Guideline for the management of Vitamin B12 (Cobalamin) deficiency in over 16s

Megaloblastic anaemia and/or strong clinical suspicion of deficiency e.g., visual disturbance related to optic nerve dysfunction (blurred vision, optic atrophy, visual field loss [scotoma]), cognitive difficulties (short-term memory loss and difficulty concentrating), glossitis, neurological or mobility problems (pins and needles [paraesthesia], numbness, peripheral neuropathy, balance issues and falls, impaired gait), unexplained fatigue, and symptoms and signs of anaemia that suggest iron treatment is not working during pregnancy or breastfeeding

Check total (serum) vitamin B12 (and folate*). Ensure to state whether patient is pregnant or a known recreational Nitrous oxide user on request as holotranscobalamin assay (HoloTC) will be used in isolation to improve accuracy

<300ng/L

Check HoloTC (reflex tested automatically by pathology lab)

≥300ng/L B12 deficiency very unlikely

HoloTC <25: deficiency likely- Check Intrinsic Factor Antibody (IFAB)*** if suspected autoimmune gastritis (AIG) and no history of causative surgical procedure (total gastrectomy or terminal ileal resection)

Proceed to treatment regardless of result. Check folate levels *

HoloTC >70 and asymptomatic: deficiency unlikely- investigate alternative cause for symptoms.

HoloTC 25-70 indeterminate: strong clinical suspicion or high-risk group**
Consider empirical trial of treatment or follow up laboratory monitoring of B12 status

IFAB positive: autoimmune gastritis (AIG) confirmed

Consider starting treatment while awaiting B12 result in those with suspected megaloblastic anaemia and neurological symptoms, and in those with suspected deficiency because of taking medications listed below **

IFAB negative: consider causes of B12 deficiency, if AIG still suspected, consider alternative investigations ****

Treatment-see table 1 for details

Notes:

* Megaloblastic anaemia can also be caused by folate deficiency. If both B12 and folate deficiency is identified, treatment should be initiated with cobalamin therapy before adding in folate therapy.

** High risk groups:

- People with diets low in vitamin B12 without the use of over the counter (OTC) preparations e.g.:
  - Diet low in foods from animal sources such as vegan or strict vegetarian diets.
  - People who do not consume foods or drinks fortified with B12.
  - Food allergies with restrictions to intake of milk, eggs, or fish.
  - Restricted diets e.g., eating disorders.
  - Difficulties in preparing or sourcing foods rich in B12 e.g., frailty, dementia, mental health conditions, or on low incomes.
- Family history of B12 deficiency or autoimmune condition.
- Medical conditions: atrophic/autoimmune gastritis (AIG), coeliac disease, other autoimmune conditions such as Sjögren's syndrome or type 1 diabetes.
- Previous abdominal or pelvic radiotherapy.
- Previous gastrointestinal (GI) surgery e.g., bariatric surgery (Roux-en-Y gastric bypass or sleeve gastrectomy), total gastrectomy or terminal ileal resection.
- People taking certain medicines: colchicine, H_2-receptor antagonists, metformin, phenobarbital, pregabalin, primidone, proton pump inhibitors (PPIs), and topiramate.
- Recreational nitrous oxide use.

*** Intrinsic Factor Antibody (IFAB): Raised intrinsic factor (IF) antibodies indicate AIG- an autoimmune condition that causes destruction of the parietal cells which produce IF, therefore vitamin B12 cannot be absorbed in the distal ileum. Raised IFAB are only present in approx. 50% of those with AIG.

**** Alternative tests for AIG following negative IFAB are not routinely available: Please seek specialist advice from secondary care e.g. gastroenterology who may be able to perform an endoscopy.

