

POLICY STATEMENT FOR VITAMIN B12 PRESCRIBING

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1. INTRODUCTION

1.1 Purpose

Manx Care does not support the prescribing of Vitamin B12 tablets including modified release preparations, for the management of Vitamin B12 deficiency. For patients requiring treatment for Vitamin B12 deficiency IM Hydroxocobalamin should be used.

NICE CKS (<https://cks.nice.org.uk/topics/anaemia-b12-folate-deficiency/>) states that deficiency of Vitamin B12 or Folate is the most common causes of megaloblastic anaemia.

Vitamin B12 is involved with making red blood cells and keeping the nervous system healthy as well as releasing energy from food and using Folic Acid. Adults aged between 19-64 years of age require around 1.5mcg of Vitamin B12 a day.

The Department of Health UK advises that you should be able to get all of the Vitamin B12 you need by eating a varied and balanced diet.

Due to the low absorption rate of Vitamin B12 (Cyanocobalamin) tablets, Manx Care does not recommend their use in Primary Care.

1.2 Scope

Primary & Secondary Care Prescribers

2. POLICY

2.1 Symptoms of deficiency may include:

- a) Cognitive changes, dyspnoea (difficult or laboured breathing), headache, indigestion, loss of appetite, palpitations, tachypnoea (abnormally rapid breathing), visual disturbance, weakness, lethargy.
- b) People with pernicious anaemia may present with symptoms of associated disorder i.e, Myxoedema, other thyroid disorders, vitiligo, stomach cancer or Addison's disease.
- c) Neurological complications associated with Vitamin B12 deficiency include a loss of cutaneous sensation, loss of mental and physical drive, muscle weakness, optical neuropathy, psychiatric disturbances ranging from mild neurosis to severe dementia, symmetrical neuropathy affecting the legs more than the arms and urinary or faecal incontinence.

2.2 Diagnosis

- a) As per NICE CKS on *Anaemia, B12 and Folate Deficiency* (<https://cks.nice.org.uk/topics/anaemia-b12-folate-deficiency/>) the clinically normal level for serum B12 is unclear, although it is thought that serum B12 of less than 200 nanograms/L (148 picomol/L) is sensitive enough to diagnose 97% of people with Vitamin B12 deficiency
- b) There are few absolute indicators for Vitamin B12 to be assessed. These are:
 - Unexplained anaemia
 - Neurological signs or cognitive impairment
 - Post gastric and bariatric surgery
 - Failure to thrive, movement disorders and developmental delay in infants
 - Objective evidence of Vitamin B12 deficiency.
- c) Many non-specific symptoms may be caused by Vitamin B12 deficiency including tiredness, fatigue and other neuropsychiatric symptoms. Vitamin B12 should only be assessed if no other cause can be found.

2.3 Vitamin B12 deficiency in adults

- a) There are currently no indications for Vitamin B12 supplementation without assessment of Vitamin B12 levels.
- b) Determine whether there is an underlying cause for the Vitamin B12 deficiency.
- c) Determine whether the person has experienced complications of anaemia or Vitamin B12 deficiency.
- d) Refer or treat the person where appropriate depending on the suspected cause.
- e) Serum Vitamin B12 levels are not easily correlated with clinical symptoms, although people with levels of less than 100 nanograms/L (75 picomol/L) usually have clinical or metabolic evidence of Vitamin B12 deficiency.
- f) In the elderly, low serum Vitamin B12 concentrations (usually in the range 100-160 nanograms/L) may occur in the absence of anaemia or macrocytosis,

and clinically significant Vitamin B12 deficiency may be present even with serum Vitamin B12 levels in the normal range

- g) Women taking oral contraceptives may show decreased serum Vitamin B12 levels because of a decrease in Cobalamin carrier protein, however, this may not result in deficiency.
- h) Serum Vitamin B12 levels fall in pregnant women and are less reliable in determining deficiency
- i) For people with suspected Vitamin B12 deficiency, arrange:
 - A full blood count to determine mean cell volume (MCV), haematocrit and haemoglobin levels, and a blood film – which help to identify megaloblastic anaemia
 - Measurement of serum Vitamin B12 and folate levels to determine the cause of anaemia, if anaemia suspected.
 - Additional investigations, such as liver function tests, gamma-glutamyl transpeptidase, and/or thyroid function tests to identify the underlying cause. Determining the underlying cause may require specialist referral

