

Mersey Cluster - Guidance for Vitamin D Deficiency and Treatment Options

Recent BMJ articles^{1,2} highlighted the problem of vitamin D deficiency in the UK population. There is an increasing body of evidence associating such deficiency with an increased risk of morbidity not only due to bone/muscle disorders but a variety of other conditions³. Prescribers may encounter patients whose clinical presentation is either principally due to vitamin D deficiency or is complicated by its presence. A recent letter was sent to all healthcare professionals from the Chief Medical Officer highlighting the risk of Vitamin D deficiency. +

Consensus suggests Vitamin D is mainly obtained by the action of UV rays on our skin. A US study⁴ suggests 5-15 minutes (longer for darker skin) daily sun exposure between 10am and 3pm from April to October would be sufficient to improve vitamin D status⁵. Dietary sources of Vitamin D include oily fish, egg yolk, fortified foods e.g. cereal and margarine⁶.

Please see national advice leaflet at:

<http://www.dh.gov.uk/health/2012/02/advice-vitamin-d/>

http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_132508.pdf

or Map of Medicines <http://eng.mapofmedicine.com/evidence/map/index.html>

There is a lack of consensus regarding the precise definition of vitamin D deficiency. Some authorities recommend treatment below 25nmol/L while others recommend 50nmol/L. The Liverpool criteria for deficiency (Total 25 (OH)D concentration) is ≤ 30 nmol/L and for insufficiency $>30-50$ nmol/L. This may vary across North Mersey.

The scope of this guidance is to review the treatment and prevention of Vitamin D deficiency, please see Appendix 1 for further information and advice regarding care of patients who fall outside the scope of this guidance including those with osteoporosis and eGFR <30 mL/minute/1.73m²

nmol/L*	ng/mL*	Vitamin D Status	Health status
≤ 30	<12	Deficiency	Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults
$>30-50$	12-20	Insufficiency	Generally considered inadequate for bone and overall health in healthy individuals
>50	>20	Adequate	Generally considered adequate for bone and overall health in healthy individuals. ***Remember levels may decrease over autumn/winter***
>75	>30	Optimal	Emerging evidence links potential adverse effects to high concentrations particularly >150 nmol/L (>60 ng/mL)

Please Note: Serum concentrations of 25(OH)D reported in either nanomoles per litre (nmol/L) or nanograms per millilitre (ng/mL). 1ng/mL = 2.5nmol/L

Since 2010 clinical chemistry laboratories should be reporting results in nmol/L.

Who should be tested?

Routine testing of Vitamin D levels is NOT recommended.

Assessing the patient:

If patient is healthy with no risk factors and is symptom free – NO investigations are required. Offer lifestyle advice and consider over the counter preventative therapies.

If a patient presents with risks factors only – Offer lifestyle advice and consider long term preventative therapies

If a patient presents with risk factors and signs and symptoms - Vitamin D deficiency should be considered. Vitamin D levels should be measured **ONLY** if patients are symptomatic **AND** have other risk factors unless clinically appropriate.

Risk factors for vitamin D deficiency include:

- Black & ethnic minority patients with darker skin
- Elderly patients in residential care, housebound or institutionalised patients
- Older people aged 65 years and over
- Infants and young children under 5 years of age
- Intestinal malabsorption e.g. coeliac disease, crohns disease, gastrectomy, cholestatic liver disease
- Routine covering of face or body e.g. habitual sunscreen use factor 15 or above
- Vegan/vegetarian diet
- Liver or renal disease
- Medications including certain anticonvulsants, cholestyramine, colestipol, liquid paraffin, sucralfate, rifampicin, glucocorticoids, highly active antiretrovirals
- Obesity (BMI >30)
- All pregnant and breast feeding women, especially teenagers and young women
- Short interval pregnancies
- Patients with persistently low calcium, low phosphate or raised Alkaline Phosphatase
- Low vitamin D dietary intake
- Cystic fibrosis
- If one family member is Vitamin D deficient it is likely others in the family may also be deficient, unless that person has a specific medical condition

