

Oral vitamin B12 – what are the prescribing considerations and what formulations are available?

Prepared by a UK Medicines Information (UKMi) team for NHS healthcare professionals
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Background

Vitamin B12 deficiency is diet-related (e.g. malnutrition, vegan diet) or non-diet-related (e.g. pernicious anaemia, inflammatory bowel disease, gastrectomy) (1). The most common cause of severe non-diet-related vitamin B12 deficiency in the UK is pernicious anaemia, an autoimmune disorder causing reduced production of intrinsic factor (IF) in the stomach; IF is essential for absorption of dietary vitamin B12.

Two forms of vitamin B12 are available in the UK; hydroxocobalamin and cyanocobalamin (2).

In patients with diet-related deficiency (who retain IF production), oral cyanocobalamin at doses of 50-150micrograms daily (between meals) is an option for maintenance therapy (1,2).

In non-diet-related deficiency, intramuscular (IM) hydroxocobalamin is the preferred method of treatment as it is retained in the body longer than cyanocobalamin, allowing maintenance therapy to be given at intervals of up to 3 months (1,2). However, where administration of IM hydroxocobalamin is not tolerated, or not possible (e.g. during a pandemic), oral cyanocobalamin may be considered as an alternative, provided sufficient doses are taken (much higher than the doses used for diet-related deficiency, at least 1mg) and there is good compliance with treatment (3). Passive, IF-independent absorption of a small fraction of such large doses should suffice to meet daily requirements in some patients with non-diet-related deficiency (3). Low quality evidence suggests that these high doses of cyanocobalamin (1-2mg daily) are as safe and effective as IM cyanocobalamin (various doses) in normalising serum vitamin B12 levels (4).

High-dose oral cyanocobalamin (1-2mg) supplements are widely available via the internet and from high street pharmacies but they are not licensed medicines in the UK; however, a licensed product, *Orobalin* 1mg tablets will be available in the UK from July 2020 (5,6).

This Medicines Q&A outlines what oral vitamin B12 (cyanocobalamin) preparations are available and associated prescribing considerations.

Answer

Clinical considerations when prescribing oral cyanocobalamin

Prescribers should consider the cause of their patient's vitamin B12 deficiency before deciding on the appropriate dose of oral cyanocobalamin to be prescribed.

Patients with non-diet-related deficiency must be prescribed at least 1mg of cyanocobalamin daily to ensure sufficient IF-independent absorption, and must be counselled on the importance of good compliance (3). Patients with diet-related deficiency require much lower doses of cyanocobalamin (50-150micrograms daily); some (excluding patients with vegetarian or vegan diets) may be vitamin B12 replete if they have already been receiving vitamin B12 supplementation and may be able to stop supplementation for up to a year (1,2,7). All patients should be counselled to take their dose on an empty stomach to maximise absorption (8).

Do not prescribe oral vitamin B12 for patients presenting with neurological involvement; in these cases, seek urgent advice from a haematologist (1). IM hydroxocobalamin should be given if this advice is not immediately available.

Patients prescribed high-dose oral cyanocobalamin should be advised to monitor their symptoms carefully and contact their GP if they begin to experience neurological or neuropsychiatric symptoms, such as pins and needles, numbness, problems with memory or concentration, or irritability (7).

Prescribing oral cyanocobalamin on NHS prescriptions in primary care

In 'Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs', NHS England and NHS Clinical Commissioners recommend that vitamin or mineral products should only be prescribed for 'medically diagnosed deficiency, including for those patients who may have a lifelong or chronic condition or have undergone surgery that results in malabsorption' (9). Therefore, low-dose oral cyanocobalamin should not routinely be prescribed for patients suspected of having or likely to have diet-related vitamin B12 deficiency unless it has been medically diagnosed; such patients should be advised to purchase a supply instead. For any patient with medically diagnosed vitamin B12 deficiency (diet- or non-diet-related) or malabsorption of vitamin B12 where it is not possible to administer IM hydroxocobalamin, it is reasonable to prescribe oral cyanocobalamin at NHS expense.

