South East London Clinical Guidance for the Management of Vitamin D Deficiency and Insufficiency in Pregnancy and lactation

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This document is for guidance only and not intended to replace the health professionals' clinical judgement for individual patients. SEL APC has separate guidance for management of Vitamin D deficiency in Adults including CKD *and* management of Vitamin D deficiency in children.

1. Introduction

Vitamin D is essential for musculoskeletal health as it promotes calcium absorption from the bowel, enables mineralisation of newly formed osteoid tissue in bone and plays an important role in muscle function.[1] The term 'vitamin D' generally refers to two very similar molecules. Vitamin D_3, also known as colecalciferol, is the most abundant in humans and is produced in the skin following exposure to sunlight.[1] Vitamin D_2, or ergocalciferol, occurs naturally in some mushrooms and yeast. The amount in most other vegetables is negligible.

The body converts both forms of vitamin D to 25-hydroxyvitamin D (25OHD). Tests to assess vitamin D status measure levels of 25OHD in the blood. 25OHD is itself converted in the body to the biologically active form 1,25-dihydroxyvitamin D, also known as calcitriol.

There is little information on vitamin D intake in pregnancy and lactation and few studies on clinical outcomes. Reduced vitamin D concentrations are found in obese women BMI>30 and pre-pregnancy obesity has been associated with lower levels of vitamin D in both pregnant women and their neonates. Maternal Vitamin D deficiency is linked with higher risk of pre-eclampsia, increased caesarean section rates, low birth weight, neonatal hypocalcaemia and tetany. It may adversely affect foetal bone mineralisation and may also be linked to impaired foetal skeletal growth and impaired foetal lung development but definite evidence for this is lacking. Women should have adequate vitamin D stores for their own requirement, for their developing foetus and to build stores for early infancy particularly if they plan to breast-feed. There is a growing understanding of the importance of vitamin D in terms of its potential role in the prevention of non-skeletal disorders such as auto-immune disease, cancer, mental health problems and cardiovascular disease.

2. Purpose and Scope

This document is a South East London wide guideline broadly based on the following as well as expert opinion.

- Chief Medical Officer's recommendation on vitamin D supplementation for pregnant women and breastfeeding mothers
- NICE guidelines CG62 (2008) Antenatal care: routine care for the healthy pregnant woman
- RCOG (Royal College of Obstetricians & Gynaecologists) Impact Paper: Vitamin D in Pregnancy June 2014
- UKMi Q&A 329.1 Which oral vitamin D dosing regimens correct deficiency in pregnancy?

It sets out to provide guidance on:

- Management of Low Vitamin D Levels in Pregnancy or Breastfeeding Women
- Who to test for vitamin D deficiency
- General information and lifestyle advice
- Prescribing Information
- Product and Allergy Information for a selection of Vitamin D products
- Symptoms of Vitamin D overdose

