Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

Position Statement: Treatment of diagnosed vitamin B12 deficiency

Hertfordshire and West Essex ICS does not support prescription of oral cyanocobalamin to treat diagnosed vitamin B12 deficiency

Recommendations

1. **For all patients currently prescribed continuous oral 50 microgram or 1 milligram cyanocobalamin:**
   If treatment is still required replace oral cyanocobalamin with hydroxocobalamin injection at appropriate intervals.

   Where replacement is due to diet related vitamin B12 deficiency (and oral cyanocobalamin is appropriate for the patient), advise over the counter purchase in line with NHS England Conditions for which over the counter items should not routinely be prescribed in primary care.

2. **For all new patients with non-diet related vitamin B12 deficiency requiring treatment:**
   Hydroxocobalamin injection is recommended. Oral treatment is not recommended.

3. **For all new patients with diet related vitamin B12 deficiency requiring treatment:**
   Consider initial hydroxocobalamin injection followed by over the counter oral maintenance cyanocobalamin in line with NHS England Conditions for which over the counter items should not routinely be prescribed in primary care.

   Where oral maintenance cyanocobalamin is not considered appropriate and ongoing management is required, hydroxocobalamin injection can be continued twice a year.

4. **For patients taking metformin:**
   Consider periodic serum vitamin B12 monitoring particularly where there is a strong clinical suggestion of B12 deficiency. See below for further information.

Note: Check serum folate in B12 deficiency.
Secondary folate deficiency can occur in B12 deficiency and both deficiencies may need to be treated. In the event of combined B12 and folate deficiency, commence hydroxocobalamin intramuscular injections twenty-four hours ahead of folate to protect neuron function. In severe B12 or folate deficiency, supplementation may cause severe hypokalaemia as red blood cell production restarts.

Rationale

NICE Clinical Knowledge Summary (2020) advises that maintenance of diagnosed non-diet related vitamin B12 deficiency (i.e. due to pernicious anaemia, intrinsic factor deficiency or malabsorption) **requires administration of hydroxocobalamin 1 milligram intramuscularly every 2–3 months for life** unless advised otherwise by a haematologist.

It is important to note that patients with diagnosed non-diet related vitamin B12 deficiency are unlikely to be able to absorb sufficient oral cyanocobalamin to adequately treat deficiency in the long term. Prescribed oral cyanocobalamin is also considerably more expensive than 1 milligram injectable hydroxocobalamin as below:

Drug	Prescribed as	Dose & frequency required	Cost to the NHS per patient per year*
Hydroxocobalamin	5 x 1 milligram/ml injection = £11.85	1milligram injection every 2 – 3 months	£9.48 - £14.22
Cyanocobalamin	50 x 50 microgram tablets = £8.58	1 – 3 tablets per day	£62.63 - £187.90

*April 2024 Drug Tariff price

For diagnosed (by blood test) vitamin B12 deficiency which is thought to be diet related and without neurological involvement, after initial hydroxocobalamin injection, NICE Clinical Knowledge Summary (2020) advises maintenance treatment with either oral cyanocobalamin tablets 50–150 micrograms daily between meals, or twice-yearly hydroxocobalamin 1 mg intramuscular injection. Over the counter purchase of oral maintenance treatment should be advised in line with NHS England Conditions for which over the counter items should not routinely be prescribed in primary care.

ICB prescribing rates

In 2020, at the beginning of the COVID-19 pandemic, national guidance from the British Society of Haematologists advised "*As an alternative* [to injectable hydroxocobalamin for treating vitamin B12 deficiency], *oral cyanocobalamin can be offered ……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.*" This guidance was intended to support practices and vulnerable patients in the first few, uncertain months of the pandemic.

ePACT2 data (see Chart 1 overleaf) clearly demonstrates that prescribing of 50 microgram oral cyanocobalamin remains higher than pre-pandemic.

Vitamin B12 and Metformin

Department of Health and Social Care (DHSC) Drug Safety Update: Metformin and reduced vitamin B12 levels (2022) advises that the risk of low vitamin B12 levels is increased for those with risk factors for vitamin B12 deficiency who also take metformin in either a higher dose or for a longer period of time.

For these patients DHSC advises:

- Consider periodic vitamin B12 monitoring
- Check serum vitamin B12 levels in patients who have symptoms suggestive of vitamin B12 deficiency.

