Guideline for the management of Vitamin B12 (Cobalamin) deficiency in adults



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: Age > 65, patients with chronic GI illness or malabsorption (such as inflammatory bowel disease, undiagnosed or uncontrolled coeliac disease), patients with a history of bariatric surgery or surgical resections (especially terminal ileectomy), vegans or strict vegetarians who do not take additional oral vitamin supplementation, and those taking certain medicines (metformin, proton-pump inhibitors)

***Intrinsic Factor Antibody (IFAB): Raised IF antibodies indicate pernicious anaemia (PA)- an autoimmune condition that causes destruction of the parietal cells which produce IF, therefore vitamin B12 is unable to be absorbed in the distal ileum without binding to IF. Raised IFABs are only present in 50% of cases of PA. First line treatment for PA is intramuscular Vitamin B12

****Clinical malabsorption/Intrinsic Factor pathway disrupted e.g., Gastric surgery, short bowel syndrome or ileal resection, congenital disorders of B12 metabolism

Monitoring:

- There is no need to recheck serum B12 in patients on IM treatment. FBC should be used to monitor response to B12 replacement.
- If treating with oral B12 recheck vitamin B12 levels after 2-3 months to check responding to treatment. If not responding consider parenteral treatment

For severe megaloblastic anaemia an increase in reticulocyte is usually seen 4 days after starting treatment.

• Discuss with haematologist if anaemia not responding to treatment

If neurological problems do develop, they may be irreversible. Source: <u>https://www.nhs.uk/conditions/vitamin-b12-or-folate-deficiency-anaemia/complications/</u>

| Medication/conditions that may affect levels Vitamin B12 | Comments |
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| Metformin (for longer than 12 months) | Usually improved with dietary improvement of B12 intake Only assess if objective evidence of deficiency is present including peripheral neuropathy or macrocytic anaemia If low levels check IFAB and should be treated with a short course of oral cyanocobalamin (50 micrograms orally for 4 weeks). Response should be assessed clinically and continued if benefit is shown No need for prophylactic B12 administration |
| Proton pump inhibitors and H2 antagonists | Oral replacement (50-100 micrograms orally) may be appropriate if objective evidence of deficiency is found |
| Anticonvulsants | If no objective features of B12 deficiency- no need for replacement Oral replacement (50-100 micrograms orally) may be appropriate if objective evidence of deficiency is found |
| Oral contraceptives and hormone replacement therapy | Only be assessed if objective symptoms develop and this is the only indication for treatment Oral replacement (50-100 micrograms orally) may be appropriate if objective evidence of deficiency is found |
| Colchicine | Low levels can easily be increased with OTC oral supplementation (cyanocobalamin 50mcg daily) and by increasing B12 in the diet (see page 5) |
| Antibiotics | Low levels can easily be increased with OTC oral supplementation (cyanocobalamin 50mcg daily) and by increasing B12 in the diet (see page 5) |
| Gastrointestinal surgery | Both gastrectomy and bariatric surgery can lead to B12 deficiency and require regular monitoring and replacement if levels are falling despite good dietary intake. Oral replacement is often inadequate in these patients since the cause is likely malabsorption. Patients who have undergone gastric bypass will require 3 monthly intramuscular injections of vitamin B12. Patients who have undergone sleeve gastrectomy surgery or duodenal switch are usually recommended to have initial 3 monthly intramuscular injections of vitamin B12 but may need less frequent injections depending on blood results. |
| Pregnancy | Not routinely measured during pregnancy therefore only identified if symptoms develop – in which case follow pathway as for non-pregnant people |
| Vegetarian and vegan diets | Vegetarians and vegans are at increased risk of B12 deficiency especially during pregnancy and when breastfeeding Monitoring should be considered, especially at high-risk times, and OTC oral supplementation (cyanocobalamin 50mcg daily) may be required |

Vitamin B12 Frequently Asked Questions

- 1. What if the patient is unwilling to have the IM route?
 - If absorption is not impaired, then it is **possible** to use oral Cyanocobalamin. It is available as cyanocobalamin 50-150mcg tablets which may be **purchased over the counter (see page 6)**
 - It may be appropriate to advise using 1000mcg to treat deficiency if absorption <u>is impaired</u> and unwilling to have IM route, though this should be second line only if parenteral therapy is NOT an option and the patient should be advised this may not be as effective as injection.

(Please note that Vitamin B Co strong tablets do not contain any vitamin B12 and therefore cannot be used to treat B12 deficiency)

- 2. How do you treat low vitamin B12 in patients with Type 2 diabetes (on long term metformin longer than 12 months)? Give patient dietary advice to increase their vitamin B12 levels, advise them to supplement with OTC oral cyanocobalamin (see page 6). Monitor serum B12 every 6 months. If still low check IFAB. If positive, then treat lifelong with IM hydroxocobalamin every three months. If IFAB is negative, the reduced level may be purely as a result of metformin, increase dose of oral cyanocobalamin to 150mcg daily, if still not able to raise B12 levels, treatment with three injections of IM hydroxocobalamin with subsequent monitoring of serum B12 at 6 monthly intervals is suggested.
- 3. What if someone is unable to access timely vitamin B12 injections post bariatric surgery due to pressures on NHS services or having to self-isolate?

