

Vitamin B12 Full guidance

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Background

There are 2 causes of B12 deficiency: malabsorption and inadequate dietary intake.

Dietary Deficiency: Historically we have considered few people at risk of dietary deficiency, focusing primarily on vegans and strict vegetarians.

However, there is a recognition of greater than previously acknowledged risk of B12 deficiency in individuals who have reduced animal product consumption, limited consumption of fortified foods, or erratic/low intake of food. This includes those with social difficulties in acquiring balanced diets, or those with low mood or memory issues/chaotic lifestyles who may forget or lack motivation to eat.

Risk factors for B12 deficiency

- Those with low Dietary intake of B12
- Older Adults
- Patients with Gastrointestinal disorders such as gastrectomy, Crohn's
- Use of some medications including metformin, acid reducing medication such as PPI and H2 receptor antagonists

Dietary sources of b12

- Natural sources: Meat, eggs, fish, poultry, dairy products.
- Fortified sources: SOME dairy alternative cheeses, milks, yogurts, breakfast cereals, nutritional yeast (Nooch), toddler milks and protein shakes.

Dietary deficiency of B12 should be prevented through oral consumption of either a more balanced diet, or self-care with B12 oral supplementation.

Non-dietary deficiency occurs as a result of malabsorption, e.g. as a result of pernicious anaemia, inflammatory bowel disease, gastrectomy, pancreatic insufficiency, short bowel syndrome or bacterial overgrowth. Pernicious anaemia is the most common cause of B12 deficiency in the UK.

In non-dietary deficiency, lifelong treatment with intramuscular (IM) hydroxocobalamin is the required to maintain adequate B12 levels. (NICE 2019, BJH, BSH, BOMSS)

Diagnosis and treatment of B12 deficiency

Vitamin B12 serum levels should not be routinely tested, they should be tested in the presence of strong clinical deficiency, e.g. Visual disturbance, memory loss, psychiatric abnormalities, glossitis, paraesthesia, loss of peripheral nerve function that can result in impaired sensation, movement or organ function **with no other identifiable cause** (confirm normal folate status).

B12 deficiency is defined as serum B12 levels of **≤200 ng/L in the presence of anaemia or Neurological symptoms.**

For patients with non-specific symptoms, serum levels of **<150 ng/L** and who are IFAB positive are also treated as deficient.

Whether dietary, or malabsorptive in cause proven B12 deficiency should be treated with IM hydroxocobalamin 1mg/1ml.

Maintenance doses

Vitamin B12 tablets (cyanocobalamin) Should not be prescribed, Dietary improvement of B12 intake is recommended or patient may purchase supplements (50-150mcg/day)

Dietary deficiency – Prevention and maintenance

Once replete, patients with a nutritional deficiency of B12 should be given advice around the food sources of B12, aiming for 1.5-3microgram of B12 per day.

If patients improve their Vitamin B12 intake in their diet, there is no need for ongoing B12 supplementation. Consider using the B12 food fact sheet for patients ([B12 Food Fact Sheet](#)).

For patients who choose to use Supplemental B12 tablets for maintenance they should be recommended to purchase Cyanocobalamin supplement of 50- 150 micrograms to take daily (between meals).

Should patients require a prescription of oral Cyanocobalamin as the patient is not willing or able to purchase or improve their dietary intake, Cyanocobalamin should be prescribed by brand in 100mcg tablets, as these are more cost effective than 50mcg tablets.

Tablets	Cost/ tablet	Cost/ year treatment
50 mcg Cyanocobalamin	£0.27	£197.83
Lamberts Vitamin B12 100 mcg <i>Lamberts healthcare</i>	£0.04	£16.20
CyanocoB12 100mcg tablets <i>TriOn Pharma Ltd</i>	£0.06	£23.43

Additional advice for Vegans/ Vegetarians

Vitamin B12 is a vital nutrient that can only be found naturally in animal sources and planning how to meet their B12 requirements is an important part of a vegan individual's lifestyle choice.

- [The vegan society](#) and the British Dietetic Association recommend aiming for 3mcg of B12 from food **and/or** supplementation of at least 10mcg per day for all vegans, even if you haven't had a deficiency diagnosed.
- If you are pregnant or breastfeeding, it is strongly recommended you use vitamin B12 supplement tablets.
- **If you had a B12 deficiency diagnosed and treated with Injections by your doctor**, you should increase the Vitamin B12 in your diet or consider buying some stronger vitamin B12 supplement tablets: providing at least 50 micrograms, up to 150 micrograms.

Monitoring for vegans should not differ from the rest of the population, and clinicians should only test in the presence of clinical suspicion. However clinical risk assessment should consider various studies showing that vegetarian and vegans, but especially vegans, have a higher risk of deficiency. (Stabler & Allen, 2004).