AND

Signs/symptoms include:

- Young children or infants can present with bony deformity (rickets), irritability, reluctance to weight bear, impaired growth and even neonatal tetany
- Older children may present with lethargy and general aches & pains e.g. growing pains^{7,8}
- Adults often present with generalised musculoskeletal and or bone pain, muscle weakness and lethargy

Only test if both risk factors and symptoms are present or if clinically appropriate

Investigations:

If the patient has both risk factors and symptoms the following investigations should be carried out:

- Serum 25-hydroxyvitamin D (25(OH)D)
- Serum Calcium – to exclude hypercalcaemia and obtain baseline for monitoring. If low vitamin D confirmed and calcium result is raised or high-normal, check parathyroid hormone. Do not check parathyroid hormone routinely
- Alkaline Phosphatase and Phosphate
- Liver and renal function
- Full blood count (there may be coexisting anaemia if dietary factors are involved)

If there is a history of confirmed Vitamin D deficiency and anaemia ensure ongoing advice is provided to reduce associated risks.

Diagnosis and coding

NB If deficiency diagnosed use the Read code **.C28 Vitamin D deficiency** (for audit purposes)

All patients at risk of Vitamin D deficiency require ongoing lifestyle advice regarding sunlight exposure and diet. See Liverpool Patient leaflet for further information available at Map of Medicines <http://eng.mapofmedicine.com/evidence/map/index.html> or www.northmerseyammc.nhs.uk/

Table 2: Vitamin D treatment guidelines.

Exclude patients with hypercalcaemia or an eGFR <30mL/minute/1.73m². See Appendix 1

Patient Characteristics	Recommendations	Notes
<p>Deficiency in adults:</p> <p>≤30nmol/L Or <12ng/mL</p> <p>Deficiency: high dose treatment initially, then long term maintenance treatment required</p> <p>If deficiency is diagnosed in pregnancy please follow guidelines of your local maternity services provider</p>	<p>Most UK Guidelines suggest a loading dose of 300,000IU colecalciferol is required to replenish Vitamin D concentration. Various regimes can be considered to achieve this.</p> <p><i>Check Vitamin D concentration after 6 months to ensure adequate replacement and/or concordance.</i> <i>If >100nmol/L consider reducing dose.</i> <i>If still deficient alter dose as necessary.</i> <i>If sufficient no further monitoring recommended</i></p>	<p><u>Treatment Dose:</u> Due to compliance issues locally Liverpool are suggesting a loading dose is given by either:</p> <p>Colecalciferol 20,000IU orally ONE daily for 15 days</p> <p style="text-align: center;">OR</p> <p>Colecalciferol 20,000IU orally FIVE daily for 3 days</p> <p><u>Maintenance dose:</u> Colecalciferol 20,000 IU ONE orally once a month</p> <p><i>Prescribers can prescribe from a selection of available products to give a total dose as recommended above. See Appendix 2 for further prescribing and product information</i></p>

Alfacalcidol is not considered appropriate for community use in Vitamin D deficiency unless advised by specialists due to the risk of hypercalcaemia. See Appendix 3

Table 2: Vitamin D treatment guidelines.

