

**INTERIM RECOMMENDATION FOR DRUG ADMINISTRATION DURING THE COVID-19 PERIOD
(UPDATE: 29/04/2020)**

DRUG: Vitamin B12 (Hydroxocobalamin 1000mcg) Intramuscular Injections

In light of the COVID-19 outbreak there have been many queries regarding patients requiring regular Vitamin B12 injections. Although the preferable route is the parenteral route according to NICE guidelines, due to the current pandemic, the CCG issued updated interim advice (24/04/2020) regarding the management of patient receiving vitamin B12 Injections. This updated advice incorporated guidance from the British Society for Haematology (BSH).

Following the CCG's interim recommendation update on 24th April 2020, the British Society for Haematology (BSH) has collaborated to the Pernicious Anaemia Society (PAS) to review its stance on the management of patient non-diet related vitamin B12 deficiency. The prescribing options following the most recent update are highlighted below.

Dietary Vitamin B12 Deficiency:

Doses of 50-150 micrograms daily of cyanocobalamin may be offered as alternative to intramuscular injections using 50 microgram tablets which are a licensed medicine, This formulation may not be acceptable to all patients (as they may contain lactose), individual formulations should be checked.

Non -Dietary Vitamin B12 Deficiency:

Omit Hydroxocobalamin (where applicable):

British Society for Haematology has advised that the need for intramuscular (IM) hydroxocobalamin should be discussed with each patient individually. The BSH recommend that screening questions for COVID-19 infection are asked before patients attend their GP surgeries.

Patients who are already self-administering IM hydroxocobalamin should continue to do so but BSH do not recommend a patient switching to self-administration during the COVID-19 pandemic since instruction is likely to be difficult.

Oral Administration of cyanocobalamin:

The updated BSH advice has suggested for symptomatic patients, as an alternative, oral cyanocobalamin can be offered at a dose of 1 mg per day until regular IM hydroxocobalamin can be resumed, i.e. once GP surgeries are able to do so safely, aiming to have a shortest possible break from regular injections.

Please note, although this dose is not licenced in the UK, cyanocobalamin 1000 microgram (1mg) tablets are available as food supplements over the counter. These supplement products are also prescribable on FP10, but are unlicensed.

Patients should be advised to monitor their symptoms and should contact their GP for further review if they begin to experience neurological or neuropsychiatric symptoms such as pins and needles, numbness, problem with memory or concentration or irritability.

This updated guidance is summarised in the Appendix 1 and provides details in terms of the indication-specific use of vitamin B12, the prescribing options during this phase, any associated monitoring requirements and patient specific advice. Taking this guidance into account, the CCG is updating its previous interim advice provided (released on 24/04/2020).

The final decision in each case will be a clinical decision made by the prescriber. **When prescribing an unlicensed or off-licence treatment, GMC guidance on unlicensed and off-licence prescribing should be followed.**

For further support and prescribing guidance, please contact the CCGs Medicines Optimisation team via email: nstccg.staffsmedicineoptimisationqueries@nhs.net

Patient facing websites that provide dietary advice for reference:

<https://www.bda.uk.com/food-health/food-facts.html>

References:

1. Cyanocobalamin 50mcg Tablets <https://www.medicines.org.uk/emc/product/5716/smpc>
2. Anaemia - B12 and folate deficiency NICE: Feb 2019[Accessed 25/3/20] <https://cks.nice.org.uk/anaemia-b12-and-folate-deficiency>
3. Treatment Vit B12 or Folate Deficiency <https://www.nhs.uk/conditions/vitamin-b12-or-folate-deficiency-tment/> [Accessed 25/3/2020]
4. BNF.org [accessed 25/3/20] <https://bnf.nice.org.uk/drug/cyanocobalamin.html>
5. Oral Vit B12 Compared to Intramuscular vitamin B12 for vitamin B12 deficiency <https://www.cochrane.org/oral-vitamin-b12> [accessed 26/3/2020]
6. MedOptimise® Complete Prescribing Analysis Report March 2020 www.medoptimise.co.uk [accessed 27/3/2020]
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8. NICE CKS <https://cks.nice.org.uk/anaemia-b12-and-folate-deficiency#!scenario>
9. British Society for Haematology (BSH) guidance on Vitamin B12 replacement during the COVID-19 pandemic- updated 24/04/2020. [accessed 28/4/2020]
10. Castelli, M.C., Friedman, K., Sherry, J., Brazzillo, K., Genoble, L., Bhargava, P. and Riley, M.G.I., 2011. Comparing the efficacy and tolerability of a new daily oral vitamin B12 formulation and intermittent intramuscular vitamin B12 in normalizing low cobalamin levels: a randomized, open-label, parallel-group study. *Clinical therapeutics*, 33(3), pp.358-371.
11. Devalia, V., Hamilton, M.S., Molloy, A.M. and British Committee for Standards in Haematology, 2014. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *British journal of haematology*, 166(4), pp.496-513
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14. Kuzminski, A.M., Del Giacco, E.J., Allen, R.H., Stabler, S.P. and Lindenbaum, J., 1998. Effective treatment of cobalamin deficiency with oral cobalamin. *Blood, The Journal of the American Society of Hematology*, 92(4), pp.1191-1198.
15. National Institute for Health and Care Excellence (2019) B12 and Folate deficiency (Clinical Knowledge Summaries). Available at <https://cks.nice.org.uk/anaemia-b12-and-folate-deficiency#!scenarioRecommendation>
16. Stabler, S.P., 2013. Vitamin B12 deficiency. *New England Journal of Medicine*, 368(2), pp.149-160

