Guidance on the review of patients on intramuscular vitamin B12 (hydroxocobalamin) injections and identifying those in whom this may be stopped

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Background

There are an increasing number of patients on long-term Vitamin B12 (hydroxocobalamin) intramuscular (IM) injections in NHS Lanarkshire (NHSL) which is having a significant impact on treatment room and district nursing caseloads, up to 20-25% in some instances. Local audits have shown that Vitamin B12 injection is not clinically indicated in a number of patients. However, it is important that patients are properly assessed before long-term treatment is stopped as B12 deficiency can potentially cause irreversible neurological damage. In order to address this, a Short Life Working Group was established to develop this guideline. It aims at guiding healthcare professionals to identify patients in whom Vitamin B12 injections can be stopped.

The widespread adoption of this guideline and the associated operational protocols will support the establishment of a NHSL-wide approach which:

- Improves patient care by ensuring treatment is clinically indicated
- Reduces use of treatment room services capacity
- Addresses the current high level of testing through the reduction in unnecessary testing
- Realises savings in laboratory and prescribing costs

Step one

Identify from patient's records:

- Was the original diagnosis of PERNICIOUS ANAEMIA (PA) confirmed by a previous positive Intrinsic Factor (IF) antibody?
- Did the patient present with neurological symptoms (e.g. pins and needles, numbness, unsteadiness, cognitive changes or visual disturbance) which resolved on treatment?
- Does the patient have Glossitis (clinician confirmed inflammation of the tongue) that has failed to resolve with oral treatment?
- Does the patient have known inflammatory bowel disease (e.g. ulcerative colitis, Crohn's disease)?
- Does the patient have a previous gastrectomy/bariatric surgery/terminal ileal resection or diagnosis of short bowel syndrome?
- Does the patient have pancreatic insufficiency?
- Is the patient receiving pemetrexed based chemotherapy? These patients require IM hydroxocobalamin administered every 9 weeks (plus folic acid 400micrograms once daily) on a continuous basis during treatment. It is important that patients continue to receive this as a supportive medicine throughout their treatment as it minimises toxicity. Oncologists typically write to the patient's GP to initiate treatment at least a week before starting chemotherapy.

If the answer is YES to ANY of the above questions, IM Vitamin B12 (hydroxocobalamin) injection 1mg should be continued long-term, i.e. every 2 months for those who presented with neurological symptoms and every 3 months for others**. It is recommended that patients are issued one ampoule per prescription (not a pack of 5) in order to prevent wastage. Consider writing the prescription to clarify time of review and formalisation of indication as per Appendix 1. The health care professional that reviews the patient record has a responsibility to advise the other relevant parties (i.e. Treatment Room / District Nurse / Practice) of the outcome of the review.

There is no need to monitor B12 levels in patients on regular B12 injections. However, yearly full blood count (FBC) monitoring is recommended.

NOTE: Low B12 level is not uncommonly seen in pregnancy. This is often not clinically significant and management of this specific issue is out-with the scope of this guideline.
***Patient's on pemetrexed should follow dosing schedule and duration as noted above and as guided by the Oncologist.*

If the answer is NO to ALL of the above questions, then proceed to Step two below.

Where Vitamin B12 injections are continued long-term, consider teaching self-administration to patient/carer. There are anecdotal reports of patients sourcing auto-injectors for self-use. These products are however not licenced in the UK and should not be prescribed.

CAUTION is advised on stopping Vitamin B12 injections in patients with concomitant folate deficiency as this may cause a significant fall in the B12 level and precipitate sub-acute degeneration of the cord. Consider continuing on B12 injection if indicated or give a minimum of one injection before starting folate replacement. Repeat both B12 and folate levels in 3 months. Subsequent management of low B12 can be guided by Step two.

Step two (i.e. if answer is NO to questions above)

Please ensure all test results and subsequent decisions/actions are clearly documented and read-coded in the patient's records.

Patients will require to be assessed by a registered healthcare professional who is competent to determine the following:

1. Any neurological symptoms
2. Glossitis
3. Abnormal full blood count, i.e. anaemia/any cytopenias or macrocytosis

If any of these are present, IM Vitamin B12 (hydroxocobalamin) injection 1mg should be continued long-term, i.e. every 2 months for those who presented with neurological symptoms and every 3 months for others. It is recommended that patients are issued one ampoule per prescription (not a pack of 5) in order to prevent wastage. Consider writing the prescription to clarify time of review and formalisation of indication as per Appendix 1. **There is no need to monitor B12 levels in patients on regular B12 injections. However, yearly FBC monitoring is recommended.**

If patient has none of the above (i.e. asymptomatic):

- Discuss and document consideration of stopping Vitamin B12 injection with patient, include dietary advice as per Appendix 2. Oral Vitamin B12 (cyanocobalamin) should **not** be prescribed as an alternative (unless used as a trial in line with the specifications below and ensuring the patient hasn't already undergone a trial of oral cyanocobalamin);
- Counsel patient on potential symptoms to report after stopping regular Vitamin B12 injection i.e. symptoms of anaemia, painful tongue, neurological symptoms

such pins and needles, numbness, unsteadiness, cognitive changes or visual disturbance;
- Arrange repeat B12 level whenever next injection is due and then take action as per guidance below.