Patient Characteristics	Recommendations	Notes
<p>Insufficiency in adults:</p> <p>>30 to 50nmol/L Or >12-20ng/mL</p> <p>Insufficiency: Maintenance treatment likely to be required</p>	<p>There is currently a lack of evidence on the functional outcomes of populations with insufficient vitamin D concentration to justify the treatment of all patients with insufficiency.</p> <p>Assess patient holistically Consider prescribing if symptomatic & at risk / previously deficient/ unlikely to take supplements / breast feeding or considering pregnancy / wintertime</p>	<p><u>Maintenance dose:</u></p> <ul style="list-style-type: none"> • Vitamin D equivalent to 800IU daily e.g. Vitamin D 400IU (10mcg) tablets. One tablet twice daily for life. • A range of Vitamin D tablets are available to buy from community pharmacies, health food stores or via prescription. (See Appendix 2) • Calcium and Vitamin D tablets e.g. Calcichew D3 Forte and Adcal D3 are licensed preparations available on prescription and can be considered for maintenance treatment <p>Or where compliance may be an issue</p> <ul style="list-style-type: none"> • Colecalciferol 20,000IU one capsule per month available via prescription
<p>Healthy or at risk adults</p> <p>>50-75nmol/L Or > 20ng/mL</p> <p>Symptom free</p>	<p>Lifestyle advice</p> <p>Can consider daily self treatment with over the counter purchased supplement of 400-800IU Vitamin D daily</p>	<p>Over the counter products contain amounts likely to prevent rickets/osteomalacia, but are unlikely to raise Vitamin D concentration to optimal in most people who are deficient.</p> <p>NB prevention may be needed in older people / housebound / in institution</p>
Patient Characteristics	Recommendations	Notes
<p>Prevention in children</p>	<p><i>COMA⁹ (Committee on Medical aspects of food) recommends:</i></p> <p>All infants except those taking at least 500ml of infant formula have a total of 280-340iu Vitamin D daily for the first four years of life.</p> <p>Fully breast fed infants: see prevention in pregnancy</p> <p>At risk children supplemented up to the age of five years. This can be achieved with Healthy Start vitamins.</p> <p>Alternatives are Abidec and Dalivit drops (Vitamin A, B group, C and D) for children -available to buy or through GP</p>	<p>Healthy Start Children's Vitamin drops (Vitamin A 5000units, Vitamin D 2000units and ascorbic acid 150mg/ml)</p> <p><u>Recommended dose:</u> Child 1 month – 5years: 5 drops daily (5 drops contain approximately 700units Vitamin A, 300units Vitamin D, 20mg Ascorbic Acid; BNF 62 page 627)</p> <p>Healthy Start vitamins are usually available with vouchers through Children's Centres and many Health Centres. Only Healthy Start beneficiaries can access vouchers. However Healthy Start may be universally available in some parts of the Mersey Cluster. See Appendix 4 for further information regarding this scheme or visit http://www.healthystart.nhs.uk/ or discuss with your health visitor / midwife</p>

Table 2: Vitamin D treatment guidelines.

Patient Characteristics	Recommendations	Notes
<p>Prevention in Pregnancy and Breastfeeding</p> <p>If deficiency is diagnosed in pregnancy please follow guidelines of local maternity services provider</p>	<p>COMA⁹ (Committee on Medical Aspects of food) recommends: All pregnant and lactating women have a total of 400iu Vitamin D/day</p> <p>Pregnant women suspected of being vitamin D deficient should have their Vitamin D concentration measured.</p> <p>NICE CG62 Antenatal care¹¹ suggests that up to 1000IU daily is considered the maximum safe dose.</p> <p>Ensure Vitamin D concentrations remain above 50nmol/L throughout the year</p> <p>A recent letter was sent to all healthcare professionals from the Chief Medical officer (3/2/12) offering advice on Vitamin D supplements further information can be found via http://www.nelm.nhs.uk/en/NeLM-Area/News/2012---February/16/Products-in-UK-that-enable-adherence-to-CMO-advice-on-Vitamin-D-supplementation/</p>	<p>All women should continue with Vitamin D supplementation throughout pregnancy and breastfeeding.</p> <p>All women diagnosed with Vitamin D deficiency should continue treatment/maintenance whilst breast feeding.</p> <p>If deficient check Vitamin D concentration at 6 months post delivery. Consider lifelong maintenance.</p> <p>Advise all women about Healthy Start vitamins preconception and during pregnancy¹⁰</p> <p>If ineligible for Healthy Start advise 10 micrograms Vitamin D (400IU) daily – purchased over the counter. Vitamin supplements such as Pregnacare are available over the counter.</p> <p>Siblings under five years old should have maintenance with Healthy Start Vitamins (or Abidec/Dalvit) see Appendix 4</p> <p>NB: Women at risk (Black Minority Ethnic (BME)/darker skin) will be tested routinely by Liverpool Women’s NHS Foundation Trust and treatment advised as necessary.</p>

For advice re prevention and treatment of Vitamin D disorders in Children please refer to separate Alder Hey Guidance

References:

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12. East & South east England Specialist Pharmacy services – Vitamin d deficiency and insufficiency November 2011
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Appendix 1 – Conditions outside the scope of this guidance

The following are outside the scope of this guidance. See condition related guidelines for further information. Referral to specialist may be appropriate.