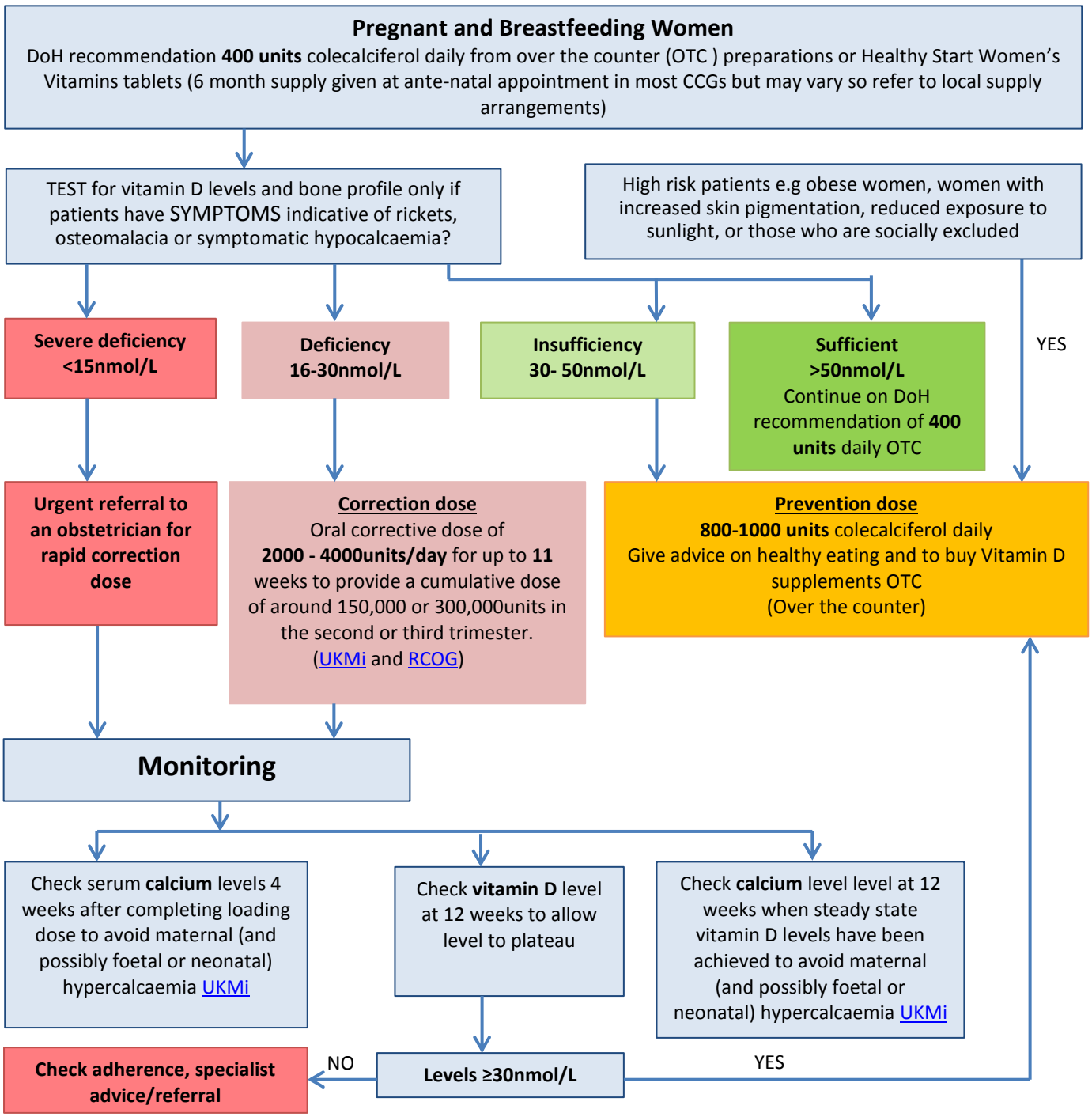
Before using this guidance consider a referral to a specialist for advice if:

1. The patient has a diagnosis of stage 3 CKD (or greater) or history of significant renal impairment/stones
2. The patient has sarcoidosis, liver disease, lymphoma, metastatic cancer
3. The patient has hypercalcaemia (hyperparathyroidism)

In the autumn and winter months **EVERYONE** including pregnant and breastfeeding women should consider taking a daily supplement containing 10 micrograms (400 IU) of vitamin D

Public Health England July 2016

Management of Low Vitamin D Levels in Pregnancy or Breastfeeding Women



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SEL Area Prescribing Committee. A partnership between NHS organisations in SEL: Bexley, Bromley, Greenwich, Lambeth, Lewisham and Southwark Clinical Commissioning Groups (CCGs) and GSTFT/KCH/SLAM/LGT/Oxleas hospital trust

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3. Testing for vitamin D deficiency in pregnancy

There are no data to support routine screening for vitamin D deficiency in pregnancy in terms of health benefits or cost effectiveness. As the test is expensive, offering vitamin D screening to all at-risk women may not be cost effective compared to offering advice on healthy eating and encouraging daily uptake of OTC supplements. Both clinical symptoms and risk factors must be present before considering testing. Those at greatest risk of vitamin D deficiency includes women who are obese, pregnancy with diabetes, risk of pre-eclampsia, women with limited skin exposure to sunlight, who are of South Asian, African, Caribbean or Middle Eastern descent or those covering their skin for religious/cultural reasons. Measurement of vitamin D in a hypocalcaemic or symptomatic woman as part of their management continues to be applicable. This includes women with , bone pain, gastrointestinal disease, alcohol abuse, a previous child with rickets and those receiving drugs which reduce vitamin D. e.g. enzyme inducing antiepileptic medications such as phenytoin, carbamazepine, and phenobarbital.

