

## **1. Introduction**

This guideline is intended for use by all prescribing members of the Adult Cystic Fibrosis (CF) multidisciplinary team (MDT) to optimise fat soluble vitamin supplementation.

## **2. Scope**

People with cystic fibrosis, particularly those with pancreatic insufficiency, are at risk of fat soluble vitamin deficiencies. A significant correlation between vitamin A and E deficiency and pancreatic insufficiency has been reported at the time of diagnosis however no correlation is reported between pancreatic status and vitamin D deficiency.

Most people with CF who are pancreatic insufficient will require supplementation with the fat soluble vitamins A,D, E and K.

Most people with CF who are pancreatic sufficient require supplementation with vitamin D and some may require additional vitamin A, vitamin E and/or vitamin K.

- Vitamin A has an important role in the eye, skin, respiratory and immune systems.
- Vitamin D is fundamental for calcium absorption from the gut and subsequently important for bone health. Without adequate vitamin D, only 15-20% of dietary calcium and 60% of phosphorus are absorbed - when Vitamin D replete 30-50% of calcium is absorbed (Holick et al, 2011). In addition to bone health, there is increasing recognition and interest in the non-skeletal roles of vitamin D in respiratory function, muscle function, diabetes and cardiovascular disease.
- Vitamin E is an important antioxidant. It reduces the effects of free radicals produced by infection and chronic inflammation, therefore helping to protect cell membranes from oxidative damage.
- Vitamin K is vital for normal blood coagulation and important for good bone health. Interest has been shown, more recently, in its role in energy metabolism and inflammation which may be of importance in CF.

This guideline includes: the recommended levels for each fat soluble vitamin; recommended maintenance supplementation doses; how to escalate doses if serum levels are low; and when to refer for discussion with the CF MDT.

## **3. Recommendations, Standards and Procedural Statements**

### **3.1 Assessment**

Vitamin A, D and E, along with eGFR, C Reactive Protein (CRP), adjusted calcium, alkaline phosphatase and phosphorus are checked routinely for each patient once a year at their annual review and following treatment adjustments.

Consider measuring PTH if deemed to be at risk of Cystic Fibrosis bone disease (e.g. previously identified bone disease or chronically low vitamin D, low phosphate, low body weight).

Acute phase response to infection (indicated by a raised CRP or an acute exacerbation of CF) can lead to falsely low vitamin A and vitamin D levels. If CRP is raised at the time of checking vitamin levels, recheck when CRP has normalised before commencing additional supplementation.

If the level reported for each fat soluble vitamin is lower than the recommended range, check the following and if additional supplementation is still required follow section 2.4

1. Check adherence to maintenance vitamin preparation(s) the patient is prescribed and confirm the strength and the number of tablets / capsules
2. Check for any over the counter (OTC) preparations or supplements
3. Check the fat soluble vitamins are taken with fat containing food to maximise absorption
4. If pancreatic insufficient, check fat soluble vitamins are taken alongside pancreatic enzymes to maximise absorption

### **3.2 Recommended Levels**

	Recommended level	Adult recommended daily dosage
Vitamin A (if >19yrs)	1.1 – 2.8 µmol/L	1500 – 10,000 international units
Vitamin A (13 – 19yrs)	0.9 - 2.5 µmol/L	1500 – 10,000 international units
Vitamin D*	>50 nmol/L*	400 – 5000 international units (10 - 125 micrograms)
Vitamin E (if >19yrs)	12 – 42 µmol/L	150 – 500 international units
Vitamin E (13 – 19 yrs)	14 – 23 µmol/L	150 – 500 international units
Vitamin K	Not routinely monitored	5 – 10mg

\*Risk of toxicity increased when serum colecalciferol concentrations exceed 220 nmol/L

### **3.3 Vitamin Preparations**

Daily Maintenance Vitamins:

Pancreatic insufficient

Preparation	Dose	Constituents	Comments
1 <sup>st</sup> line:			
Paravit CF Capsules	2 capsules once a day	Per 2 capsule dose: vitamin A 8,000 units vitamin D 3000 units, vitamin E 300 units, vitamin K 10mg	



For patients who may be at risk of exceeding 10,000 units of vitamin A per day, e.g. through diet or additional supplementation, consider switching to DEKAs Essential capsules.