The British Obesity and Metabolic Surgery Society (BOMSS) recommend the following as an interim measure: Advise people to buy oral vitamin B12 1000mcg per day over the counter (see page 6). This is an interim arrangement- recommence three monthly vitamin B12 injections within 3 months or earlier if possible.

4. What if a person is still symptomatic despite maintenance IM vitamin B12 treatment?

Review diagnosis to ensure symptoms are due to B12 deficiency. Consider increasing frequency of B12 injections to 2 monthly if B12 deficiency is still suspected. Seek specialist advice if required.

5. What dose of cyanocobalamin is recommended for purchase?

If mild deficiency is thought to be diet related, advise people to take oral cyanocobalamin tablets 50–150 micrograms daily between meals. Doses within this range are safe and sufficient to prevent dietary deficiency. Example products are shown below (page 6).



6. 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, salmon and cod; as well as foods which have been fortified with B12 (some soy products, breakfast cereals and breads). If the patient is vegan it may be harder to meet vitamin B12 requirements, see link for more information: <u>The vegan diet.</u>

Prescribing of oral Cyanocobalamin

Prescribing of oral Cyanocobalamin should only be commenced for those who meet certain criteria as these preparations will not be effective in those with absorption issues or pernicious anaemia

Criteria:

- 1) Vitamin B12 deficiency confirmed by pathology lab
- 2) Absorption of vitamin B12 NOT impaired e.g. NOT pernicious anaemia, or condition affecting gut leading to impaired absorption
- 3) If Absorption of B12 IS impaired AND the patient is unwilling to have IM hydroxocobalamin (after counselling that oral administration may not be effective to treat deficiency)
- 4) Unable or unwilling to purchase vitamin B12 OTC and risk to health deemed significant
- Please note once deficiency has resolved, maintenance oral Vitamin B12 should NOT be prescribed, but bought OTC. Dietary advice should also be given

Types of tablet to prescribe:

- Standard-release (rather than modified-release)
- 50-150micrograms cyanocobalamin is sufficient to treat deficiency that is NOT absorption related (e.g. due to dietary insufficiency)
- For those with impaired absorption who are unwilling to have IM hydroxocobalamin then cyanocobalamin 1000microgram/day (or 1mg) is required for enough vitamin B12 to be passively absorbed.



Examples of cyanocobalamin available to purchase (other products are available)

| Holland and Barrett (available on the high street or online) | 100mcg vitamin B12 tablets x 100 Take ONE tablet daily £7.69 (price at time of writing, also included in buy one get one half-price offer) |
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| Nature's Best (online) | 100mcg vitamin B12 tablets x 100 Take ONE tablet daily £4.95 (price at time of writing, plus £1 delivery charge) |
| MyProtein (suitable for vegans) | 1000mcg vitamin B12 tablets x 60 Take ONE tablet daily (dose is more than is necessary but will not cause harm) £4.99 (price at time of writing) |

Norfolk and Waveney

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| References | NICE Clinical Knowledge Summary: Anaemia- B12 and Folate deficiency (July 2020)[accessed January 2022]BMJ Best Practice: Vitamin B12 Deficiency (June 2021) [accessed January 2022]British Obesity and Metabolic Surgery Society (BOMSS) Guidelines on perioperative andpostoperative biochemical monitoring and micronutrient replacement for patients undergoingbariatric surgery—2020 update (August 2020) [accessed January 2022]Guidelines for the diagnosis and treatment of cobalamin and folate disorders (June 2014)[accessed January 2022] |
| Guidelines adapted from | Mid Essex CCG Medicines Optimisation Team Guidelines 2019 <u>https://midessexccg.nhs.uk/about-us/the-library/medicines-management/clinical-pathways-and-medication-guidelines-1/chapter-9-nutrition-and-blood-2/3002-vitamin-b12-deficiency-in- <u>adults-september-2018-new/file</u> Ipswich and East Suffolk CCG, North East Essex CCG and West Suffolk CCG Medicines Management Team Guidelines 2020 <u>https://www.westsuffolkccg.nhs.uk/wp-content/uploads/2021/02/Guideline-for-the-management-of-Vitamin-B12-deficiency-in-adults-November-2020.pdf</u></u> |
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| Available at online locations | Knowledge Anglia: Home > Prescribing, Pharmacy and Medicines Optimisation > Therapeutic Advisory Group (TAG) > TAG Guidance |

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| Previous Version | V1.1 Changes made May 2022- added table on page 5 re oral prescribing of cyanocobalamin V1.2 Changes made June 2022- changes to flow chart on page 1 (initial treatment) V1.3 added new ICB header as no longer N&W CCG V2.1 January 2024 Redated to April 2024 review date in preparation for NICE B12 update in |
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