Additional advice for Care home residents

Low dose Cyanocobalamin (50-150mcg) is of particular importance to address in care homes, as over 30% of the oral B12 tablets are prescribed to those over the age of 80.

Prescriptions of oral cyanocobalamin 50-150mg should not be provided to residents in a care home setting. Under Regulation 14 of the Care Quality Commission (CQC) Guidance for Providers must meet their resident's nutrition & hydration needs.

Similarly, to the recent DHSC guidance on Vitamin D, social care should provide a diet adequate in B12, or should this consumption be hindered due to food preferences/ food refusal such as in dementia, the Residential setting should provide an OTC B12 supplement of 50-150mg.

Considerations for those on Metformin

MHRA have recently updated their advice to reflect that reduced B12 levels, or vitamin B12 deficiency is now considered a common side effect for patients on Metformin, especially for those on higher treatment doses or with existing risk factors.

Patients should not be routinely monitored for B12 deficiency unless there is strong clinical suspicion of Vitamin B12 deficiency.

For Patients who have had a confirmed deficiency treated with Hydroxocobalamin, maintenance of Serum B12 levels, patients should be recommended to increase their dietary intake of B12 or purchase Vitamin B12 (at least 50mcg tablets) to consume daily.

If the patient is not a resident in a care home, or not willing or able to self-purchase, 100 mcg tablets can be prescribed daily for the duration of the metformin treatment.

Nitrous Oxide Abuse consideration

Recreational use of nitrous oxide (N2O) has increased rapidly in recent years and is now the second most used recreational drug among young people in the UK.

The risk of developing Subacute combined Degeneration of the cord (SACD) symptoms increases with greater N2O use: those using one canister per session have around a 1.9% risk of experiencing distal paraesthesia compared with 8.5% in people who use over 100 canisters per session. ([Amussen et al 2020](#)) In general, people presenting to the hospital with N2O-SACD report heavy recreational use over months to years.

Patients often do not spontaneously disclose N2O use and are unlikely to be aware of the risk of SACD, a lower threshold should be used to initiate investigations in those who disclose recreational use.

Advice and guidance from specialist services should be sought.

Non-dietary deficiency maintenance doses

IM injections

Hydroxocobalamin Injections are the recommended treatment. Cyanocobalamin Injections are less cost effective and have no greater clinical benefits.

Given the serious consequences of vitamin B12 deficiency, routine supplementation should remain as Intramuscular injections.

For patients who are unable to tolerate intramuscular injections, Oral high dose supplementation may be considered, however the low-quality evidence for efficacy and increased risk of deficiency /blood tests should be explained to the patient. See [high dose oral section](#).

Self-administration of IM injections:

Consideration of off license self-administration of Hydroxocobalamin injections may be suitable on a patient-by-patient basis. Individual surgeries would be responsible for the training of patients, and the consumables required including sharps bins (FP10 prescribable) and needles (cannot be provided through FP10).

High Dose Oral treatment

There is interest in the oral treatment of B12 deficiency with high dose cyanocobalamin (1mg).

However, the evidence to support the safety and efficacy of high dose oral B12 supplementation is low to very low quality with non-effectiveness of high dose oral treatment ranging from 13-18% in some studies. More robust research with adequate sample sizes and long term follow up are required. (All considered papers are listed in [Appendix 1](#)).

For patients who are unable to tolerate intramuscular injections, High dose (1mg) oral supplementation is a reasonable alternative provided there is good compliance with treatment, and they do not meet any of the following criteria: (BHS 2014).

Oral High dose treatment should not be offered to patients who:

- Require higher doses than 1mg to maintain adequate serum B12 levels
- Have impaired intestinal tracts (e.g. Crohn's, Ulcerative Colitis, strictures, or resections)

Patients who choose high Dose Oral B12 should be informed of the limited evidence base for effectiveness of long term oral B12 supplementation and will require regular monitoring.

Cost and staffing implications of Oral vs IM Vitamin B12 maintenance

	Orobalin 1mg Film-Coated tablets	Hydroxocobalamin 1mg/1ml solution for injection ampoules
Dose and frequency	Oral 1mg tablet/ day	IM injection 5 x 1mg/ml injection every 2 months (for neuro-involvement) And 2-3 months for non-Neuro
Cost per year	£119.9	£4.11 - £6.17
Appointment time	n/a	4-6 appointments/ year (Hollingshurst et al 2006) £38-£57
Monitoring test	£20	n/a
Total per year	£140	£42.11- £63.14