Most of the vitamin A in DEKAs is given as  $\beta$ -carotene, which is a precursor to vitamin A and is converted by the body to vitamin A as needed. Therefore, there is no risk of hypervitaminosis A.

**Renal Impairment**

If eGFR less than 30mls/min/1.73m<sup>2</sup> discuss with MDT

**Raised CRP**

If CRP level is raised at the time of checking vitamin D wait three months or until CRP is normal and check level again. A raised CRP can lead to a falsely low vitamin D. If both CRP and PTH level are raised this would indicate vitamin D deficiency and supplementation required.

**3.4 Dose Adjustment if Vitamin Levels Lower than Recommended Range:**

Refer to 3.1 before adjusting vitamin therapy

	Dose Adjustment	Monitoring
Vitamin A <1.1 $\mu$ mol/L	If taking full dose Paravit CF, discuss with CF MDT  Check CRP, zinc and retinol binding protein	After adjusting supplementation, repeat levels at 3 months
	If taking vitamin A and D, increase up to 3 capsules once a day. If remains low, discuss with CF MDT  Check CRP, zinc level and retinol binding protein	
Vitamin E <12 $\mu$ mol/L if >19 years <14 $\mu$ mol/L if 13 – 19 years	If taking full dose Paravit CF, discuss with CF MDT	After adjusting supplementation, repeat levels at 3 months
	If taking vitamin E, increase up to 500 units daily. If remains low, discuss with CF MDT	
Vitamin D <50nmol/l	Supplement with a ‘booster’ of 300,000 units of Vitamin D3 orally in divided doses over 5-10 weeks alongside maintenance dose e.g.	Follow monitoring algorithm - Appendix A

	60,000 units per week for 5 weeks 20,000 units twice a week for 7 weeks  On completion of booster dose, continue maintenance treatment	
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### **3.5 Dose Adjustment if Vitamin Levels Higher than Recommended Range**

- Check for OTC supplements
- Check for other nutritional preparations
- Refer to CF MDT for discussion

### **4. Education and Training**

None

### **5. Monitoring and Audit Criteria**

All guidelines should include key performance indicators or audit criteria for auditing compliance, if this template is being used for associated documents (such as procedures or processes) that support a Policy then this section is not required as all audit and monitoring arrangements will be documented in section 8 of the Policy.

Key Performance Indicator	Method of Assessment	Frequency	Lead
Appropriate prescribing of fat soluble vitamins in adult patients with CF	Audit prescribing practice within CF MDT	Bi-annually	Pharmacist and Dietitian

### **6. Supporting Documents and Key References**

Guidelines for Use of Pancreatic Enzyme Replacement Therapy Trust ref: B10/2019

Nutritional Management of Cystic Fibrosis, Cystic Fibrosis Trust, Second Edition Sept 2016

