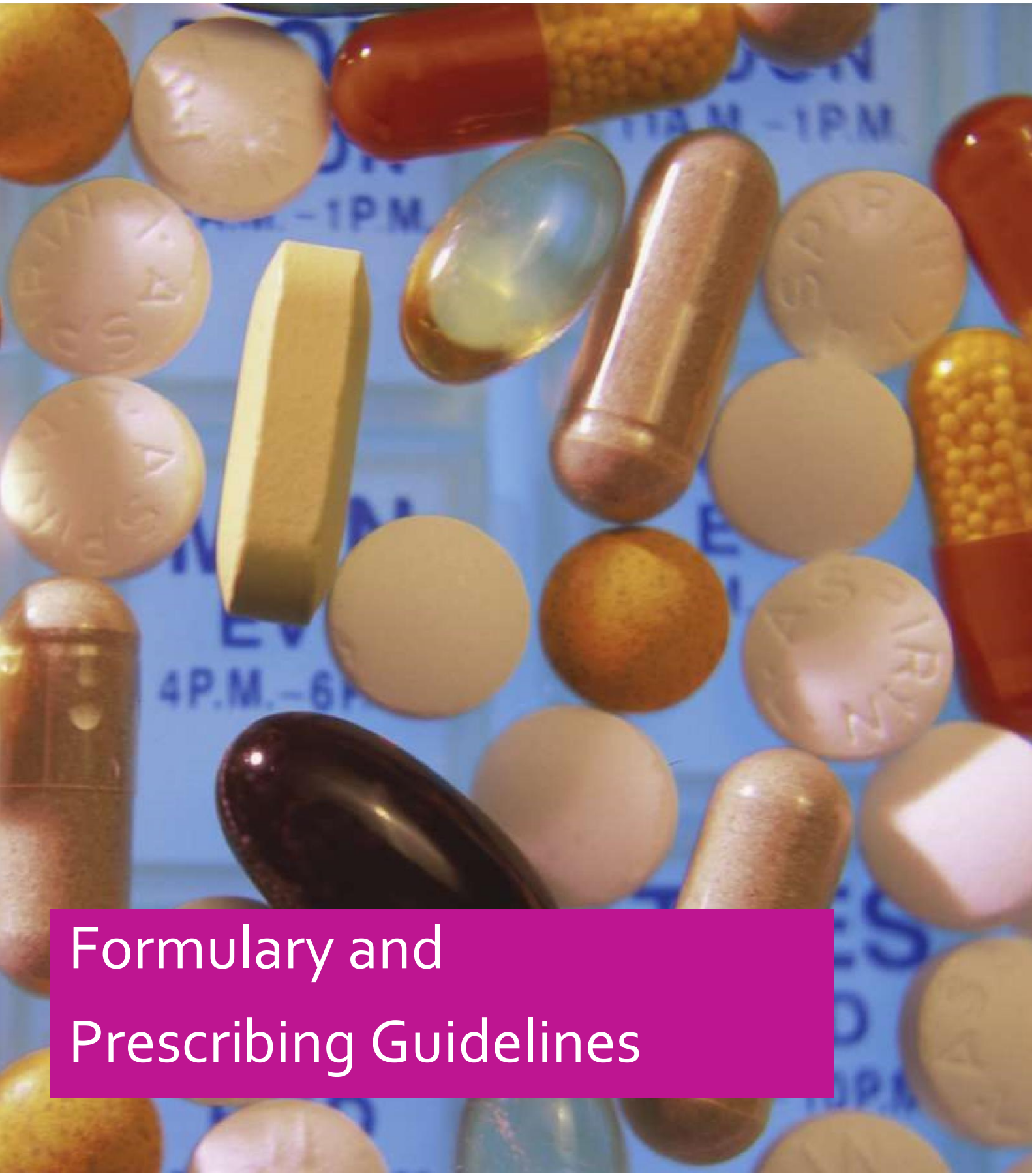
Essex Partnership University
NHS Foundation Trust

SECTION 23: MANAGEMENT OF VITAMIN D DEFICIENCY AND THE USE OF VITAMIN D SUPPLEMENTS



Formulary and Prescribing Guidelines

23.1 INTRODUCTION

Vitamin D is a fat-soluble vitamin that regulates calcium and phosphate homeostasis and is therefore vital for musculoskeletal health. In addition, with less robust evidence, it arguably plays a role in non-skeletal disorders, including autoimmune disease, cancer, mental health problems and cardiovascular disease.
Vitamin D circulates in the blood as both vitamin D_3 (colecalciferol) and vitamin D_2 (ergocalciferol). Measurement of plasma 25-hydroxyvitamin D (25-OHD) is the best way of estimating vitamin D status in patients.

Recommended vitamin D thresholds in the UK in respect to bone health are:

- Vitamin D **deficiency** occurs at plasma 25-OHD levels **less than 25 nmol/L**.
- Vitamin D levels may be **inadequate (or insufficient)** if plasma 25-OHD is **25–50 nmol/L**.
- Vitamin D levels are **sufficient** when plasma 25-OHD is **greater than 50 nmol/L**.