Table 1: Treatment of B12 deficiency based on suspected cause

Suspected cause of Vitamin B12 deficiency	Initial treatment	Maintenance
Malabsorption (autoimmune gastritis [AIG], total gastrectomy, terminal ileal resection, gastrointestinal surgery (GI), or abdominal/ pelvic radiotherapy)	• Intramuscular (IM) hydroxocobalamin **1mg x3 per week for 2-3 weeks** (3 weeks and review if neuro symptoms) • Oral treatment can be considered, but only in people with deficiency **NOT caused** by AIG, total gastrectomy, or complete terminal ileal resection as it may not be as effective (e.g. malabsorption caused by other GI surgeries, radiotherapy, or coeliac disease) ○ **Oral: Cyanocobalamin 4mg/day for 8 weeks (see table 2)**	• Offer lifelong IM vitamin B12 replacement for those with an irreversible cause of B12 deficiency e.g. AIG, gastrectomy and terminal ileal resection **1mg hydroxocobalamin every 2-3 months.** • If vitamin B12 deficiency is thought to be due to other GI surgeries, radiotherapy, or coeliac disease then lifelong IM Vitamin B12 replacement can be offered **but** oral replacement can also be considered- doses should be 1mg/d (1000mcg) in this group (**OTC only**- see appendix 1 for options).
Medication (e.g., colchicine, H2-receptor antagonists, metformin, phenobarbital, pregabalin, primidone, proton pump inhibitors [PPIs], and topiramate)	• If appropriate review the medicine that is the suspected cause of Vitamin B12 deficiency to see if it is still required or can be changed to a suitable alternative. • Offer IM or oral replacement depending on clinical judgement and the patient's reference. IM treatment should be used if neuropathy is suspected. ○ **IM: 1mg Hydroxocobalamin x3 per week for 2-3 weeks** **OR** ○ **Oral: Cyanocobalamin 4mg/day for 8 weeks (see table 2)**	• If the medicine causing the deficiency has been stopped or changed then ongoing vitamin B12 supplementation should not be required if dietary intake is sufficient (give PIL Oral treatment of Vitamin B12 deficiency). OTC vitamin B12 could be considered (see appendix 1). • If medication suspected of causing deficiency cannot be changed **OTC Vitamin B12 at 1mg/day should be purchased by the patient (see appendix 1 and give PIL linked above).**
Dietary cause- diet low in Vitamin B12 (e.g., vegan, strict vegetarian diets, food allergies, or low food intakes)	• Ask about the patient's diet, including any foods or food groups they avoid, and sources of Vitamin B12 (e.g., meat, fish, milk, cheese, eggs, and fortified foods). • Give Patient Information Leaflet associated with this guidance Oral treatment of Vitamin B12 deficiency)	• If diet remains low in vitamin B12, OTC preparations should be used to supplement the diet. Recommended dose: at least 10mcg/day (see appendix 1), higher doses can be used. • Long term supplementation may not be required if dietary changes are made (link to PIL Oral treatment of Vitamin B12 deficiency).

	• Advise on increasing dietary intake of Vitamin B12. • Recommend OTC **oral Cyanocobalamin 50-150mcg daily for 3 months (see appendix 1).** • Consider prescribing oral tablets **50-150mcg daily for 3 months ONLY if patient unable or unwilling to self-care.**	https://www.bda.uk.com/news-campaigns/campaigns/sustainable-september/nutritional-considerations-for-dietitians.html
Recreational Nitrous Oxide use	• Only to be assessed if objective symptoms develop and this is the only indication for treatment. • Refer as appropriate to drug and alcohol services. • Recommend OTC oral Cyanocobalamin 50-150mcg daily for 3 months. • Consider prescribing oral tablets **50-150mcg daily for 3 months ONLY if patient unable or unwilling to self-care.**	• If nitrous oxide use has stopped, then ongoing supplementation may not be required if dietary intake is sufficient (give PIL Oral treatment of Vitamin B12 deficiency). If supplementation is required then the recommended dose should be at least 10mcg/day (OTC only), higher doses can be used. (see appendix 1 and give PIL Oral treatment of Vitamin B12 deficiency).
Unknown cause	• Offer IM or oral replacement depending on clinical judgement and the patient's preference. IM treatment should be used if neuropathy is suspected. ○ **IM: 1mg Hydroxocobalamin x3 per week for 2-3 weeks** **OR** ○ **Oral: Cyanocobalamin 4mg/day for 8 weeks** • Offer serological testing for coeliac disease where the cause of vitamin B12 deficiency is still unknown after further investigations.	• If the cause of the deficiency has been identified see maintenance information for above causes. • OTC vitamin B12 supplementation for maintenance may be required following initial treatment (see appendix 1). • Give PIL (Oral treatment of Vitamin B12 deficiency).

