Vitamin D Prescribing for Children – supplementary

Coventry & Warwickshire
Area Prescribing Committee

Resource Document

The APC approves this document as appropriate for use within the health economy by those clinicians, or group of clinicians, that choose to. This resource has not received the extensive scrutiny required for it to be designated as an APC clinical guideline.

Children with vitamin D levels indicative of deficiency or insufficiency should be referred to a specialist, particularly if there are serious concerns about bone growth and development (e.g. suspicion of Rickets) or if there is evidence of atypical physiology or simply if the primary care physician decides the best interests of the child are best served by a referral. Provision of lifestyle advice, dietary information and occasionally, prescription or purchase of low dose maintenance Vitamin D therapy can be performed in primary care.

This document has been produced for the use of the Medicines Management Team and/or physicians in primary care as a source of evaluated information to use in the management of cases, where simple supplementation is considered sufficient for the *prevention* of vitamin D insufficiency or deficiency in a child. **Information on the *management* of vitamin D insufficiency and deficiency in children is also included here for completeness but it is expected that physicians will refer these cases.**

Preventing Bone Disease in Children - National Guidance

- National Guidance suggests that all children aged 6 months to 5 years should take a daily supplement containing vitamin D in the form of vitamin drops, to help them meet the requirement set for this age group of 280–340 units (7-8.5 micrograms) per day.(1,2)

- Infants who are fed infant formula will not need vitamin D supplements unless they are receiving less than 500ml of infant formula a day, as these formulas are fortified with vitamin D. Breastfed infants may need supplements containing vitamin D from one month of age if their mother may be deficient in vitamin D and has not taken vitamin D supplements throughout pregnancy.(1,2)

- Clinical evidence, which is weak in this area, is largely based on consensus and is used here to inform practice. (3) The following, based on the Royal College of Paediatrics and Child Health recommendations, as well as product literature, represents the local consensus and suggests doses of vitamin D for all children aged from birth to 18 years, to prevent bone disease. (1-4)

- Since the latest RCPCH guidelines were written in 2013, there are several new licensed products marketed in the UK for the treatment and prevention of vitamin D deficiency related bone disease in children. We have mentioned only licensed products (and licensed dosing regimens) in this guidance document (see Table 1 and Table 2), omitting nutritional supplements and unlicensed products. Some of these licensed products offer alternative dosing regimens that may be given less frequently but achieve similar cumulative doses of vitamin D as the daily regimens suggested by the 2013 RCPCH guidelines. We have tried to point out where such differences exist and have included a range of licensed product and dose options in order to provide choice. GP's can decide which regimen to use based on several factors; cost-effectiveness, likelihood of compliance, the child's/parent preference and product suitability.

Preventing Vitamin D deficiency related bone disease in Children - National Guidance

- The Royal College of Paediatrics and Child Health (RCPCH) guidelines recommend the following regimens for preventing vitamin D deficiency related bone disease in children.

    - New born to 1 month: 300 - 400 units daily
    - 1 month to 18 years old: 400 – 1000 units daily

Treating Vitamin D deficiency related bone disease in Children - National Guidance

- The Royal College of Paediatrics and Child Health (RCPCH) guidelines recommend the following regimens for treating vitamin D deficiency related bone disease in children.

    - Up to 6 months old: 1000-3000 units/daily for 4-8 weeks
    - 6 months to 12 years old: 6000 units/daily for 4-8 weeks
    - 12 years to 18 years old: 10,000 units daily for 4-8 weeks

