Medicines & Healthcare products Regulatory Agency

10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom
gov.uk/mhra

[redacted]

10 November 2023

Dear [redacted]

FOI 23/724: Vitamin B12

Thank you for your communication, dated 01 October 2023, in which you requested information concerning Vitamin B12 injectable medicines. Please find below, our responses to your queries:

MHRA response:

Background
Table 1 below includes summary details of the injectable Vitamin B12 medicinal products containing hydroxocobalamin (or a hydroxocobalamin salt), authorised as prescription only medicines in the UK or Great Britain (GB, consisting of England, Scotland and Wales).

Further information on these Marketing Authorisations is available on the MHRA website: https://products.mhra.gov.uk/.

Additionally, the European Public Assessment Report for Cyanokit 2.5g and 5 g powder for solution for infusion (PLGB 43956/0004) can be found on the European Medicines Agency's website at:
https://www.ema.europa.eu/en/medicines/human/EPAR/cyanokit.

Table 1: Hydroxocobalamin Marketing Authorisations

Authorisation Number	Product Name	Active Substance	Indication	Maintenance dose
PL 12762/0008	Hydroxocobalamin 1 mg/ml Solution for Injection	Hydroxocobalamin acetate	Addisonian pernicious anaemia, prophylaxis and treatment of other macrocytic anaemias associated with vitamin B12 deficiency, tobacco amblyopia and Leber's optic atrophy	Addisonian pernicious anaemias and other macrocytic anaemias without neurological involvement: 1000 micrograms every two to three months Addisonian pernicious anaemias and other macrocytic anaemias with neurological involvement: 1000 micrograms every two of three months Tobacco amblyopia and Leber's optic atrophy: 1000 micrograms every one to three months as required
PL 20072/0217	Cobalin-H/ Hydroxocobalamin 1000 microgram/ml Injection	Hydroxocobalamin	Treatment of Addisonian pernicious anaemia, prophylaxis and treatment of other macrocytic anaemias due to vitamin B12 deficiency, treatment of tobacco amblyopia and treatment of Leber's atrophy	Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement: 1000 micrograms every two or three months Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement: 1000 micrograms every two months Tobacco amblyopia and Leber's optic atrophy: 1000 micrograms every three months or as required
PL 20075/0691	Hydroxocobalamin 1mg in 1 ml, solution for injection	Hydroxocobalamin acetate	Treatment of Addisonian Pernicious anaemia, prophylaxis and treatment of other macrocytic anaemias associated with Vitamin B12 deficiency, treatment of tobacco amblyopia and treatment of Leber's optic atrophy	Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement: 1 mg every two or three months Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement: 1 mg every 2 months Tobacco amblyopia and Leber's optic atrophy: 1 mg monthly
PL 21597/0060	Hydroxocobalamin 1mg/ml Solution for Injection	Hydroxocobalamin acetate	Addisonian pernicious anaemia, prophylaxis and treatment of other macrocytic anaemias associated with vitamin B12 deficiency, tobacco amblyopia and Leber's optic atrophy	Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement: 1000 micrograms every two to three months Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement: 1000 micrograms every two or three months Tobacco amblyopia and Leber's optic atrophy: 1000 micrograms every one to three months as required

Table 1 (cont'd): Hydroxocobalamin Marketing Authorisations

Authorisation Number	Product Name	Active Substance	Indication	Maintenance dose
PL 36301/0011	Neo-Cytamen 1000 micrograms/ml solution for injection/ Hydroxocobalamin 1000 micrograms/ml solution for injection	Hydroxocobalamin chloride	Addisonian pernicious anaemia, prophylaxis and treatment of other macrocytic anaemias associated with vitamin B12 deficiency, tobacco amblyopia and Leber's optic atrophy	Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement: 1000 micrograms every two to three months Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement: 1000 micrograms every two months Tobacco amblyopia and Leber's optic atrophy: 1000 micrograms monthly
PLGB 43956/0003-0004	Cyanokit 2.5 g and 5 g powder for solution for infusion	Hydroxocobalamin	Treatment of known or suspected cyanide poisoning in all age ranges Cyanokit is to be administered together with appropriate decontamination and supportive measures (see section 4.4 of the Summary of Product Characteristics).	Maintenance dose: Not applicable Refer to the product information for details of dosage.