In Wales, cyanocobalamin tablets can be prescribed for patients who are vegan or have a proven vitamin B12 deficiency of dietary origin only for treatment or prevention of vitamin B12 deficiency as specified under the 'Selected List Scheme' (SLS) (in part XVIIIIB 'Drugs, Medicines and Other Substances that may be ordered only in certain circumstances' of the Drug Tariff), and the prescriber must endorse the prescription with 'SLS' to enable community pharmacies to dispense the prescription (10). This is not applicable to prescriptions for cyanocobalamin tablets in England, Northern Ireland or Scotland (11,12), or when prescribing cyanocobalamin tablets for non-diet-related vitamin B12 deficiency in any of the countries. In England, cyanocobalamin tablets were previously included in the SLS scheme, but this restriction was removed from May 2013 and therefore no longer applies.

"Vitamin B12 tablets" are listed on the "Blacklist" of UK drug tariffs (10-12); therefore, prescriptions must be written as "cyanocobalamin tablets" as opposed to "vitamin B12 tablets", for dispensing by a UK community pharmacy. Also on the 'Blacklist' are all strengths of cyanocobalamin oral solution.

Several branded and generic formulations of cyanocobalamin 50microgram tablets are listed in the BNF (2). Some of these preparations are available to purchase as food supplements; others are licensed medicines for treatment of nutritional (diet-related) vitamin B12 deficiency, vitamin B12 deficiency following partial gastrectomy, tropical sprue (alone or with folic acid), and pernicious anaemia when parenteral administration is not possible or not advised (13-15). Although some cyanocobalamin 50microgram tablets are licensed for the treatment of conditions that cause non-diet-related vitamin B12 deficiency (e.g. pernicious anaemia), the 50microgram dosage formulation is less suitable to provide the high doses of cyanocobalamin required by these patients.

In addition to the 50microgram tablets, the following are available: 100microgram tablets, 1mg tablets, 1mg modified-release (MR) tablets and 1mg sublingual nuggets (2,16). None of these preparations or strengths are currently included in any drug tariff in the UK (10-12). Although currently available cyanocobalamin 1mg tablets (immediate-release or MR) are unlicensed in the UK, they can be obtained through community pharmacies (some stock is classified as a wholesaler 'special') (17). Before prescribing, it is advisable to discuss the cost of supply with local pharmacies as this may vary depending on the availability options.

Although effective, sublingual cyanocobalamin is generally not used in the treatment of vitamin B12 deficiency due to limited evidence and limited knowledge regarding optimal dosing via this route (8). No published evidence for the use of cyanocobalamin MR in preference to immediate-release tablets was identified.

Which oral cyanocobalamin preparations are available?

A licensed cyanocobalamin 1mg tablet preparation (*Orobalin*) is due to be launched as a branded product in the UK in July 2020 (6). This will be a prescription only medicine (POM) indicated for the treatment of haematological, neurological and other symptoms secondary to vitamin B12 deficiency, malabsorption of vitamin B12, such as due to the absence of intrinsic factor (pernicious anaemia), stomach resection or disease of the small intestine (5,6). It will also be indicated for use during para-aminosalicylic acid therapy, which can cause impaired vitamin B12 resorption.

Table 1 shows the oral cyanocobalamin preparations currently available to prescribe on the NHS, as well as details of pack size and cost (if known).

Table 1: Oral cyanocobalamin preparations currently available for prescribing (16)

Product	Pack size	Licensed status	Cost [#]
Cyanocobalamin 50microgram tablets			
Cyanocobalamin 50microgram (prescribed generically; various products available)	50 tablets	Available as Pharmacy only (P) medicines or food supplements	£15.86
Cyanocobalamin 100microgram tablets			
Lamberts Vitamin B12 100microgram <i>Lamberts Healthcare Ltd</i>	100 tablets	Food supplement	£4.44
Cyanocobalamin 1mg tablets			
CyanocoMinn 1mg <i>Essential-Healthcare Ltd</i>	28 tablets (2x14 pack)	Food supplement	£2.87
Cyanovit-B12 1000microgram <i>Synergy Pharmaceuticals</i>	28 tablets	Food supplement	£6.68
CyanocoB12 1mg <i>TriOn Pharma Ltd</i>	50 tablets	Food supplement	£5.68
Lamberts Vitamin B12 1000microgram <i>Lamberts Healthcare Ltd</i>	60 tablets	Food supplement	£5.00
Quest Vitamin B12 High Potency 1000microgram <i>Quest Vitamins Ltd</i>	60 tablets	Food supplement	£5.85
Quest Vitamin B12 High Potency 1000microgram <i>Quest Vitamins Ltd</i>	90 tablets	Food supplement	£7.50
Behepan 1mg (Imported from Sweden)	100 tablets	Prescription only medicine (POM)	Contact Community Pharmacy
Cyanocobalamin 1mg modified-release tablets			
CyanocoB12 1mg modified-release <i>TriOn Pharma Ltd</i>	50 tablets	Food supplement	£3.47