TABLE 1 Standard prevention / supplementation / maintenance with Vitamin D for children (1-4)		
Age group	**Dosing regimens**	**Suggested products and dose range** (for more on products see Appendix)
Formula fed infants >500ml formula/day	Not needed	Infant formulas are fortified with vitamin D
Newborn babies to infants aged to 1 month (including breast fed infants or infants taking <500ml formula/day)	RCPCH recommends 300 - 400 units daily	**Fultium D3 oral drops** (3-6 drops = 200-400 units)* (Licensed) **InVita D3 oral drops** (3-6 drops = 200-400 units)* (Licensed) **THORENS oral drops** (1-2 drop = 200-400 units)* (Licensed) **Healthy Start Vitamins** if eligible (5 drops=300 units)* (Licensed) **Abidec and Dalivit drops are not for GP's to prescribe but may be purchased over the counter**
Newborn babies to infants aged to 1 year (including breast fed infants or infants taking <500ml formula/day)	Alternative regimen: 25,000 units every 8 weeks	**InVita D3 oral solution** (1 ampoule for oral use [25,000 units]) (Licensed) **THORENS oral solution** (1 x 2.5mL bottle for oral use [25,000 units]) (Licensed)
Infants and Children aged from 1month to 11 years (including breast fed infants or infants taking <500ml formula/day)	RCPCH recommends 400 units-1,000units daily	**Fultium D3 oral drops** (6-15 drops= 400-1000 units)* (Licensed) **InVita D3 oral drops** (6-9 drops = 400-600 units)* (Licensed) **THORENS oral drops** (2-5 drops = 400-1000 units)* (Licensed) **Healthy Start Vitamins** if eligible up to 4 years (5 drops=300 units)* (Licensed) **Abidec and Dalivit drops are not for GP's to prescribe but may be purchased over the counter.**
Infants and Children aged from 1 to 11 years	Alternative regimen: 25,000 units once every 6 weeks	**InVita D3 oral solution** (1 ampoule for oral use [25,000 units]) (Licensed) **THORENS oral solution** (1 x 2.5mL bottle for oral use [25,000 units]) (Licensed)
Children† aged from 12 to 18years	RCPCH recommends 400 units-1,000units daily	**Fultium D3 capsules** (One capsule = 800 units) (Licensed) **InVita D3 oral drops** (9 drops = 600 units) (Licensed) **THORENS oral drops** (3-5 drops = 600-1000 units)* (Licensed)
	Alternative regimen: 20,000 to 25,000 units every 6 weeks	**Aviticol capsules** (One capsule =20,000 units) (Licensed) **Fultium D3 capsules** (One capsule =20,000 units) (Licensed)

Notes

** Licensed doses may vary slightly from RCPCH recommendations but are broadly consistent overall. Check SPC's to check age appropriate dose.*

† In children with risk factors but no symptoms, consider supplementation in winter only.

Note the InVita D3 oral solution is a different product to InVita D3 oral drops.

Likewise THORENS oral solution is a different product to THORENS oral drops.

Whilst Coventry & Rugby CCG does not endorse any particular commercial product, licensed products are preferred and prescribers should try to use these where possible. The options above are examples of products which could be used to meet the suggested dosing regimens. Please note, however, that the options listed are not exhaustive and that other products (e.g. nutritional supplements) may be available to buy and these might be appropriate in some cases where children will not comply with the options listed above. **Also please see** Disclaimer

Correcting vitamin D deficiency and preventing bone disease in children

What levels of vitamin D are considered a deficiency in children?

The Royal College of Paediatrics and Child Health (2) suggest that vitamin D deficiency in the paediatric population is defined as:

≤ 25nmol/L= vitamin D deficiency

25 to 50nmol/L = insufficiency

≥ 50-75nmol/L= sufficient levels of Vitamin D (though 'sufficient levels' are not well defined)

Why does vitamin D deficiency in infants and children need correcting? What is the evidence to support correction of deficiency?

- These values are based on robust evidence of benefit to bone health when levels are more than 50nmol/L. Vitamin D deficiency can cause seizures and cardiomyopathy in infants, rickets and it could lead to poor growth in children.(1-5)

Which children should have their vitamin D levels tested? (1-6)

- There is no clear consensus on which children should be tested for vitamin D deficiency. Generally, if children display symptoms and signs of deficiency **and** if they are in at-risk groups, testing may be considered. If children have no risk factors, then offer lifestyle advice and advise doses of vitamin D for prevention of deficiency.
- **Signs and symptoms** include; seizures, tetany and cardiomyopathy in infants; aches and pains, myopathy causing delayed walking, rickets with bowed legs, knock knees, poor linear growth and muscle weakness in children and; aches and pains, muscle weakness, bone changes of rickets or osteomalacia in adolescents.
- **Risk factors** for Vitamin D deficiency include living at northern latitude in an area of air pollution, wearing occlusive garments, having pigmented skin, malabsorption disorders, habitual sunscreen use or being institutionalised or housebound, vegetarian or breast fed.

If children are tested, and they are found to be vitamin D deficient, how should this be managed? (1-6)

- Lifestyle advice on obtaining vitamin D via sunlight and diet should be provided to parents and children as the first line intervention.
- Therapeutic intervention should be considered using doses below which are recommended by the Royal College of Paediatrics and Child Health,(2) the BNF for children (4) or product information for the licensed products. (7,8)

TABLE 2 Standard Treatment/Corrective doses (1-4)