1. **Please provide me with details of why Vitamin B12 injectable (hydroxocobalamin) is a prescription only medicine, including medical supporting documentation.**

The approval of the legal supply status or classification (Prescription Only Medicine status (POM), Pharmacy (P) status or General Sales List status (GSL)) of an authorised medicinal product is determined on the basis of the assessment of the data submitted to support the application for the Marketing Authorisation.

The criteria for classification of medicines are set out in Regulation 62 of the Human Medicines Regulations 2012 [SI 2012/2016 as amended]. Regulation 62(3) is clear that if the medicine is usually prescribed for parenteral administration – that is by injection – then the medicinal product must by law be classified as a prescription only medicine. Other aspects within Regulation 62 also apply in consideration of the most suitable legal status of vitamin B12 (hydroxocobalamin) injection. An important aspect is that conditions which require diagnosis and management by a physician, as is the case for which vitamin B12 (hydroxocobalamin) injection medicinal products are authorised in UK, will also fall to be considered as POM products. Therefore, the reclassification of vitamin B12 injections to non-prescription medicines to enable these to be purchased over-the counter is not supported by current legislation.

To note, there are injectable vitamin B12 products available which are not licensed medicinal products and are administered for general health supplementation and intended, or marketed, for non-medicinal purposes. These products are not included under the definition of a medicinal product within the Human Medicines Regulations 2012 and consequently fall outside the remit of MHRA. It must be clear in the advertising of these products that they do not have a medical purpose; for example, they are not intended to treat a deficiency or an underlying condition which is a consequence of a deficiency, and they must be clearly distinguishable from licensed medicines.

2. **In addition, why maintenance doses of vitamin B12 injectable are only prescribed on a 1 ml dose every three months**.

Please note that the approved maintenance doses in the UK for injectable Vitamin B12 medicinal products containing hydroxocobalamin (or a hydroxocobalamin salt) indicated for Vitamin B12 deficiency or related disorders vary from 1000 micrograms (1 ml) every 1, 2 or 3 months, depending on the Marketing Authorisation and the indication.

The approval of the instructions of use of an authorised medicinal product is determined on the basis of the assessment of the data submitted to support the application for the Marketing Authorisation.

We have searched our records (including the records for the original UK brand leader Neo-Cytamen 1000 Injection (PLR 00004/5026)) and have not found the original justification that was submitted that would address your query. Therefore, having exhausted all the usual avenues in our search for this information, we have concluded that, it is no longer on our systems in a retrievable form.

3. **Finally, why it is not possible for doctors to prescribe vitamin B12 methylcobalamin injectable.**

There is no vitamin B12 methylcobalamin medicinal product authorised by the MHRA for use within the UK.

Prescribers may resort to unlicensed medicine if they believe it to be required. We refer you to the page on the General Medical Council (the public body that maintains the official register of medical practitioners within the United Kingdom) on the prescribing of unlicensed medicines: https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines.

We now consider this FOI request closed.

If you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within 2 months of the date you receive this response and addressed to: info@mhra.gov.uk.

Please remember to quote the reference number above in any future communications.

If you were to remain dissatisfied with the outcome of the internal review, you would have the right to apply directly to the Information Commissioner for a decision. Please bear in mind that the Information Commissioner will not normally review our handling of your request unless you have first contacted us to conduct an internal review. The Information Commissioner can be contacted at:

Information Commissioner's Office
Wycliffe House
Water Lane, Wilmslow
Cheshire
SK9 5AF.

Yours sincerely,

The FOI Team,
Healthcare Quality and Access.