- Renal disease*
- Osteoporosis **
- Secondary prevention post fractures
- Failure to respond to treatment after 3 months
- All children under 1 year
- Atypical biochemistry
- Atypical clinical manifestations or biochemistry
- Deficiency due to malabsorption
- Focal bone pain
- Liver disease
- Lymphoma
- Metastatic cancer
- Parathyroid disorders
- Renal stones
- Sarcoidosis
- Short stature and Skeletal deformity
- Tuberculosis
- Unexplained deficiency
- Unexplained weight loss

***Renal Disease – eGFR less than 30mL/minute/1.73m²**

NICE clinical guideline CG73 on chronic kidney disease, published in 2008, advises on which vitamin D preparations should be used and when, according to the stage of renal impairment.

NICE CG73 Chronic kidney disease. NICE Guideline. 2008. Available at <http://www.nice.org.uk/nicemedia/live/12069/42117/42117.pdf>

The information has been summarized in a NICE pathway see <http://pathways.nice.org.uk/pathways/chronic-kidney-disease>

**** Osteoporosis and Falls**

See NICE Technology Appraisals TA160 and TA161 for further information re Osteoporosis www.nice.org.uk

Local osteoporosis guideline currently in development – <http://www.northmerseyamc.nhs.uk/>

Alternatively refer to your local Medicines Management Team for further advice

Appendix 2 – Prescribing Guidance

There are numerous issues surrounding Vitamin D products and availability and the Department of Health are aware of the need for a licensed product and are in discussion with the Medicines and Healthcare products Regulatory Agency (MHRA) and pharmaceutical industry.

Although licensed products should be used where available in some circumstances unlicensed or special products may be suitable following appropriate consideration of the increased risks and substantial costs of such medicines.¹²

For further information please see

<http://www.nelm.nhs.uk/en/NeLM-Area/Other-Lib-Updates/Drug-Discontinuation-And-Shortage/Vitamin-D-product-availability/>

<http://www.nelm.nhs.uk/en/NeLM-Area/Other-Lib-Updates/Drug-Discontinuation-And-Shortage/Vitamin-D---Available--products-for-DOH-recommendations/>

Prescribing Options:

- **Pro D3 Colecalciferol 20,000IU capsules** - *This is not a licensed medicine as it is classed as a food/vitamin product.* Capsules and liquid are available in various strengths ranging from 400IU to 30,000IU. This product is suitable for patients with nut allergies is gelatin free, suitable for vegetarians and halal diets. The 20,000IU capsules are available at a set price of £19.99 per 30 capsules and are not classed as a 'special' so there should be no price variation. Pro-D3 is available directly from the manufacturer, AAH and Phoenix wholesalers so there should not be any supply problems in primary care. Please prescribe on acute prescriptions. A liquid preparation and other strengths of Vitamin D are also available. Further information can be found at <http://www.prod3.co.uk/> ***Nutritional supplements are generally subject to food safety labelling legislation and whilst this excludes them from a formal licensing process they may be considered a potentially useful option in some circumstances following consideration of the risks¹².***
- **Dekristol 20,000IU capsules** – *Unlicensed special import from EU (price variable) specify “order from IDIS, Martindale or Pharmarama” on the prescription. Prescribe on acute prescriptions. Pack size available 50capsules. This product is licensed in Germany and manufactured by MIBE pharmaceuticals*
NB Dekristol contains gelatin and is NOT suitable for nut allergies – for more information please see MHRA warning
<http://www.mhra.gov.uk/Publications/Safetywarnings/DrugAlerts/CON140797>
- **Fultium-D3 800IU capsules** - Newly licensed product available. Contains peanut oil. 25 x 800IU caps equivalent to 1x 20,000IU. Not recommended for use in under 12years. Manufacturers licensed dose:
 - Deficiency: 1-4caps daily (800-3200IU) for 12 weeks.
 - Insufficiency / Maintenance / Prevention: 1-2caps (800-1600IU) daily.
- **Ergocalciferol 300,000IU intra-muscular injection** - once or twice a year (variable availability)
- **Over the counter products** - Patients can be directed to purchase over the counter products. A dose of 800IU per day should be recommended for **maintenance and prevention regimes**. Brands of Vitamin D tablets include:
 - Solgar® (Vitamin D3 – Colecalciferol) vegetarian capsules available in various strengths (suitable for nut allergy sufferers),
 - Pro D3 products available in a range of strengths from 400IU (10mcg) to 30,000IU,
 - Boots and Holland & Barrett also offer a range of Vitamin D products.