Nutrition guidelines for Cystic Fibrosis in Australia and Newzeland, August 2017

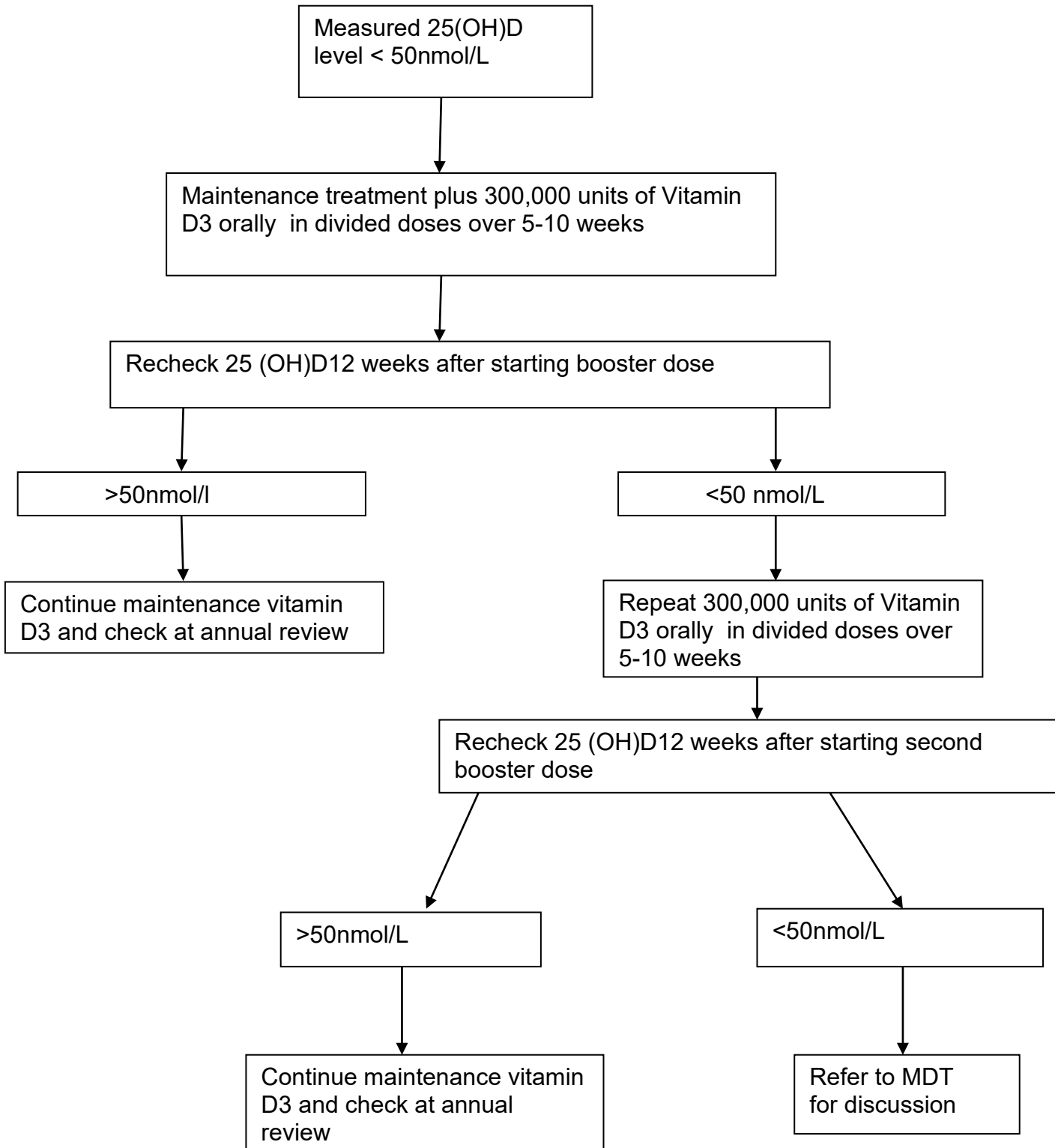
Holick, MF, Binkley, NC, Bischoff-Ferrari, HA, Gordon, CM, Hanley, DA, Heaney, RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 96, 1911-1930 (2011).

### **7. Key Words**

Cystic Fibrosis, fat soluble vitamins, vitamin A, vitamin D, vitamin E, vitamin K

**Oral Vitamin D supplementation guide if 25(OH)D level <50nmol/L for pancreatic insufficient cystic fibrosis adult patients**

Before escalating treatment of vitamin D deficiency, check adherence to current supplementation/Pancreatic Enzyme Replacement Therapy (PERT) and at every dose adjustment



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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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