Monitoring

- There is no need to recheck serum B12 in patients on IM treatment. FBC should be used to monitor response to B12 replacement.
- Discuss with haematologist if anaemia not responding to treatment.
- Please note B12 (serum or active) cannot be retested within 90 days of initial assay.
- Review for improvement in symptoms at approximately 3 months after starting treatment, or 1 month if pregnant/breastfeeding (or earlier if no improvement/worsening symptoms).
- Ensure those taking oral replacement are taking the correct dosage.

Vitamin B12 Frequently Asked Questions

1. **What if the patient is unwilling to have the IM route?**
   It is **possible** to use oral Vitamin B12. If the deficiency is thought to be caused by malabsorption or altered metabolism (caused by some medications) oral treatment may not be as effective as an injection (see table 2). This should be explained to the patient, any decision to inject will require informed patient consent.
   (*Please note that Vitamin B Co strong tablets do not contain any vitamin B12 and therefore cannot be used to treat B12 deficiency)*

2. **What if a patient is still symptomatic despite maintenance IM vitamin B12 treatment?**
   If levels were indeterminate initially and only treated due to symptoms/high risk group, then this suggests the B12 has not been effective. Trial withdrawal and investigate other causes of symptoms. If initially B12 deficient, retest the active B12 level: if levels remain low, seek specialist advice. If levels are corrected to normal, continue maintenance dose interval and investigate other causes of symptoms. If a patient's symptoms recur before the next injection is due, seek specialist advice from a haematologist.

3. **Are high intakes of vitamin B12 dangerous or toxic?**
   High intakes of vitamin B12 are not dangerous. Injected amounts as large as 3mg/d (3000 micrograms) have not been associated with harmful effects.

4. **What foods can I advise patients to eat to increase their dietary intake of Vitamin B12?**
   Foods that are a good source of B12: eggs, meat, milk and other dairy products, fish; as well as foods which have been fortified (some soy products, breakfast cereals and breads). If the patient is vegan or has a restricted diet it may be harder to meet vitamin B12 requirements. Give patients this leaflet to advise: (PIL Oral treatment of Vitamin B12 deficiency).

5. **What if the patient was switched to oral cyanocobalamin instead of IM injections during the COVID pandemic?**
   We would advise these patients are reviewed to see whether it can be stopped and/or switched to OTC preparations if the deficiency has been 'treated', see appendix 1 for OTC options.

6. **Can patients be trained to self-administer their B12 injections if required long term?**
   Some GP practices may choose to allow some patients to self-administer their B12 injections e.g. those who are unable to regularly attend the practice due to work/caring commitments. Suitability for this must be assessed on an individual basis with training provided by an appropriate clinician.