Age group	Dose, frequency & duration	Products (for more on products see Appendix)
Babies and Infants <6 months	RCPCH recommends 1,000 units - 3,000 units daily for 4-8 weeks#	**Fultium D3 oral drops** (6-15 drops= 400-1000 units)* (Licensed) * *Doses of 6-15 drops/day (400-1000 units) licensed for treatment in this age group. Use of higher doses using this product would be off-label use.* **THORENS oral drops** (10 drops = 2000 units)*. (Licensed) * *Doses of 10 drops/day (2000 units) for 6 weeks licensed for treatment. Use for >6 weeks of this product would be off-label for infants aged <6 months.*
	Alternative regimen: 25000 units once every 2 weeks for 6 weeks #	**InVita D3 oral solution** (1 x 1ml ampoules of 25,000 units). (Licensed) This can be mixed with a small amount of children's foods (e.g. yoghurt, milk, cheese).(7) **THORENS oral solution** (1 x 2.5mL bottle for oral use [25,000 units]) (Licensed)
Infants & Children 6 months - 12 years	RCPCH recommends 6,000 units daily for 4-8 weeks #	**Fultium D3 oral drops** (6-30 drops= 400-2000 units)* (Licensed) * *Doses of 6-30 drops/day (400-2000 units) licensed for treatment. Higher doses (>30drops/day) using this product would be impractical and off-label for infants aged <12 years* **THORENS oral drops** (10 drops = 2000 units)*. (Licensed) * *Doses of 10 drops/day (2000 units) for 6 weeks licensed for treatment. Higher doses (>10drops/day for >6 weeks) of this product would be off-label for infants aged <12 years.*
	Alternative regimen: 25,000 units once every 2 weeks for 6 weeks#	**InVita D3 oral solution** (1 x 1ml ampoules of 25,000 units). (Licensed) This can be mixed with a small amount of children's foods (e.g. yoghurt, milk, cheese).(7) **THORENS oral solution** (1 x 2.5mL bottle for oral use [25,000 units]) (Licensed)
Children 12 to 18 years	RCPCH recommends 10,000 units daily for 4-8 weeks# but licensed treatment doses for this age group are often different (lower).	**Fultium D3 oral drops** (6-60 drops= 400-4000 units)* (Licensed) * *Licensed dose but using higher doses of this product would be impractical.* Or **THORENS oral drops** (10 drops = 2000 units)* for 6 weeks . (Licensed) * *Doses of 10 drops/day (2000 units) for 6 weeks licensed for treatment. Higher doses (>10drops/day for >6 weeks) of this product would be off-label.*
	Alternative regimen: 20 to 25,000 units once every 2 weeks for 6 weeks#	**Aviticol capsules** (One capsule =20,000 units) (Licensed) **Fultium D3 capsules** (One capsule =20,000 units) (Licensed) Or **InVita D3 oral solution** (1 x 1ml ampoules of 25,000 units). (Licensed) This can be mixed with a small amount of children's foods (e.g. yoghurt, milk, cheese).(7) **THORENS oral solution** (1 x 2.5mL bottle for oral use [25,000 units]) (Licensed)

Notes

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Note the InVita D3 oral solution is a different product to InVita D3 oral drops.

Likewise THORENS oral solution is a different product to THORENS oral drops.

Whilst Coventry & Rugby CCG does not endorse any particular commercial product, licensed products are preferred and prescribers should try to use these where possible. The options above are examples of products which could be used to meet the suggested dosing regimens. Please note, however, that the options listed are not exhaustive and that other products (e.g. nutritional supplements) may be available to buy and these might be appropriate in some cases where children will not comply with the options listed above. Also please see Disclaimer

Should patients be given 'maintenance therapy' with vitamin D after completing a treatment/ corrective regimen? Yes, maintenance regimens should be given following treatment or correction and should be given in conjunction with advice on implementing lifestyle changes. These should continue until lifestyle changes can be assured to achieve adequate vitamin D levels or until the child has stopped growing. Maintenance regimens are the same as regimens for prevention (refer to Table1). (1-4)

When should vitamin D levels be checked again in children? Should any other parameters be monitored? At baseline, the following investigations should be carried out; renal function, calcium, phosphate, magnesium, parathyroid hormone level, alkaline phosphatase and 25-OH Vitamin D levels. Compliance should be assessed and encouraged. Weekly or even monthly dosing has been suggested to support this. (3,7,8) After treatment, to prevent relapse there is no need for routine Vitamin D re-testing, except for those under age 6 months. If re-testing vitamin D levels, note that they take 3-6 months to achieve steady state levels. (3) Calcium should be re-checked for all babies, infants and children being treated after 1 month of treatment.