Product	Pack size	Licensed status	Cost [#]
CyanocoMinn 1mg modified-release <i>Essential-Healthcare Ltd</i>	50 tablets	Food supplement	£3.19
HealthAid Vitamin B12 1000microgram modified-release <i>HealthAid Ltd</i>	50 tablets	Food supplement	£4.46
HealthAid Vitamin B12 1000microgram modified-release <i>HealthAid Ltd</i>	100 tablets	Food supplement	£8.09
Cyanocobalamin 1mg sublingual tablets			
Solgar Vitamin B12 1000microgram sublingual <i>Solgar Vitamin and Herb</i>	100 nuggets	Food supplement	Not available
Solgar Vitamin B12 1000microgram sublingual <i>Solgar Vitamin and Herb</i>	250 nuggets	Food supplement	Not available

Notes to support table 1:

[#] Prices obtained from dm+d browser, except for cyanocobalamin 50microgram tablets where price was obtained from the June 2020 edition of UK drug tariffs.

Not all products may be acceptable to all patients (e.g. patients with a vegan diet). To check if a product is suitable for vegans, contact the manufacturer directly as formulations/excipients may differ between products. See also the UKMi Medicines Q&A [“Excipients: What are the general considerations for vegan patients?”](#)

Summary

- Hydroxocobalamin 1mg administered intramuscularly (IM) is the preferred method of treatment for non-diet-related vitamin B12 deficiency (e.g. pernicious anaemia) as it is retained in the body longer than cyanocobalamin.
- Oral cyanocobalamin 50-150micrograms daily is used to treat diet-related vitamin B12 deficiency.
- Where administration of IM hydroxocobalamin is not possible (e.g. during a pandemic) or not tolerated, oral cyanocobalamin may be considered as an alternative, provided sufficient doses are taken (at least 1mg for non-diet-related deficiency) and there is good compliance with treatment.
- Cyanocobalamin 1mg tablets are available as a food supplement (immediate-release, modified-release or sublingual tablets) or as a prescription-only medicine that is unlicensed in the UK but can be imported; they can be obtained through community pharmacies (some stock is classified as a wholesaler 'special').
- A licensed cyanocobalamin 1mg tablet (Orobalin) is due to be launched in the UK in July 2020.
- Cyanocobalamin 50microgram tablets are available as Pharmacy only medicines or as food supplements.
- Cyanocobalamin tablets must be prescribed as "cyanocobalamin tablets" and should not be written as "vitamin B12 tablets".
- In Wales, cyanocobalamin tablets can be prescribed for patients who are vegan or with a proven diet-related vitamin B12 deficiency only for the purpose of treating or preventing vitamin B12 deficiency, and the prescription must be endorsed 'SLS'; this does not apply in England, Northern Ireland or Scotland, or when prescribing for patients with non-diet-related vitamin B12 deficiency in any of the countries.

Limitations

- Many more preparations, formulations and strengths of oral vitamin B12 are also available to purchase as food supplements online or in health food shops, which have not been included in this Q&A.
- Availability and cost of oral cyanocobalamin preparations are correct at the time of writing and are subject to change.

References

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Search strategy

1. Embase exp CYANOCOBALAMIN/ AND exp "CONTROLLED RELEASE FORMULATION"/ (conducted by West Midlands Medicines Information Service in December 2019). Search repeated exp CYANOCOBALAMIN/ AND exp "CONTROLLED RELEASE FORMULATION"/ [DT 2019-2020] on 01/06/20.
2. Medline exp "VITAMIN B 12"/ AND exp "DELAYED-ACTION PREPARATIONS"/ (conducted by West Midlands Medicines Information Service in December 2019). Search repeated exp "VITAMIN B 12"/ AND exp "DELAYED-ACTION PREPARATIONS"/ [DT 2019-2020] on 01/06/20.
3. In-house database/ resources
4. Google, search for cyanocobalamin products.
5. Manufacturer - Northumbria Pharma Ltd. Communication by telephone and email on 28/05/20, 08/06/20 and 09/06/20.
6. NHS Prescription Services at the NHS Business Services Authority (NHSBSA). Communication by telephone on 23/06/20.