2.4 Recommendations:

- a) Recommend dietary changes by introducing foods that are a good source of Vitamin B12. These include: meat, eggs, milk and other dairy products, salmon, cod and foods fortified with Vitamin B12 which are a good alternative to meat.
- b) Advise patients with a mild-deficiency (150 - 180 pg/ml) or patients requiring maintenance therapy following treatment with hydroxocobalamin to take an oral cyanocobalamin (50-150mcg daily between meals) which can be purchased over the counter.
- c) Do not prescribe Vitamin B12 (Cyanocobalamin) tablets, including modified release preparations, as they can be purchased over the counter. Vitamin B12 tablets (Cyanocobalamin) should only be prescribed if the patient is of low body weight / with muscle wastage and cannot tolerate the injections. However the absorption from the tablets will be limited.
- d) Review all existing patients being prescribed Vitamin B12 (Cyanocobalamin) tablets and advise them that these items are no longer available on prescription due to the low absorption rates. If they would like to continue taking these supplements, they are available to be purchased in local pharmacies and health food stores.
- e) Review all patients being prescribed IM Hydroxocobalamin with a mild deficiency (level 145-179ng/L) and advise them that they should be taking Vitamin B12 tablets which will need to be purchased. If no blood test completed within the last 12 months, review and repeat bloods if required.

2.5 Treatment

- a) Do not initiate cyanocobalamin tablets due to poor absorption rates. The B12 Society recommends treatment in the form of injections. Patients with dietary causes (such as vegans) for low levels should purchase Vitamin B12 tablets from a pharmacy or health food store.
- b) People who are vegan should aim to include foods fortified with Vitamin B12 at least three times a day. If these foods are not consumed in adequate quantities, the Vegan society recommends that a Vitamin B12 supplement should be taken, which can be purchased from a health food store or pharmacy. Some products

may not be suitable for Vegans and they should be advised to check labels before purchasing.

- c) Apart from dietary deficiency, all other causes of Vitamin B12 deficiency are attributed to malabsorption. There is little place for Vitamin B12 given orally.
- d) The need for IM hydroxocobalamin should be discussed with each patient individually with regards to appropriateness.
- e) Hydroxocobalamin has completely replaced cyanocobalamin as the drug of choice for therapy as it is retained in the body for longer and only requires maintenance therapy every three months.
- f) If prescribing hydroxocobalamin 1mg IM injection is inappropriate (eg, under a pandemic situation), prescribers are advised to use the licensed 1mg cyanocobalamin tablets (Orobalin®) ; Modified release tablets are not licensed and therefore should not be prescribed.
- g) Parenteral therapy is preferred for faster remission and liver repletion

2.6 Patient with NO neurological involvement

- a) Non-Dietary related deficiency: Initially administer hydroxocobalamin 1mg intramuscularly three times a week for 2 weeks
- b) Vitamin B12 deficiency in adults: For maintenance in non-dietary deficiency, administer hydroxocobalamin 1mg intramuscularly every 2-3 months for life or alternatively, if IM administration is inappropriate (pandemic situation), prescribe 1mg cyanocobalamin (Orobalin®) tablets once a day until regular IM injections can be resumed
- c) Patients should be advised to monitor their symptoms and contact the GP if they begin to experience neurological symptoms such as pins and needles or lack of concentration/problems with memory
- d) Manx Care does not support prescribing for dietary related deficiency. These patients should be sign posted to purchase these supplements at a pharmacy or health food store and given advice on foods that are a good source of Vitamin B12
- e) In vegans, self-care supplementation may need to be life-long
- f) Give dietary advice about foods that are a good source of Vitamin B12

2.7 Monitoring

- All patients should be reviewed on a yearly basis to assess continued need. Some patients may become psychologically dependant on this medication, however if there is no clinical need to continue they should be sign posted to a private service.
- The following monitoring is recommended after treatment has started:

2.8.1 For IM ONLY:

Within 7-10 days of starting treatment: FBC, reticulocyte count

- A rise in the haemoglobin level and an increase in the reticulocyte count to about the normal range indicates the treatment is having a positive effect
- If there is no improvement, check serum folate level (if this has not been done already)

2.8.2 For IM and PO:

After 8 weeks of treatment: FBC, reticulocyte count, iron and folate levels

- The mean cell volume (MCV) should have normalised
- Ongoing monitoring is unnecessary unless a lack of compliance with treatment is suspected, anaemia recurs, or neurological symptoms do not improve or progress.
- Measuring serum Vitamin B12 levels is unhelpful as levels increase with treatment regardless of how effective it is, and retesting is not usually required. However, serum Vitamin B12 can be measured 1-2 months after starting treatment if there is no response.
- Neurological recovery may take some time – improvement begins within one week and complete resolution usually occurs between six weeks and three months.