Table 2: Prescribed oral Cyanocobalamin options
Norfolk and Waveney ICB only commissions the prescribing of vitamins and minerals to **treat a diagnosed deficiency**. Once the deficiency has been corrected patients are expected to purchase OTC products to maintain their health if required as per NHSE guidance. See appendix 1 for suitable OTC products. Expectations for prescribers: • **Do not prescribe** unlicensed 100 microgram tablets (TAG recommendation?) • **Do not prescribe** modified release (MR) versions (TAG recommendation?) Information for prescribers: • Dose advised below suitable for adult patients 18 years or over • **In pregnancy or breastfeeding:** Cyanocobalamin is considered safe for use during pregnancy and breastfeeding • Advise patients to take tablets between meals
Treatment of deficiency 1) **Deficiency related to malabsorption, medication, or unknown cause: 4 milligrams (4000 micrograms) per day. Take TWO tablets TWICE daily between meals (4 x 1000 micrograms per day) for 8 weeks** • Orobalin 1mg (1000 microgram) cyanocobalamin tablets (30 tablets £9.99) Northumbria Pharma Ltd. 2) Deficiency related to low dietary intake or recreational nitrous oxide use **AND patient is unable or unwilling to self-care**: 50-150 micrograms per day (take 1-3 **50 microgram** tablets per day) between meals for 3 months. **Most patients should be advised to source Vitamin B12 OTC 100 micrograms daily** (give PIL Oral treatment of Vitamin B12 deficiency). • Generic Cyanocobalamin 50microgram tablets (50 tablets £3.09) • CyanocoB12 **50microgram** tablets (50 tablets £3.59) TriOn Pharma Ltd • CyanocoMinn **50microgram** tablets (50 tablets £3.57) Essential-Healthcare Ltd

Appendix 1: Over-the-counter vitamin B12 supplements

OTC options - Suitable forms of Vitamin B12: cyanocobalamin, methylcobalamin, adenosylcobalamin). Please give patient this PIL which has written information: Oral treatment of Vitamin B12 deficiency. **Prices checked July 2025.** List is not exhaustive

Superdrug 10 microgram tablets (cyanocobalamin)

- 10mcg tablets x 60
- **Low dose** may be suitable to supplement diets which are naturally low in vitamin B12 such as vegetarian/vegan diets
- Take ONE tablet daily
- £2.99 (part of 3 for the price of 2 offer)

Holland and Barrett 100 microgram tablets (methylcobalamin)

- 100mcg vitamin B12 tablets x 60
- Take ONE tablet daily
- £6.25 (part of 3 for the price of 2 offer)

Nature's Best 100 microgram tablets (methylcobalamin)

- 100mcg vitamin B12 tablets x 100
- Take ONE tablet daily
- £4.95

Asda 100 microgram tablets (methylcobalamin)

- 100mcg vitamin B12 tablets x 30
- Take ONE tablet daily
- £1.51

Holland & Barrett 1000 microgram tablets (cyanocobalamin)

- 1000mcg vitamin B12 tablets x 180 (6 months supply)
- Take ONE tablet daily
- £20.99 (part of 3 for the price of 2 offer)

Natures best 1000 microgram tablets (methylocobalamin)

- 1000mcg vitamin B12 tablets x 180 (6 months supply)
- Take ONE tablet daily
- £11.95

Title	**Guideline for the management of Vitamin B12 (Cobalamin) deficiency in over 16s**
Author	Anna Samkin (Lead Medicines Optimisation Dietitian) Norfolk and Waveney ICB
References	NICE Vitamin B12 Deficiency in over 16s: diagnosis and management (March 2024) [accessed July 2025] NHSE Conditions for which over the counter items should not be routinely prescribed in primary care (March 2024) [accessed July 2025] PrescQIPP Bulletin 296: Vitamins and Minerals (Nov 2021) [accessed July 2025] Sanz-Cuesta T, Escortell-Mayor E, Cura-Gonzalez I, et al. Oral versus intramuscular administration of vitamin B12 for vitamin B12 deficiency in primary care: a pragmatic, randomised, non-inferiority clinical trial (OB12). BMJ Open 2020;10 [accessed July 2025] Devalia V, Hamilton M, and Molloy A. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. British Journal of Haematology 2014; 166 [accessed July 2025]
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Available at online locations	Vitamin Guidance - Knowledge NoW