What about calcium, does this need to be prescribed too? It is essential to check the child has a sufficient dietary **calcium** intake. The recommended intakes for children for optimal bone health according to the Institute of Medicine (IOM) are (9)

- 1 to 3 years old — 700 milligrams of calcium daily (=17.5mmol)
- 4 to 8 years old — 1000 milligrams (25mmol)
- 9 to 18 years old — 1,300 milligrams (32.5mmol)

The BNF for children also has a useful section on calcium supplementation and management of deficiency in children. (4) It is important that a dietician is involved in assessing calcium intake and suggesting the amount to supplement. Tools used to do this in adults include websites such as http://www.cgem.ed.ac.uk/research/rheumatological/calcium-calculator.

If vitamin D deficiency is tested for and confirmed in a child, it is often better, and more cost effective, to prescribe a pure Vitamin D product as above and to optimise calcium levels using dietary measures. Where this is not possible, calcium supplements (+/- vitamin D) may be considered, though if vitamin D deficiency exists, combined products do not contain enough vitamin D and over the counter products usually don't contain enough vitamin D or calcium. Therefore do NOT prescribe combination calcium and vitamin D products in children. Multivitamin products should also be used with caution since they usually offer a low dose of vitamin D relative to other vitamins, such as vitamin A which can cause toxicity if too much is ingested. (4) If calcium is required alone or in addition to vitamin D in a child, consider contacting a member of the Medicines Management team for case specific advice.

Lifestyle Advice (1-5)

Sunlight

The amount of exposure to sunlight required depends very much on the skin type. Fair skin requires less time than pigmented skin. For all skin types, exposure time should be **less** than is required to cause reddening. For example exposure of face, arms and legs for 15-20mins daily (longer if dark pigmented skin) would provide a good source of Vitamin D. In the UK April to September between 11am and 3pm will provide the best source of UVB. Application of sunscreen will reduce the Vitamin D synthesis by >95%. Advise to avoid sunscreen for the first 15-20 minutes of sunlight exposure. Persons wearing traditional black clothing can be advised to have sunlight exposure of face, arms and legs in the privacy of their garden.

Diet

Diet is a poor source of Vitamin D compared to sunlight. Vitamin D can be obtained from dietary sources (e.g. salmon, mackerel, tuna, egg yolk), fortified foods (e.g. fortified cow, soya, oat or rice milk and dairy products), and supplements. There are no plant sources that provide a significant amount of vitamin D naturally. Consider dietary supplementation especially during the winter months.

Family members might also be at risk if they have similar diet and lifestyles.

References

1. Vitamin D - advice on supplements for at risk groups. Ref: CEM/CMO/2012/04. Gateway ref: 17193. Welsh Government, Department of Health, Social Services and Public Safety. The Scottish Government and Department of Health.
2. Royal College of Paediatrics and Child Health, Vitamin D in Childhood. October 2013. Available at http://www.rcpch.ac.uk/system/files/protected/page/vitdguidancedraftspreads%20FINAL%20for%20website.pdf <Accessed 16.1.15>
3. Dr Benjamin Jacobs, Consultant Paediatrician Royal National Orthopaedic Hospital London. Vitamin D in children: Frequently asked questions about Vitamin D in childhood, June 2013. Available at http://www.rnoh.nhs.uk/clinical-services/paediatric-adolescents/vitamin-d-children <Accessed 16.11.15>
4. Paediatric Formulary Committee. BNF for Children (online) London: BMJ Group, Pharmaceutical Press, and RCPCH Publications via www.medicinescomplete.com <Accessed 16.11.15>
5. The National Osteoporosis Society. Vitamin D and Bone Health: A practical clinical guideline for patient management. April 2013. Available at http://www.nos.org.uk/document.doc?id=1352 <Accessed 16.11.15>
6. East & South East England Specialist Pharmacy Services, East of England, London, South Central & South East Coast. Vitamin D deficiency and insufficiency: Using appropriate available products. August 2014. Available via www.evidence.nhs.uk <Accessed 16.11.15> OUT OF DATE – new licensed products launched since Aug 14.
7. Consilient Health, Summary of Product Characteristics (InVita D3 25,000 IU oral solution), Last Updated on eMC 24-Jun-2014. Available from www.medicines.org.uk <Accessed 01.09.2014>
8. Dietary Reference Intakes for Calcium and Vitamin D. Institute of Medicine (IOM) Revised March 2011. Available via www.iom.edu <Accessed 16.11.15>
9. UKMI Q&A 387.2. 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 March 2013, updated, Available via www.evidence.nhs.uk <Accessed 16.11.15>

Practical information on licensed products mentioned in this guidance (10)