In the UK, 80–90% of vitamin D is derived from skin exposure to ultraviolet B radiation from sunlight, with the remaining 10–20% being derived from dietary sources. People that are at increased risk of developing vitamin D deficiency include those:

- Aged 65 years and over.
- Who have limited exposure to the sun, for example those who cover their skin; who are housebound or confined indoors for long periods.
- Who have darker skin pigmentation
- With a malabsorption disorder, or following weight loss surgery.
- With severe liver or end-stage chronic kidney disease.
- Taking certain drugs that increase the risk of vitamin D deficiency e.g. antiepileptics, glucocorticoids.
- Who are pregnant or breastfeeding.
- With obesity.

Complications of vitamin D deficiency include increased risk of:

- Osteomalacia, which may present with lower back pain, bone pain in the shoulder, ribs, pelvis, or legs; muscle pain and weakness; waddling gait; and impaired physical function
- Osteoporosis
- Falls and fragility fracture.

This document should be read in conjunction with the following documents:

- *Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management*, by the Royal Osteoporosis Society (ROS)
- *Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management in Children and Young People*, by ROS

The document offers pharmacological context, and a good overview of existing evidence and study limitations.

- The NICE/CKS guidance on *Vitamin D deficiency in adults* and *Vitamin D deficiency in children* refer to the ROS guidelines above and can be consulted, if required.

And depending on the location of practice within the Trust, the following documents from primary care offer helpful clinical algorithms, further support for clinical decision making, and useful (prescribing) information on available vitamin D products.

- The *West Essex CCG Clinical Guidelines and Prescribing Formulary on Vitamin D deficiency management*
- The *Mid and South Essex Health Care Partnership Vitamin D Deficiency Prescribing Guidance*.

23.2 MANAGEMENT OF VITAMIN D DEFICIENCY

Treatment is recommended for vitamin D deficiency (plasma 25-OHD levels **less than 25 nmol/L**)

For **inadequate (or insufficient)** vitamin D levels (plasma 25-OHD **25–50 nmol/L**), maintenance treatment is recommended in patients with the following:

- Fragility fracture, confirmed osteoporosis or high fracture risk
- Receiving antiresorptive medication for bone disease
- 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, dark skin, etc.
- Raised Parathyroid Hormone (PTH)
- Receiving treatment with antiepileptic drugs or oral glucocorticoids

Key aims for treating vitamin D deficiency includes using adequate doses to ensure correction of vitamin D deficiency (ideally > 50 nmol/l), reversing the clinical consequences of vitamin D deficiency in a timely manner, and avoiding toxicity.

Seek specialist advice or arrange referral if the patient has a condition predisposing to hypercalcaemia; a malabsorption disorder; renal stone disease; severe kidney or liver disease; or is pregnant.

23.2.1 Testing for vitamin D Deficiency

Do not routinely test for vitamin D deficiency in people who are asymptomatic.

Indications for testing vitamin D status include:

In adults:

- Patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency, such as chronic widespread pain, muscle aches and weakness.
- Patients with suspected bone disease such as osteomalacia or osteoporosis that may be improved with vitamin D treatment.
- Patients with bone disease such as osteoporosis or Paget's disease, prior to specific treatment where correcting vitamin D deficiency is needed.
- Patients considered to be at particularly high risk of deficiency (for example, they have very low exposure to sunlight).

In children and adolescents:

- Symptoms and signs of rickets;
- Other conditions associated with vitamin D deficiency, including long-standing bone pain, muscular weakness, tetany due to low plasma calcium, seizures due to low plasma calcium, and infantile cardiomyopathy;
- Abnormally low plasma calcium or phosphate, or high alkaline phosphatase;
- Radiographs showing osteopenia, rickets or pathological fractures;
- Chronic diseases, including chronic renal disease, chronic liver disease, and malabsorption syndromes; and
- Treatment with antiresorptive agents.

Note: asymptomatic people at higher risk of vitamin D deficiency (as in section 23.1) *do not need routine testing* for vitamin D deficiency, but should be advised on the need for preventing vitamin D deficiency which includes taking daily vitamin D supplementation all year round (see section 23.3).

People with osteoporosis or fragility fracture who are treated with vitamin D supplements and an oral antiresorptive agent do not need routine testing for vitamin D deficiency.

23.2.2 Prescribing guidance for treating vitamin D Deficiency

<u>In adults</u> – a loading dose regimen may be prescribed to deliver a total of approximately 300,000 units over 6 to 10 weeks, when rapid correction of vitamin D deficiency is required, such as in:

- Patients with symptomatic disease
- Patients about to start treatment with a potent antiresorptive agent (zoledronate or denosumab or teriparatide)

followed by **maintenance therapy in doses equivalent to 800-2000 units daily**, given either daily or intermittently.

Several loading and maintenance dose regimens are available, but for the sake of simplicity, uniformity and to reduce prescribing and administration errors, EPUT prescribers are requested to use once daily doses for both loading and maintenance.