The health care professional that assesses the patient has a responsibility to advise the other relevant parties (i.e. Treatment Room / District Nurse / Practice) of the outcome of the assessment.

Management of repeat B12 levels in asymptomatic patients who have stopped Vitamin B12 injections:

Normal/High B12 level (>200 pg/ml)

- Stop long-term Vitamin B12 injections.
- Monitor B12 level every 6 months for 3 years.

Low B12 level (<150 pg/ml)

- Check IF antibody:
  - If positive, i.e. diagnostic of PA, offer long-term IM Vitamin B12 injection 1mg every 3 months.
  - If negative, and still asymptomatic, offer 2-month trial of oral cyanocobalamin 50-150micrograms per day as an acute prescription. Repeat B12 level in 3 months. If patient has responded to oral treatment, manage with dietary adjustment long-term (see Appendix 2) and monitor B12 level every 6 months for 3 years. If B12 level remains persistently low, review compliance history and consider long-term IM Vitamin B12 injection 1mg every 3 months.

Borderline low B12 level (150-200 pg/ml)

- Review diet and offer dietary advice as per Appendix 2.
- In the absence of haematological or neurological symptoms, avoid rechecking in patients on **hormonal preparations** (e.g. oral and depot contraception, HRT) as this class of drugs can cause a low (or apparent low) B12 level, which does not need treatment.
- Repeat B12 level in 3 months. If still low (i.e. <200 pg/ml), check IF antibody:
  - If positive, this will be diagnostic of PA and merit long-term IM Vitamin B12 injection 1mg every 3 months.
  - If negative, and still asymptomatic, offer 2-month trial of oral cyanocobalamin 50-150 micrograms per day as an acute prescription. **Pernicious anaemia cannot be excluded as IF can be negative in 50% of patients.** Repeat B12 level in 3 months. If patient has responded to oral treatment, manage with dietary adjustment long-term (see Appendix 2) and monitor B12 level every 6 months for 3 years. If B12 level remains persistently borderline low, review compliance history and consider long-term IM Vitamin B12 injection 1mg every 3 months.

NOTE: A normal B12 level after a course of oral B12 makes PA unlikely as a cause of previous low B12 level. Potential causes could have been dietary insufficiency or food cobalamin malabsorption syndrome, which is more common in the elderly with

atrophic gastritis or chronic *H. pylori* infection. Repeat B12 level again in 6 months and if still low, consider 3-monthly IM Vitamin B12 1mg injections.