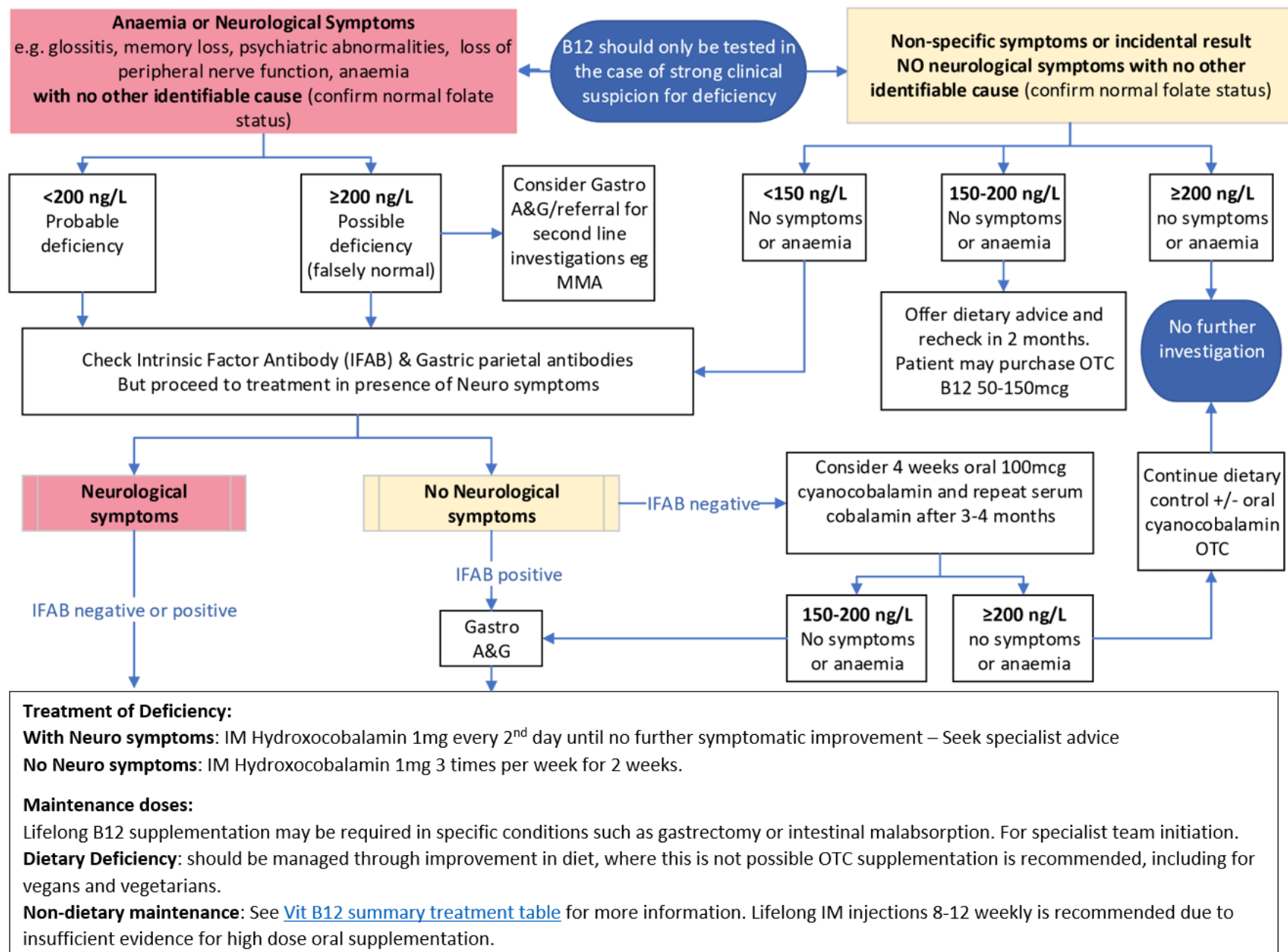
Document ratification details

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Appendix 1: High Oral Dose Evidence Summary Table