Product	Suitable for Vegetarians?	Suitable for Vegans?	Information to help support patients on Halal/Kosher diets. See **Disclaimer**	Suitable for patients with peanut/ soy allergies?	Costs (List price)
DROPS					
Healthy Start drops 300iu/5 drops (Licensed)	Yes	Colecalciferol is derived from sheep's wool fat	Does not contain any animal products or alcohol. Halal certified.	Yes	Free to low income families £2.31 (10ml, 280 drops)
Fultium D3 drops (66.7iu/drop = 200iu/ 3 drops) (Licensed)	Yes	Colecalciferol is derived from sheep's wool fat	Does not contain any animal products or alcohol. Not certified.	Yes – made with palm kernel and coconut oil	£10.70 (25ml, 1025 drops)
InVita D3 drops (67iu/drop = 200iu/3 drops) (Licensed)	Yes	Colecalciferol is derived from lanolin in live sheep's wool fat.	Does not use any ingredients from slaughtered animals. Does not contain pork gelatine. Not certified.	No issues; olive oil based.	£3.60 (10ml, 360 drops)
THORENS drops (200iu/drop) (Licensed)	Yes	No	Manufacturer states it is certified as suitable for halal/kosher diets – contact manufacturer for detail.	No issues; refined olive oil based. Trace amounts of peanut oil may be present although efforts are made to exclude this.	£5.85 (10ml, 500 drops)
Abidec drops (Licensed) 400iu/0.6ml *(BLACKLISTED – for purchase only)*	Yes	Yes	Does not contain any animal products or alcohol. Not certified.	No. Contains refined peanut oil. Does not contain soy but cross-reactivity possible.	£3.33 (25ml) – *BLACKLISTED – for purchase only)*
Dalivit drops (Licensed) 400iu/0.6ml *(BLACKLISTED – for purchase only)*	Yes	Yes	Does not contain any animal products or alcohol. No detail on certification.	Yes. Does not contain peanut or soy derivatives.	£3.32 (25ml) £6.65 (50ml) *BLACKLISTED – for purchase only)*
Abidec and Dalivit are multivitamins and, as well as vitamin D as ergocalciferol 400 iu, they also contain vitamin A, vitamin B (as thiamine hydrochloride, riboflavine, pyridoxine hydrochloride and nicotinamide and vitamin C ascorbic acid. Maximum licensed doses must not be exceeded in order to avoid hypervitaminosis. They are BLACKLISTED for prescription in Coventry and Rugby and are for purchase only. **Healthy Start drops** are also multivitamin drops and they contain 300iu of vitamin D as well as some vitamin C and vitamin A. They can only be accessed by some families under the Healthy Start Scheme. For more information, see https://www.healthystart.nhs.uk/for-health-professionals/vitamins/					
High strength ampoules/bottles for single doses (for oral use).					
InVita D3 (Licensed) 25,000 iu/ml x 1 ml ampoule	Yes	Colecalciferol is derived from lanolin in live sheep's wool fat.	Does not use any ingredients from slaughtered animals. Does not contain pork gelatine. Not certified as halal /kosher.	No issues; olive oil based.	£4.45 (3x1ml doses)
THORENS (Licensed) 25,000 iu/2.5ml x 2.5 ml bottle	Yes	No	Manufacturer states it is certified as suitable for halal/kosher diets – contact for more detail.	No issues; refined olive oil based. Trace amounts of peanut oil may be present although efforts are made to exclude this.	£5.85 (4 x 2.5ml doses)

Oral Capsules					
Aviticol capsules 20,000 units/cap (Licensed)	No – contains bovine and pork gelatine	No – contains bovine and pork gelatine	No – contains bovine and pork gelatine	Does not contain peanut or soya protein.	£29.00 for 30 capsules
Fultium D3 capsules 20,000 units/cap (Licensed)	No – contains gelatine	No – contains gelatine	Contains beef gelatine. Halal/ kosher certification available on request from manufacturer.	No information	£17.04 for 15 capsules £29.00 for 30 capsules
Fultium D3 capsules 800 units/caps (Licensed)	No – contains gelatine	No – contains gelatine		No information	£3.60 for 30 capsules

Patients and their parents may want to know if certain products are suitable for vegetarian, vegan, halal or kosher diets or if the patient has allergies to peanut or soybean oil. See disclaimer below regarding this. The information above was collected from manufacturers in November 2015. However, manufacturers regularly change the contents of their products so it is prudent to check the currency of the information.

Disclaimer: *Statements made by manufacturers regarding the terms 'halal' or 'kosher' certification or suitability are subject to interpretation. Individuals' religious belief systems are known to vary considerably and the authors of this guideline cannot broadly advise on the religious acceptability of products. To support patients and healthcare professionals in selecting an acceptable product, manufacturers contact details can be supplied so that the individuals are able to find out whether the products comply with their own belief systems.*