribing%20Committee/Clinical%20Guidelines/Comparison%20table%20of%20licensed%20Vitamin%20D%20preparations%20for%20adults%20Nov%202015.pdf> <Accessed 21.04.2016>
23. Summary of Product Characteristics for Fultium-D3 Drops. Last updated on: 27.08.2015
<https://www.medicines.org.uk/emc/medicine/30438>
24. Chemist and Druggist Prices. February 2016.
25. Summary of Product Characteristics for Desunin 800 IU tablets. Available via:
<https://www.medicines.org.uk/emc/medicine/27007>
26. Summary of Product Characteristics for Fultium-D3 800IU capsules. Available via:
<https://www.medicines.org.uk/emc/medicine/25664>
27. Summary of Product Characteristics for Plenachol 20 000IU capsules. Available via:
<https://www.medicines.org.uk/emc/medicine/31196>
28. Summary of Product Characteristics for Aviticol 20 000IU capsules. Available via:
<https://www.medicines.org.uk/emc/medicine/29660>
29. Summary of Product Characteristics for Fultium-D3 20 000IU capsules. Available via:
<https://www.medicines.org.uk/emc/medicine/29815>
30. Summary of Product Characteristics for Thorens 25 000 IU/2.5ml oral solution. Available via:
<https://www.medicines.org.uk/emc/medicine/30775>
31. Summary of Product Characteristics for InVita D3 25 000IU oral solution. Available via:
<https://www.medicines.org.uk/emc/medicine/28998>
32. Summary of Product Characteristics for Plenachol 40 000IU capsules. Available via:
<https://www.medicines.org.uk/emc/medicine/31197>
33. Summary of Product Characteristics for Stexerol 1,000 IU and 25 000IU tablets. Available via:
<https://www.medicines.org.uk/emc/medicine/31223>
34. Summary of Product Characteristics for Colecalciferol 3,000IU/ml oral solution. Available via:
<http://www.mhra.gov.uk/home/groups/spcpil/documents/spcpil/con1454653985022.pdf>