Paper	Population	Main points
Cochrane review (2018); Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency.	3 RCT's (Bolaman 2003, Kuziminski 1998, Sarawathy 2012) (total patients 154 across 3 trials, 3-4 month follow up)	- No significant difference between oral and IM - Short term follow-up - Low to very low quality - Small population groups
Oral vitamin B12 replacement: an effective Treatment for vitamin B12 deficiency after total gastrectomy in gastric cancer patients Kim et 2011	60 patient total 35 enrolled gastrectomy patients (oncology), 30 completed oral arm (1500 mcg daily for 3 months). 30 IM (1000 lg weekly for 5 weeks and monthly thereafter.) all with B12 deficiency <200ng/L.	- Incomplete resolution of neuro symptoms in 12/28 patients in oral arm after 3 months - Short term follow-up of 3 months - Small sample group - IM and oral equally effective across 3-month trial
Oral Cyanocobalamin is Effective in the Treatment of Vitamin B12 Deficiency in Crohn's Disease - PubMed (nih.gov) Gomollon et al 2017	94 CD patient total 76 patients with B12 deficiency 18 with history of B12 deficiency Poor quality evidence, not randomised, no blinding, no standardised dose or treatment. Limited analysis per subgroup and inadequately powered.	23 % of oral patients consumed IM liquid orally (unlicensed) 18% did not maintain B12 levels with 1-2mg of oral cyanocobalamin. - A lack of treatment adherence was admitted by 46.6% of patients in who the oral route failed
Efficacy of Long-Term Oral Vitamin B12 Supplementation after Total Gastrectomy: Results from a Prospective Study - PMC (nih.gov) Moleiro et al 2018	26 gastrectomy patients (oncology) 65 months follow-up 1mg daily oral B12 Protocol limitation; no standardised dose or treatment for IM, small sample size	- No differences in deficiency rates between IM and oral at 6,12,18 and 24 months - IM and oral equally effective in maintenance of adequate B12 levels
Oral versus intramuscular administration of vitamin B12 for vitamin B12 deficiency in primary care: a pragmatic, randomised, non-inferiority clinical trial Sanz-Cuesta et al 2020	283 patients ≥65 years with B12 deficiency were randomly assigned to oral (n=140) or IM (n=143) 52 week follow up Sample size reached only 88.4% of the calculated necessary size, inadequately powered study. Non-inferiority established by Bayesian methods set at 10%	- Oral equally effective as IM in charging period. - At 52 weeks oral administration of 1 mg/week had a probability of being inferior (by more than 10%) to the IM route by 20% in PPT analysis. 83.4% of patients preferred oral route, however no significant difference in QOL outcomes between groups. 13.6% of patients withdrawn from oral treatment due to non-effectiveness of treatment (0.6% in IM group).

Appendix 2: B12 deficiency diagnosis and treatment pathway



Appendix 3: Vitamin B12 Treatment Summary Regimens (Table 1)

Treatment	Conditions/ Indication	Regimen	Formulary choice	Cost	Course duration
Deficiency Treatment	Neuro symptoms	IM 1mg every 2nd day until not symptomatic	Hydroxocobalamin 1mg/1ml solution for injection ampoules	£1.03 per dose	As required
Deficiency Treatment	No neuro symptoms	IM 1mg 3 times a week for 2 weeks	Hydroxocobalamin 1mg/1ml solution for injection ampoules	£6.17 per year	2 weeks
Maintenance Dose for non dietary cause	IFAB positive	IM Hydroxocobalamin injections every 8-12 weeks	Hydroxocobalamin 1mg/1ml solution for injection ampoules	£4.25-6.18 per year	lifelong
Maintenance Dose for non dietary cause	IFAB negative: Metformin	Oral 100mcg Cyanocobalamin daily	SELF CARE RECOMMENDED Cyanocobalamin 100 microgram tablets	£25.5 per year	For duration of metformin treatment
Maintenance Dose for non dietary cause	Oral treatment should not be offered to patients who: - Require higher doses than 1mg to maintain adequate serum B12 levels - Have impaired absorption	Lifelong oral 1mg Film-Coated tablets daily High dose (1mg) oral is licensed for the management of non dietary B12 deficiency.	Orobalin 1mg Film-Coated tablets <i>High dose oral Cyanocobalamin should only be used in exceptional cases where patient is unable to tolerate intramuscular injections</i>	£120 per year	Lifelong. regular monitoring of B12 status will be required
Maintenance Dose Dietary cause	Should only be prescribed in exceptional cases where dietary change and purchase of B12 supplements are not possible. Carehome residents should be provided adequate B12 through their diet.	IM Hydroxocobalamin 1mg/1ml injection 6 monthly Or Daily 100mcg Cyanocobalamin	Hydroxocobalamin 1mg/1ml solution for injection ampoules Or Cyanocobalamin 100 microgram tablets	£2.06 per year Or £25.5 per year	Lifelong unless dietary intake of B12 improves

Appendix 4: Vitamin B12 Over the Counter Summary (Table 2)

Product/ Licences status / Constituents	Approximate price and pack size	Suitability for vegetarians/vegans
Boots, Extra strength B12 tablets, 250µg	60 tablets, £6.50 (10.8p per tablet)	Yes
Nature's aid B12 tablets, 1000µg	90 tablets £6.03 (6.7p per tablet)	Yes
Holland and Barret, Vitamin B12 tablets, 100µg	100 tablets £7.63 (7.6p per tablet)	Yes
Asda, Vitamin B12, 100µg tablets	30 tablets £1.50 (5p per tablet)	Yes