Appendix 1

B12 Deficiency Cause	NICE CKS: Anaemia - B12 and folate deficiency	BSH guidance on B12 supplements during COVID pandemic	Management during COVID pandemic			
			Prescribing Options	Monitoring	Patient Counselling	Product Selection
<p>NOT thought to be diet related</p> <p>(Examples include: Pernicious anaemia, prior gastrectomy, bariatric surgery, achlorhydria, pancreatic insufficiency, short bowel syndrome, bacterial overgrowth, inflammatory bowel disease)</p>	<p>Administer hydroxocobalamin 1 mg intramuscularly every 2–3 months for life.</p>	<p>BSH advise that the need for intramuscular (IM) hydroxocobalamin should be discussed with each patient individually during COVID19 outbreak.</p> <p>The BSH recommend that screening questions for COVID-19 infection are asked before patients attend their GP surgeries. Alternatives to attending the GP surgery such as local pharmacies or home administration by district nurses should be explored.</p>	<p>Oral (cyanocobalamin) B12 1mg per day* can be offered as an alternative until regular IM hydroxocobalamin can be resumed, i.e. once GP surgeries are able to do so safely, aiming to have a shortest possible break from regular injections.</p> <p>If still very symptomatic then B12 injection can be given with clear understanding that the interaction with healthcare increases transmission risk of COVID19.</p>	<p>BSH suggests taking the opportunity to measure B12. (please note: taking the opportunity to measure B12 - this applies if a patient is still very symptomatic and is attending for a B12 injection)</p>	<p>Patients should be counselled regarding the symptoms of vitamin B12 deficiency (mouth ulcers, sore mouth, tiredness, neurological or neuropsychiatric symptoms such as pins and needles (paraesthesia), numbness, problem with memory or concentration, or irritability) and should contact their GP if they begin to experience these symptoms</p>	<p>The cyanocobalamin 50mcg tablets are available as a licenced product in the UK.</p> <p>*Higher strengths (1000mcg) are available as food supplements OTC from the local Community Pharmacy, Supermarkets and Health Shops. These supplementary products are also prescribable but are unlicensed.</p>
<p>Thought to be diet related</p>	<p>Advise people either to take oral cyanocobalamin tablets 50–150 micrograms daily between meals or have a twice-yearly Hydroxocobalamin 1 mg injection.</p> <p>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.</p>	<p>An alternative is to offer oral cyanocobalamin tablets, 50–150 micrograms, daily between meals. The BSH recommends reassessing serum B12 prior to recommencing IM hydroxocobalamin.</p> <p>However, many of these patients may be vitamin B12 replete with adequate levels within the liver, and therefore may be able to safely stop taking vitamin B12 supplements possibly for up to a year (<i>Hoffbrand 2016</i>).</p>	<p>This group of patients can be offered oral (cyanocobalamin) B12 50-150 mcg daily between meals if needed.</p>	<p>BSH suggests measuring serum B12 level before recommencing IM hydroxocobalamin</p>	<p>Give dietary advice about foods that are a good source of vitamin B12: Good sources of vitamin B12 include Eggs, meat, milk and other dairy products and fish (salmon and cod). Foods which have been fortified with vitamin B12 (for example some soy products, and some breakfast cereals and breads) are good alternative sources.</p> <p>Dietary advice should be given to all patients. Patients on vegetarian and especially vegan diets should continue taking oral supplements</p>	<p>To check whether a product is suitable for vegans, manufacturers may need to be contacted directly as formulations may differ between products. For instance, Advanz Pharma state that their cyanocobalamin 50 microgram tablets are not suitable for vegans as they contain lactose of animal origin.</p>