2.8.3 Costing Information (Drug Tariff prices)

- Cyanocobalamin 50 microgram tablets x 50 costs £16.44
 - 50 microgram daily – annual cost/patient = £119.68
 - 150 microgram daily – annual cost/patient = £359.04
- Hydroxocobalamin 1mg/ml solution for injection x 5 costs £7.13
 - 1mg every 2 months – annual cost/patient = £8.55
 - 1mg every 3 months – annual cost/patient = £5.70
- Cyanocobalamin (Orobalin®) 1mg tablets x 30 costs £9.99
 - Treatment – 2mg twice daily for 8 weeks/patient = £74.59
 - Maintenance – 1mg daily – annual cost/patient = £121.55

2.9 Raised B12

- a) Vitamin B12 does not accumulate at toxic levels.
- b) Raised Vitamin B12 is associated with underlying medical conditions such as liver disease and renal failure.
- c) Raised Vitamin B12 should lead to assessment and referral to the appropriate speciality.

2.10 Treatment Schedules:

2.10.1 Patients with suspected neurological involvement:

DO NOT delay treatment if there is (or is a strong suspicion of neurological involvement

- Seek urgent specialist advice from the haematologist
- Ideally, management should be guided by a specialist, but if specialist advice is not immediately available, consider the following:
 - Initially administer hydroxocobalamin 1mg intramuscularly on alternate days until there is not further improvement, then administer hydroxocobalamin 1mg intramuscularly every 2 months

2.10.2 Patient with NO neurological involvement:

Non-Dietary related deficiency:

- Initially administer hydroxocobalamin 1mg intramuscularly three times a week for 2 weeks

Vitamin B12 deficiency in adults:

- For maintenance in non-dietary deficiency, administer hydroxocobalamin 1mg intramuscularly every 2-3 months for life or alternatively, if IM administration is inappropriate (pandemic situation), prescribe 1mg cyanocobalamin (Orobalin®) tablets once a day until regular IM injections can be resumed

Patients should be advised to monitor their symptoms and contact the GP if they begin to experience neurological symptoms such as pins and needles or lack of concentration/problems with memory

Manx Care does not support prescribing for dietary related deficiency. These patients should be sign posted to purchase these supplements at a pharmacy or health food store and given advice on foods that are a good source of Vitamin B12.

In vegans, self-care supplementation may need to be life-long

Give dietary advice about foods that are a good source of Vitamin B12

3. REFERENCES AND/OR RESOURCES

- NICE CKS on Anaemia, B12 and Folate Deficiency (July 2020)
[https://cks.nice.org.uk/topics/anaemia-b12-folate-deficiency/#:~:text=Megaloblastic%20anaemia%20is%20characterized%20by,\(gr eater%20than%20100%20femtolitres\)](https://cks.nice.org.uk/topics/anaemia-b12-folate-deficiency/#:~:text=Megaloblastic%20anaemia%20is%20characterized%20by,(gr eater%20than%20100%20femtolitres)))
- Pan Mersey Vitamin B12 deficiency in adults
https://www.panmerseyapc.nhs.uk/media/2445/b12_adult.pdf
- Drug Tariff June 2021 <https://www.drugtariff.nhsbsa.nhs.uk/#/00804172-DD/DD00804163/Home>
- British Society for Haematology Guidelines Diagnosis of B12 and Folate Deficiency
- British Society for Haematology (BHS) guidance on Vitamin B12 Replacement during the COVID-19 Pandemic
- Orobalin® Summary of Product Characteristics
<https://www.medicines.org.uk/emc/product/11887>
- BNF Online <https://bnf.nice.org.uk/>
- B12 Society <https://www.theb12society.co.uk/>