A loading dose regimen of daily oral 4,000 units for 10 weeks, followed by **a *maintenance regimen of daily oral 800 units*** one month after loading is completed, is recommended.

A maintenance regimen, as above, can be started straight away without the need for a loading regimen, when rapid correction of vitamin D deficiency is not needed, such as in:

- Patients with fragility fracture, confirmed osteoporosis or high fracture risk
- Patients receiving antiresorptive medication for bone disease (other than those mentioned above)
- Patients with increased risk of developing vitamin D deficiency in the future because of reduced exposure to sunlight, religious/cultural dress code, dark skin, etc.
- Patients with raised Parathyroid Hormone (PTH)
- Patients on treatment with antiepileptic drugs or oral glucocorticoids;

In children – As with adults, a loading dose may be prescribed if rapid correction is indicated, followed by a maintenance dose to be started one month after loading is completed.

Prescribe loading doses as below for 8-12 weeks:
3,000 units orally daily in babies **one to five months old**.
6,000 units orally daily in **six months to 11 year old**.
10,000 units orally daily in **12-17 year old**.

followed by **a *maintenance regimen of daily oral 400 units*** one month after loading is completed.

Maintenance dosing may be started without the use of loading doses if correction of vitamin D deficiency is less urgent.

Advise patients receiving maintenance therapy as inpatients that following discharge, this may need to be bought over the counter as GPs may not continue to prescribe. Discharge prescriptions should be marked for GPs not to continue following discharge. At least 2 weeks supply will be provided on discharge.

Available preparations

- **Oral vitamin D_3 (colecalciferol) is the preparation of choice** for treatment of vitamin D deficiency.
- **Vitamin D_2 (ergocalciferol) can be used in people who cannot take vitamin D_3** for cultural, dietary, or religious reasons because of the animal sourcing, or the use of gelatine in some preparations.

Contact the pharmacy department for guidance in prescribing for people with specific dietary requirements or for whom oral administration is not feasible.

23.2.3 Clinical monitoring in the management of vitamin D Deficiency

In adults – monitor adjusted plasma calcium levels within one month after administration of the last loading dose of vitamin D, or after starting lower dose maintenance treatment, to detect calcium deficiency or unmasked primary hyperparathyroidism.

If hypercalcaemia is detected, stop vitamin D supplementation (and calcium, if taking), arrange investigations and manage as indicated.

If hypocalcaemia is detected, advise on the need to increase dietary calcium intake and consider the need for calcium supplements. Combination calcium and vitamin D preparations (such as Calcichew D3®) are not recommended for people needing high-dose vitamin D treatment, as they contain very low levels of vitamin D (200–400 IU per tablet) and may increase the risk of hypercalcaemia.

Routine monitoring of plasma 25-OHD levels is unnecessary following treatment, but may be appropriate in:

- Patients with symptomatic vitamin D deficiency
- Situations where malabsorption or poor compliance with medication is suspected

- Patients taking antiresorptive therapy who have extremely low levels at baseline assessment.

Wait for a minimum of three months after the start of treatment to monitor plasma 25-OHD levels.

Refer adults with poor response to treatment (i.e., level of 25-OHD below 50 nmol/l) despite good adherence, and/or ongoing symptoms despite adequate treatment to specialist care to consider alternative diagnosis and appropriate management.

In children – monitor bone profile (calcium, phosphate and alkaline phosphatase) and plasma 25-OHD level at the end of the course of treatment.

If the 25-OHD level is greater than 50 nmol/l and bone profile is normal, give advice on preventing vitamin D deficiency including taking daily multivitamins containing vitamin D.

If the 25-OHD level is below 50 nmol/l, consider poor compliance, drug interactions and underlying disease, such as renal disease, liver disease or malabsorption.

Refer children to specialist care with repeated low plasma calcium concentration with or without symptoms, underlying complex medical disorders (e.g., liver disease, intestinal malabsorption), deformities and abnormalities probably related to rickets, poor response to treatment (i.e., level of 25-OHD below 50 nmol/l) despite good adherence, and persisting low plasma phosphate or low/high alkaline phosphatase.

23.3 PREVENTION OF VITAMIN D DEFICIENCY

Advice on the prevention of vitamin D deficiency should be provided to all patients.

Information on safe sunlight exposure and dietary sources of vitamin D should be given.

Adults with risk factors (see section 23.1) should take a daily supplement containing 400 units of vitamin D throughout the year.

Other adults should consider taking a daily supplement containing 400 units of vitamin D, particularly in the autumn and winter (from October until the end of March).

Children, one month to 18 years, except infants fed with formula, should take daily multivitamins containing 400-600 units of vitamin D to maintain adequate vitamin D status.

Advise patients receiving low dose vitamin D to prevent deficiency as inpatients that following discharge, this may need to be bought over the counter as GPs may not continue to prescribe. Discharge prescriptions should be marked for GPs not to continue following discharge. At least 2 weeks supply will be provided on discharge.

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