Information correct as of 21st February 2012 – product availability and licensed indications change frequently, please contact your Medicines Management Team if you have any queries

Appendix 3 - Alfacalcidol

Alfacalcidol is not considered appropriate for community use in Vitamin D deficiency unless advised by Renal or Clinical Blood Sciences (Clinical Chemistry) Specialists due to risk of hypercalcaemia

A recent signal alert from the National Patient Safety Alerts (NPSA) highlights the risks associated with alfacalcidol prescribing

<http://www.nrls.npsa.nhs.uk/resources/?entryid45=132827>

Risks of hypercalcaemia

Alfacalcidol and excessive intake of products containing Vitamin D can lead to hypercalcaemia and its associated effects.

Symptoms of toxicity include:

- apathy
- anorexia
- constipation
- diarrhoea
- dry mouth
- fatigue
- headache
- nausea & vomiting
- thirst and weakness

Toxicity can lead to:

- calcification of soft tissues and bone pain,
- cardiac arrhythmias,
- hypertension,
- kidney damage (increased urinary frequency, decreased urinary concentration; nocturia, proteinuria),
- psychosis (rarely) and weight loss.

If toxicity is suspected, vitamin D must be withdrawn and serum calcium and renal function checked urgently, since emergency inpatient care with rehydration is usually indicated¹³

Patients receiving treatment with alfacalcidol should have plasma-calcium levels initially checked once or twice weekly as per product SPC when initiating treatment with alfacalcidol and whenever nausea and vomiting or other symptoms of toxicity occur during treatment. Once stabilised plasma calcium levels should be checked at intervals as per BNF 62.

Appendix 4 – Healthy Start Scheme

What is the Healthy Start Scheme?

The Healthy Start Scheme is a statutory scheme which started in 2006 and replaced the Welfare Food Scheme. The scheme aims to improve the health of pregnant women and families on benefits or low incomes. The scheme provides a nutritional safety net, encourages breastfeeding / healthy eating and is used as a public health tool.

How do you sign women / children up?

The application forms need to be signed by GPs, midwives, health visitors or other registered nurses. Health professionals are not required to check eligibility they just need to sign the application form. Any subsequent changes in personal circumstances must be reported by the beneficiary not the health professional.

The application forms (HS01) can be ordered via www.orderline.dh.gov.uk or by calling 0300 123 1002. The forms should be available in health and children centres.

N.B. Re-application for healthy start vitamins is required following the birth of child.

What are the beneficiaries entitled to?

Beneficiaries are sent vouchers that can be exchanged for cow's milk, fresh / frozen fruit, vegetables and infant formula.

Beneficiaries are also sent vitamin coupons which can be exchanged for vitamin supplements for pregnant women, new mothers and children up to 4 years. Women's tablets contain Vitamin C, D and folic acid and Children's drops contain Vitamin A, C and D.

N.B. Healthy Start Vitamins may be universally available in some parts of the Mersey Cluster

Further information - www.healthystart.nhs.uk