Vegans/Vegetarians

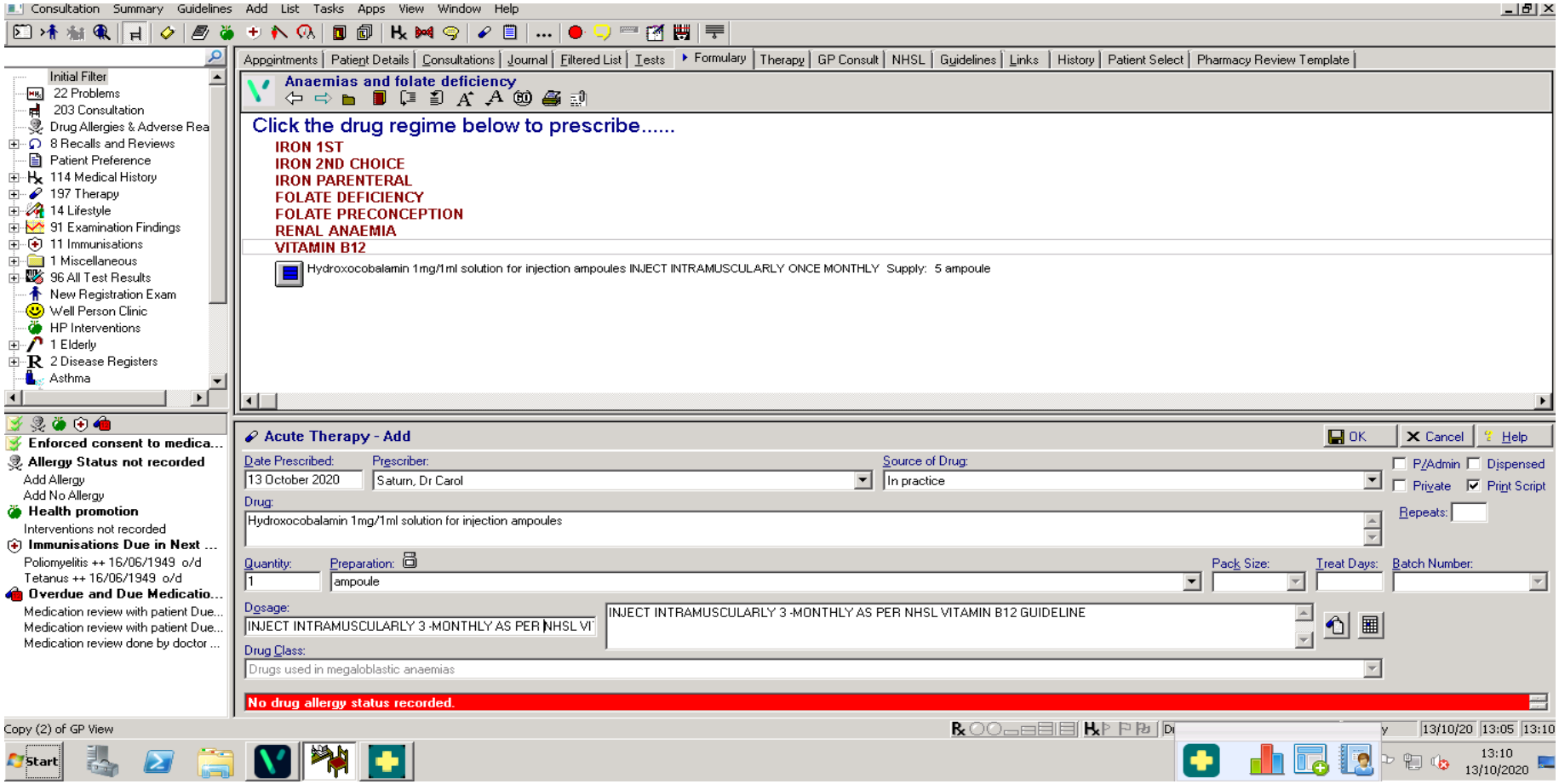
Vegans and vegetarians are at increased risk of B12 deficiency. Unless there are any of the conditions identified in Step one (above) i.e. meriting long-term Vitamin B12 injection, this should be corrected by dietary adjustment and patients advised to supplement with suitable oral vitamin preparations containing B12 that can be purchased from pharmacies, health food shops and supermarkets. **Avoid checking B12 level in this group of patients unless there are haematological or neurological features of B12 deficiency.**

The Vegan Society recommends B12 supplements of at least 10 micrograms **daily** or at least 2000 micrograms **weekly**. Vitamin supplements have variable bioavailability. Nutrients within foods are much more readily absorbed than those in an artificial supplement form. If an individual has a well-balanced vegetarian or vegan diet, a B12 supplement of 10 micrograms **daily** should be adequate. However, in those individuals who eat very few vegetables a B12 supplement of 2000 micrograms **weekly** is probably necessary. For further dietary information refer to Appendix 2.

Appendix 1 Suggested prescription wording to aid visibility of review completion

It is recommended that patients are issued one ampoule per prescription (not a pack of 5) in order to prevent wastage.

When a patient's record has been reviewed in line with this guideline it is recommended that a readcode is included in the VISION/EMIS entry, e.g. readcode 8BI.00 'Other Medication Review' and add the text 'B12 injection reviewed in line with the NHSL guideline and treatment to be reviewed/continued/stopped'.



Appendix 2 Dietetic advice for B12 enriched diet

Diets Suitable for People with Anaemia – Foods containing vitamin B12:

https://patient.info/allergies-blood-immune/anaemia-leaflet/diets-suitable-for-people-with-anaemia

Food facts:

https://www.bda.uk.com/foodfacts/home

Nutritional considerations:

https://www.bda.uk.com/news-campaigns/campaigns/one-blue-dot/sustainable-september/nutritional-considerations-for-dietitians.html

Vegan sources:

https://www.nhs.uk/live-well/eat-well/the-vegan-diet/

Appendix 3

Algorithm for review of patients on intramuscular Vitamin B12 (hydroxocobalamin) injections