4. General information and lifestyle advice

Natural ways of increasing Vitamin D levels

1. Safe Sun exposure

Sun exposure is the main source of vitamin D and this should be balanced with the risks of excessive exposure. **Sunburn should always be avoided**. Little and often sun exposure is best for Vitamin D synthesis. On 21st July 2016 Public Health England issued new advice on vitamin D based on the recommendations of the Scientific Advisory Committee on Nutrition. The advice notes that vitamin D is made in the skin on exposure to UVB in sunlight and that in spring and summer, the majority of the population get enough vitamin D through sunlight on the skin and a healthy, balanced diet. However since it is difficult to quantify, a daily dietary intake of 10 micrograms equivalent to 400 international units (IU) is being recommended for everyone particularly in the autumn and winter months. Women from ethnic minority groups with dark skin, from African, Afro-Caribbean and South Asian backgrounds, may not get enough vitamin D from sunlight in the summer and therefore should consider taking a supplement all year round.

Prescribing of vitamin D purely for supplementation following Public Health England advice should be avoided and patients should be requested to purchase Vitamin D supplements over the counter.

Unprotected sun exposure should be avoided in patients with the following conditions:sensitive skins, skin cancer, porphyrias, xeroderma pigmentosum, albinism, granulomatous disease (sarcoid but not tuberculosis) and lymphoma.

Unprotected sun exposure should also be avoided in patients who are taking following medications: sulphonamides, phenothiazines, tetracyclines, quinolones, psoralens, isotretinoin or other photosensitising medications.

Sunbed use increases the risk of skin cancer, and is not recommended as a method for enhancing vitamin D status. From mid-October to the beginning of April in the UK there is no ambient ultraviolet sunlight of the appropriate wavelength so there is no benefit from sun exposure.

2. Dietary advice

All pregnant women should be encouraged to eat plenty of vitamin D rich foods, including:

- Oily fish such as salmon, mackerel and sardines
- Eggs
- Fortified spreads and breakfast cereals and some yoghurts

These should be taken as part of a healthy balanced diet. However adequate vitamin D intake may be difficult to achieve with diet alone, and pregnant women are advised to buy over the counter (OTC) vitamin supplements or signposted to Healthy Start Clinics where Healthy Start Women's vitamins are available.
A wide range of vitamin D preparations specially tailored for pregnancy (containing 400 units of vitamin D), are available to buy OTC from pharmacies and health food shops. These products do not have a UK marketing authorisation and are marketed as nutritional supplements.

New guidance from NICE recommends that people who are at risk of low vitamin D should be given better access to supplements to protect their health. This includes pregnant and breast feeding mothers.
Healthy Start Women's vitamin tablets are supplied **free of charge** to pregnant & breastfeeding women who are eligible beneficiaries under the Healthy Start government led scheme. Healthy Start Women's vitamin tablets contain:

70 milligrams of vitamin C
10 micrograms (400 units) of vitamin D
400 micrograms of folic acid

The responsibility for distributing Healthy Start vitamins lies with clinical commissioning groups, resulting in variable local arrangements. Some CCGs provide Healthy Start vitamin supplements via specific health clinics and/or childrens' centres, while in other CCGs they are distributed by midwives and health visitors. Some CCGs choose to provide free Healthy Start vitamins to all pregnant women, breastfeeding women (with children up to the age of 1) and all children under 4 via selected community pharmacies. However, this has to be funded from existing local NHS budgets.

It is therefore very important for prescribers to refer to local CCG vitamin D supply arrangements via the Healthy Start scheme. Contact local Medicines Management teams if unsure of supply arrangements.

5. Prescribing Information

Free uptake of Healthy Start Women's vitamin tablets should be recommended for eligible pregnant women ahead of issuing FP10 prescriptions.