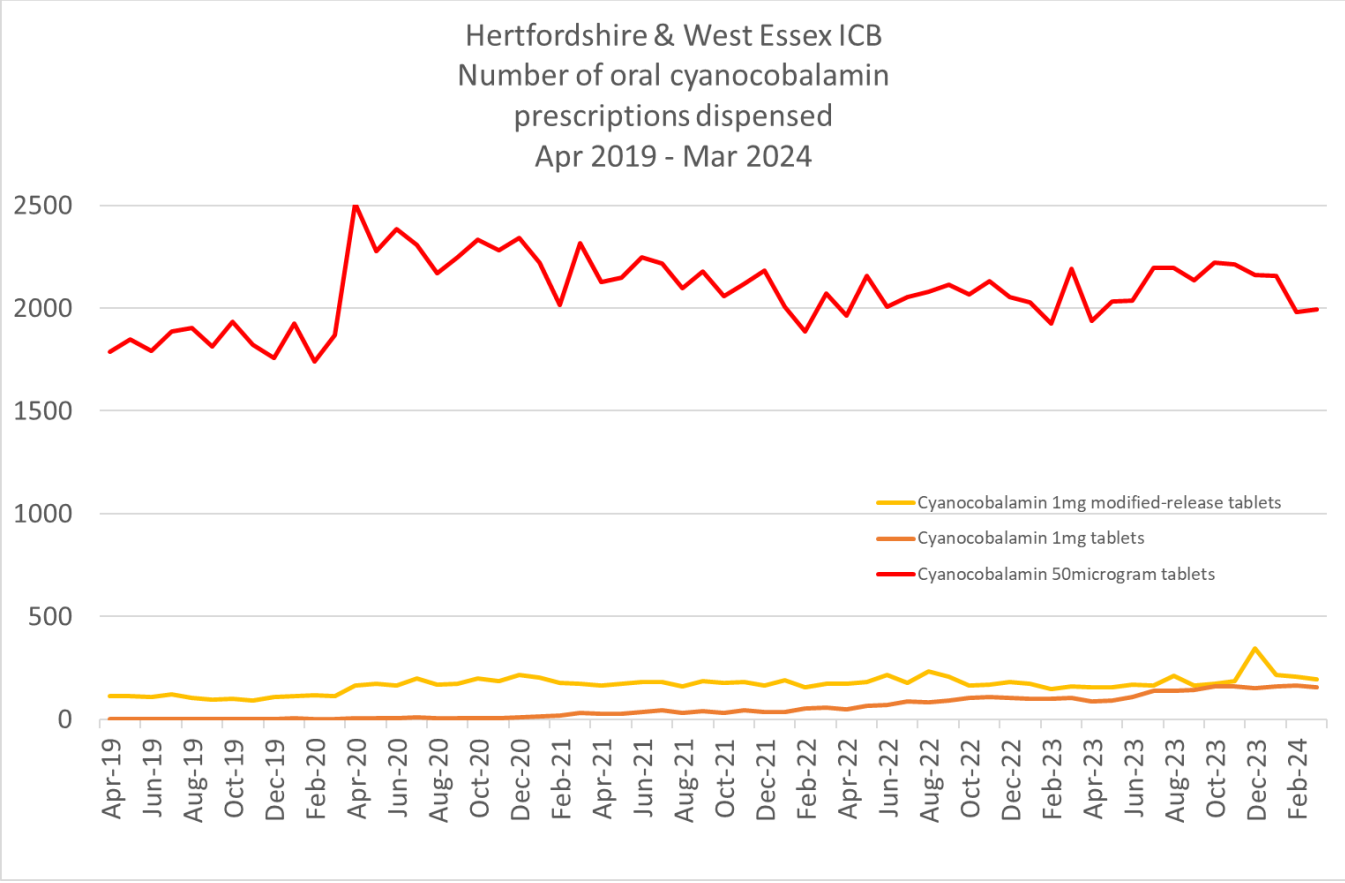
There is no consensus guideline on how best to treat low serum vitamin B12 levels related to

metformin therapy and low levels could co-exist with other causes. Whether to advise purchase of oral vitamin B12 replacement or prescribe injectable replacement should be based on clinical assessment.

In patients taking metformin the British Journal of Haematology stresses the importance of ruling out pernicious anaemia, which would require lifelong hydroxocobalamin injections *(Br J Haematol. 2014, 166(4): 496-513)*.

There is no evidence to support prophylactic oral vitamin B12 treatment in patients taking metformin.

Chart 1 - Hertfordshire and West Essex ICB - Monthly dispensed oral cyanocobalamin prescriptions



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