

New Medicine Assessment

Cyanocobalamin 50 mcg Tablets

Indication Treatment of: nutritional Vitamin B12 deficiency; vitamin B 12 deficiency following partial gastrectomy; tropical sprue, alone or with folic acid; pernicious anaemia

Recommendation:

BLACK for Treatment of nutritional Vitamin B12 deficiency; Treatment of vitamin B 12 deficiency following partial gastrectomy; Treatment of tropical sprue, alone or with folic acid; Treatment of pernicious anaemia

NOT recommended for use by the NHS in Lancashire.

Includes medicines that NICE has not recommended for use and terminated technology appraisals, unless there is a local need.

This category includes medicines for which there is insufficient evidence of their effectiveness.

Exception: Patients who require treatment of more complex conditions may be considered an exception to the policy on recommendation of a specialist

Summary of supporting evidence:

NHSE: Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs (2018) states:

- There is insufficient high quality evidence to demonstrate the clinical effectiveness of vitamins and minerals. Exceptions include medically diagnosed deficiency, including for those patients who may have a lifelong or chronic condition or have undergone surgery that results in malabsorption. Continuing need should however be reviewed on a regular basis. This does not differentiate between oral and intramuscular administration.¹

SPC: In pernicious anaemia intramuscular therapy is preferable for initial correction of vitamin B12 deficiency. However, if necessary, the oral route may be used to follow this, in which case an adequate dose (at least 300 micrograms) should be given daily and the blood picture must be examined regularly at least every three months for 18 months until stabilised, and then annually.²

NICE CKS Anaemia - B12 and folate deficiency (February 2019)³ advises that a patient with vitamin B12 deficiency anaemia should be treated as follows:

For people with neurological involvement

- Seek urgent specialist advice from a haematologist.
- Ideally, management should be guided by a specialist, but if specialist advice is not immediately available, consider the following:
- Initially administer hydroxocobalamin 1 mg intramuscularly on alternate days until there is no further improvement, then administer hydroxocobalamin 1 mg intramuscularly every 2 months.

For people with no neurological involvement

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

- The maintenance dose depends on whether the deficiency is diet related or not. For people with B12 deficiency that is:
 - Not thought to be diet related: administer hydroxocobalamin 1 mg intramuscularly every 2–3 months for life.
 - Thought to be diet related: advise people either to take oral cyanocobalamin tablets 50–150 micrograms daily between meals, or have a twice-yearly hydroxocobalamin 1 mg injection.
- In vegans, treatment may need to be life-long, whereas in other people with dietary deficiency replacement treatment can be stopped once the vitamin B12 levels have been corrected and the diet has improved.
- Give dietary advice about foods that are a good source of vitamin B12

BNF states Cyanocobalamin is less suitable for prescribing.⁴

A randomized, parallel-group, double-blind, dose-finding trial⁵ to determine the lowest oral dose of cyanocobalamin required to normalize biochemical markers of vitamin B12 deficiency in older people with **mild** vitamin B12 deficiency, defined as a serum vitamin B12 level of 100 to 300 pmol/L (135-406 pg/mL) and a methylmalonic acid level of 0.26 µmol/L or greater has been carried out (in the setting of vitamin B12 deficiency, methylmalonyl–coenzyme A is hydrolyzed to methylmalonic acid (MMA)). Thus, elevated plasma concentrations of MMA and total Hcy (tHcy) can be used as biochemical markers to aid in the diagnosis of vitamin B12 deficiency and to monitor the response to cobalamin supplementation. This study concluded that the lowest dose of oral cyanocobalamin required to normalize mild vitamin B12 deficiency is more than 200 times greater than the recommended dietary allowance, which is approximately 3 mcg daily. The lowest daily oral dose of cyanocobalamin that resulted in 80% to 90% of the maximum reduction in MMA concentrations varied from 647 to 1032 mcg. On average, such doses of cyanocobalamin reduced plasma MMA concentrations by approximately 33%.

A retrospective review of two randomized controlled trials, three prospective papers, one systematic review, and three clinical reviews concluded that oral vitamin B12 replacement at 1000 mcg daily was adequate to replace vitamin B12 levels in patients with pernicious anaemia.⁶

Another systematic review of randomized controlled trial evidence for the effectiveness of oral versus intramuscular vitamin B12 to treat vitamin B12 deficiency suggested that 2000 mcg doses of oral vitamin B12 daily and 1000 mcg doses initially daily and thereafter weekly and then monthly may be as effective as intramuscular administration in obtaining short-term haematological and neurological responses in vitamin B12-deficient patients.⁷

Drug Tariff Prices:⁸

Cyanocobalamin 50microgram tablets x 50 costs £11.42.

At a daily dose of 50mcg, annual cost / patient = £83.37

At a daily dose of 150mcg, annual cost / patient = £250.10

At a daily dose of 300mcg, annual cost / patient =£500.20

At a daily dose of 1000mcg, annual cost per patient = £1,667.32

Hydroxocobalamin 1mg/ml solution for injection x 5 costs £10.28

At a dose of 1mg / 2 months, annual cost / patient = £ 12.34

At a dose of 1mg / 3months, annual cost/ patient = £ 8.22

At a dose of 1mg / 6 months, annual cost / patient = £ 4.11 (as per NICE CKS- diet related)

References

¹ NHSE Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs <https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-guidance-for-ccgs.pdf>

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- ² SPC Cyanocobalamin 50 mcg Tablets <https://www.medicines.org.uk/emc/product/5716>
- ³ NICE CKS Anaemia - B12 and folate deficiency <https://cks.nice.org.uk/anaemia-b12-and-folate-deficiency#!scenario>
- ⁴ BNF Cyanocobalamin <https://bnf.nice.org.uk/drug/cyanocobalamin.html#indicationsAndDoses>
- ⁵ Eussen et al; Oral Cyanocobalamin Supplementation in Older People With Vitamin B12 Deficiency A Dose-Finding Trial Arch Intern Med. 2005;165(10):1167-1172
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/486565#ref-oi40807-11>
- ⁶ Chan et al; Oral Vitamin B12 Replacement for the Treatment of Pernicious Anaemia . Frontiers in Medicine August 2016; Vol 3; Article 38
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4993789/#targetText=Oral%20vitamin%20B12%20was%20effective,after%203%20months%20of%20treatment>.
- ⁷ Butler CC et al., Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency: a systematic review of randomized controlled trials, Family Practice 2006 Jun;23(3):279-85. Epub 2006 Apr 3 <https://academic.oup.com/fampra/article/23/3/279/476697>
- ⁸ Drug Tariff September 2019 <http://www.drugtariff.nhsbsa.nhs.uk/#/00730181-DC/DC00729655/Part%20VIII%20products%20C>