Vitamin D supplements are measured in both micrograms (µg or mcg) and International Units (IU) or units.
1 microgram (mcg) is equivalent to 40 units of vitamin D_2 or D_3 and 10mcg is equivalent to 400 units

- **Dose for correction (vitamin D <30nmol/L) UKMi :**
  It would be rational to use an oral dose of 2000-4000units per day for up to 11 weeks to provide a cumulative dose of around 150,000 or 300,000units in pregnancies that are in the 2nd or 3rd trimester . Correction should begin in the 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.
- **Dose for rapid correction (vitamin D <15nmol/L) UKMi :**
  A level of less than 15nmol/L, would be considered as being very low by most clinicians. Contact a specialist for advice. If the baseline vitamin D level is very low and the woman is in the 3rd trimester of her pregnancy, then rapid correction may be required particularly if there are unmodifiable risk factors.
- **Calcium intake:** Combined calcium and vitamin D products should not be used to correct deficiency in pregnancy due to the risk of hypercalcaemia; instead pregnant women should try to have an adequate

calcium intake (700mg) through their diet. Calcium supplements are essential in pregnant women who are at risk of pre-eclampsia.[14] Calcium calculators (e.g.http://www.rheum.med.ed.ac.uk/calcium-calculator.php) are available to help patients and clinicians determine whether the woman is getting enough calcium from her food and whether dietary modification and/or supplementation should be used.

- To avoid maternal (and possibly foetal or neonatal) hypercalcaemia, it is suggested that pregnant women being treated for vitamin D deficiency have their serum calcium levels checked a month after starting treatment and then three months later, when steady state vitamin D levels have been achieved.
- Pregnant mothers should be advised not to take supplements containing vitamin A such as Cod Liver Oil because this is a known teratogen[11]
- If a mother has been advised to take vitamin D supplementation because of diagnosed Vitamin D deficiency, they should be advised to continue this throughout the period of pregnancy and lactation.
- A number of licensed oral vitamin D products (Table A) are available in a variety of strengths and formulations such as tablets, capsules and drops. These enable recommended dosing regimens of 1000units/day, 2000units/day or 4000 units/day and do not contraindicate use in pregnancy.

Table A : Licensed colecalciferol products available on prescription

Product	Suitable in soy or peanut allergy?	Suitable for vegetarians	Kosher and Halal considerations	Additional Information	Pack Size	Drug Tariff Cost April 2017
Desunin ® tablets Colecalciferol 800 units	Yes	Yes	Contains no gelatin or porcine sourced excipients	Tablets can be swallowed whole or crushed or taken with food.	30	£3.60
Desunin ® tablets Colecalciferol 4000 units	Yes	Yes	Contains no gelatin or porcine sourced excipients	Tablets can be swallowed whole or crushed or taken with food.	70	£15.19
Fultium-D3® caps Colecalciferol 800 units	Yes	No	Gelatin is of bovine origin, no porcine sourced excipients	Only licensed product in pregnancy & breast feeding for doses up to and including 4000 units daily Lactose free Contains maize oil	90	£8.85
Fultium-D3® caps Colecalciferol 3200 units	Yes	No	Gelatin is of bovine origin, no porcine sourced excipients	Lactose free Contains maize oil Only licensed product in pregnancy & breast feeding	30	£13.32
Fultium D_3 drops® Colecalciferol 2740 units/ml 12 drops = 800 units	Yes	No	Gelatin is of bovine origin, no porcine sourced excipients	Lactose free Contains maize oil Only licensed product in pregnancy & breast feeding	25mls	£10.70
Stexerol-D3® tablets Colecalciferol 1000 units	Yes	Yes	Contains no gelatin	Lactose free	28	£2.95

6. Symptoms of Vitamin D Overdose

The Food and Nutrition Board of the Institute of Medicine (IOM) has summarised the evidence from a number of supplementation studies of vitamin D [13], which covered a range of doses (800 to 300,000 units/day) and duration (months to years). They concluded that vitamin D 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, including documented hypercalcaemia. Safety data for high dose oral vitamin D regimens used during human pregnancy are limited. Bolus injections or oral doses of more than 10,000units **per day** should be avoided in pregnancy.[12]

The symptoms of vitamin D overdose can vary from mild to serious. Some, like nervousness and irritability, are emotional. But physical signs can present as nausea, vomiting, loss of appetite and accompanying weight loss. Sufferers may also become dehydrated and experience increased thirst and severe headaches. As symptoms progress, the nerves and muscles become affected**, leading to itchy skin**, fatigue and weakness. More serious issues of vitamin D toxicity in the body leads to elevated levels of calcium that reside in the blood and soft tissues (like the lungs, heart and kidneys). At this point, bone pain or bone loss can occur. Sufferers will also exhibit urinary tract symptoms ranging from excessive production of urine to kidney stones or renal failure. High blood pressure and an increased risk of heart disease are concerns and ultimately can lead to irrevocable damage to major organs.

7. References

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