Guidelines for the Management of Vitamin B12 Deficiency in Primary Care

Key Points

- If suspicion of neurological symptoms, start treatment whilst waiting for any results.
- IM treatment will be required for most patients, as apart from dietary deficiency, all other causes of vitamin B12 deficiency are attributable to malabsorption. There is little place for the use of low-dose vitamin B12 orally and although larger oral doses of Vitamin B12 using the 1mg tablets may be effective in some patients, prescribing costs would be significantly higher than IM treatment.
- Ongoing monitoring of B12 levels is not required for patients being treated with I.M. hydroxocobalamin.
- If anti-intrinsic factor antibody (IFAB) is present, pernicious anaemia is very likely, but its absence does not rule out a diagnosis of pernicious anaemia.
- The prescribing of oral cyanocobalamin 50microgram or 1mg tablets at NHS expense is not supported in Herefordshire and Worcestershire.

Management

Vitamin B12 reference range in non-pregnant adult: Worcestershire Acute NHS Trust (WAHT) 133-675pmol/L, Wye Valley Trust (WVT) 197-771ng/L. In pregnancy seek advice from secondary care.

- ≥133pmol/L (WAHT)
- ≥197ng/L (WVT)
  - Normal levels no further action required
  - If there is a strong clinical suspicion despite normal levels then seek secondary care advice

- ≥83pmol/L to <133pmol/L (WAHT)
- ≥150ng/L <197ng/L (WVT)
  - Any of the following?
    - Symptomatic – megaloblastic anaemia, †MCV, neurological symptoms, cytopenia
    - GI or intestinal cause e.g. gastrectomy, Zollinger-Ellison syndrome, malabsorption, ileal resection, Cohn’s disease

- <83pmol/L (WAHT)
- <150ng/L (WVT)
  - I.M. hydroxocobalamin
    - See Section A

- B12 dropped <83pmol/L (WAHT)
- <150ng/L (WVT)
  - Positive

- B12 dropped: <83pmol/L or remains at 83-133pmol/L (WAHT)
- <150ng/L or remains at 150-197ng/L (WVT)
  - Check IFAB
    - Negative

  - If B12 remains at 83-133pmol/L (WAHT) or 150-197ng/L (WVT): Check IFAB

  - Continue with dietary advice Section B
    - Oral cyanocobalamin

  - Consider drug induced causes e.g. metformin and drugs that can worsen deficiency e.g. PPIs

  - Recheck levels after 3 months

  - ≥133pmol/L (WAHT)
  - ≥197ng/L (WVT)

  - Continue with dietary advice Section B
    - Oral cyanocobalamin

  - Consider drug induced causes e.g. metformin and drugs that can worsen deficiency e.g. PPIs

  - Recheck levels after 3 months
Section A: Hydroxocobalamin Doses

- **Patients with neurological symptoms** – initially hydroxocobalamin 1 mg I.M. on alternate days until there is no further improvement (review 3 weeks), then hydroxocobalamin 1 mg I.M. every 2 months.
- **Patients with no neurological involvement** - hydroxocobalamin 1 mg I.M. three times a week for 2 weeks. Then maintenance dose depending on cause:
  - Not thought to be diet related — administer hydroxocobalamin 1 mg I.M. every 2–3 months for life.
  - Thought to be diet related — see below

Section B: Diet related vitamin B12 deficiency

- Patients should be given dietary advice about foods that are a good source of vitamin B12 for example eggs, meat, milk and other dairy products, salmon or cod or food such as breakfast cereal or bread which has been fortified with vitamin B12. Where improvement to diet is not enough or not possible (e.g. vegan) over the counter (OTC) oral cyanocobalamin can be recommended to purchase.
- In vegans, treatment may need to be life-long; for other people with dietary deficiency, it may be possible to stop replacement treatment once vitamin B12 levels have been corrected and the diet has improved.
- Where self-care is not appropriate and clinical discretion suggests that prescribing vitamin B12 supplementation would be appropriate, hydroxocobalamin IM 1mg every 6 months should be used.

Notes

**Diagnosis** of anaemia caused by vitamin B12 or folate deficiency should be made through history, examination, and investigations. If there are strong clinical features of B12 deficiency such as megaloblastic anaemia, despite a normal serum vitamin B12 level, consider asking the lab to retain the sample and discuss further testing with them. If there is a suspicion of neurological symptoms start treatment whilst awaiting any additional results.¹

**Evidence** A Cochrane Review² in 2018 looked at three small trials reporting that oral replacement can be as effective as IM vitamin B12 replacement when given at doses of 1000-2000 microgram, as enough can be absorbed by passive diffusion. This was felt to be low quality evidence. This is more common practice in the USA and some European countries but differs from standard CKS and BNF guidance. A licensed 1mg tablet is now available in the UK, but prescribing costs are significantly higher than IM hydroxocobalamin. There remains a concern that the tablets may be less effective if there is malabsorption across the GI tract and concordance would need to be assured if used in non-diet related deficiency, so this is not recommended as a prescribed treatment option.

**Anti-intrinsic factor antibodies**³ are highly specific for pernicious anaemia. It has a PPV of 95% so most patients with a positive result have pernicious anaemia. Sensitivity is low so only about half of patients with pernicious anaemia will have a positive result so it cannot be used to rule it out.

**Drug induced vitamin B12 deficiency** is rare but can be associated with drugs e.g. metformin, colchicine or anticonvulsants. Long term use of H2-receptor antagonists & PPIs can worsen deficiency. B12 deficiency should only be assessed in patients taking medication if objective evidence of deficiency is present. Where deficiency is thought to be a **side effect of medication**, prescribing supplements would be appropriate and in line with the Guidance for over the counter items which should not routinely be prescribed in primary care.

References: