

1 **NATIONAL INSTITUTE FOR HEALTH AND CARE**
2 **EXCELLENCE**

3 **Guideline scope**

4 **Pernicious anaemia: diagnosis and**
5 **management**

Proposed new title: Vitamin B12 deficiency, including pernicious anaemia:
diagnosis and management

6

7 NHS England has asked NICE to develop a guideline on pernicious anaemia.

8 The guideline will be developed using the methods and processes outlined in
9 [developing NICE guidelines: the manual](#).

10 This guideline will also be used to develop the [NICE quality standard](#) for
11 pernicious anaemia.

12 **1 Why the guideline is needed**

13 Most vitamin B12 deficiencies occur because not enough vitamin B12 is
14 absorbed into the body. Causes of vitamin B12 deficiency include pernicious
15 anaemia, gastrointestinal conditions or surgery (including surgical removal of
16 part of the stomach, small intestinal disease such as coeliac disease or
17 Crohn's disease), or not enough dietary intake.

18 Pernicious anaemia is the most common cause of vitamin B12 deficiency
19 (over 60% of cases). It has a prevalence in the UK of 0.1% in the general
20 population and around 2% in people over 60. Pernicious anaemia is an
21 autoimmune condition that causes a lack of intrinsic factor, which is needed to
22 absorb vitamin B12 from digested food.

23 Vitamin B12 deficiency causes the body to produce abnormally large red
24 blood cells (macrocytosis) that cannot function properly. Symptoms of vitamin

1 B12 deficiency are non-specific and may include fatigue, lethargy, pale and
2 dry skin, and shortness of breath. Neurological complications such as
3 peripheral neuropathy and subacute combined degeneration of the spinal cord
4 can develop if vitamin B12 deficiency is not treated early. Pernicious anaemia
5 causes inflammation in the stomach that can damage the mucosa. Some
6 people with pernicious anaemia may develop gastric cancer (less than 1%).

7 **Current practice**

8 Vitamin B12 deficiency is generally diagnosed and treated in primary care.
9 Testing for vitamin B12 deficiency usually happens when people present with
10 non-specific complaints such as tiredness and there are abnormal findings in
11 their full blood count, such as macrocytosis. Access to tests such as
12 methylmalonic acid testing, which can diagnose vitamin B12 deficiency when
13 B12 levels are at the lower end of the normal range, is variable.

14 Once vitamin B12 deficiency is diagnosed it is uncertain which further
15 investigations should be used to diagnose the cause, including pernicious
16 anaemia.

17 Treatment for vitamin B12 deficiency depends on the cause but the main aim
18 is to replace vitamin B12. Traditional treatment for pernicious anaemia is
19 intramuscular injections given by a healthcare professional, which is more
20 costly than oral treatment. It is uncertain whether everyone with vitamin B12
21 deficiency needs treatment with intramuscular injections.

22 Better awareness of vitamin B12 deficiency and improved diagnosis and
23 management would reduce delayed and missed diagnosis. This is a particular
24 problem for pernicious anaemia where a delay to diagnosis can lead to
25 neurological complications. Diagnosing and treating pernicious anaemia in
26 children and young people is challenging because of a lack of guidance. This
27 guideline aims to improve the diagnosis and management of vitamin B12
28 deficiency, including pernicious anaemia, and improve quality of life for people
29 with vitamin B12 deficiency.

1 **2 Who the guideline is for**

2 This guideline is for:

- 3 • health and social care practitioners providing NHS-commissioned services
- 4 • commissioners of health and social care services
- 5 • people using services, their families and carers, and the public.

6 NICE guidelines cover health and care in England. Decisions on how they
7 apply in other UK countries are made by ministers in the [Welsh Government](#),
8 [Scottish Government](#) and [Northern Ireland Executive](#).

9 **Equality considerations**

10 NICE has carried out an [equality impact assessment](#) during scoping. The
11 assessment:

- 12 • lists equality issues identified, and how they have been addressed
- 13 • explains why any groups are excluded from the scope.

14 The guideline will look at inequalities relating to age, pregnancy and maternity,
15 race, religion and belief and sex.

16 **3 What the guideline will cover**

17 **3.1 Who is the focus?**

18 **Groups that will be covered**

19 Children, young people and adults with suspected and diagnosed vitamin B12
20 deficiency, including pernicious anaemia.

21 Specific consideration will be given to pregnant women with a vitamin B12
22 deficiency including pernicious anaemia.

23 **3.2 Settings**

24 **Settings that will be covered**

25 All settings where NHS health and social care is provided or commissioned.

1 **3.3 Activities, services or aspects of care**

2 **Key areas that will be covered**

3 We will look at evidence in the areas below when developing the guideline,
4 but it may not be possible to make recommendations in all the areas.

5 1 Information and support

- 6 – for people with suspected or diagnosed vitamin B12 deficiency (and
7 their families or carers)

8 2 Initial identification and assessment of people with suspected vitamin 9 B12 deficiency

- 10 – signs and symptoms
- 11 – risk factors for vitamin B12 deficiency, such as comorbidities that
12 increase the risk of vitamin B12 deficiency.

13 3 Diagnosing vitamin B12 deficiency

- 14 – testing to diagnose vitamin B12 deficiency.

15 4 Identifying the causes of vitamin B12 deficiency

- 16 – testing for the cause of vitamin B12 deficiency and pernicious
17 anaemia.

18 5 Managing vitamin B12 deficiency

- 19 – treatment options for vitamin B12 replacement.

20 6 Ongoing care and monitoring

- 21 – frequency and content of monitoring of vitamin B12 deficiency.

22 7 Monitoring for gastric cancer (subject to discussion between NICE and 23 the UK National Screening Committee).

24

25 Note that guideline recommendations for medicines will normally fall within
26 licensed indications; exceptionally, and only if clearly supported by evidence,
27 use outside a licensed indication may be recommended. The guideline will
28 assume that prescribers will use a medicine's summary of product
29 characteristics to inform decisions made with individual patients.

30 **Areas that will not be covered**

- 31 • Newborn screening for vitamin B12 deficiency.

- 1 • Management of the general symptoms of vitamin B12 deficiency (e.g.
- 2 fatigue).
- 3 • Blood transfusion.
- 4 • Investigation and management of complications related to vitamin B12
- 5 deficiency.

6 **Related NICE guidance**

7 **Published**

- 8 • [Antenatal care](#) (2021) NICE guideline NG201
- 9 • [Suspected neurological conditions: recognition and referral](#) (2019) NICE
- 10 guideline NG127
- 11 • [Blood transfusion](#) (2015) NICE guideline NG24
- 12 • [Coeliac disease: recognition, assessment and management](#) (2015) NICE
- 13 guideline NG20
- 14 • [Type 1 diabetes in adults: diagnosis and management](#) (2015) NICE
- 15 guideline NG17
- 16 • [Suspected cancer: recognition and referral](#) (2015) NICE guideline NG12
- 17 • [Active B12 assay for diagnosing vitamin B12 deficiency](#) (2015) medtech
- 18 innovation briefing MIB40

19 **NICE publications that will be updated by this guideline**

- 20 • Active B12 assay for diagnosing vitamin B12 deficiency (2015) medtech
- 21 innovation briefing MIB40

22 **NICE guidance about the experience of people using NHS services**

23 NICE has produced the following guidance on the experience of people using
24 the NHS. This guideline will not include additional recommendations on these
25 topics unless there are specific issues related to vitamin B12 deficiency and
26 pernicious anaemia:

- 27 • [Babies, children and young people's experience of healthcare](#) (2021) NICE
- 28 guideline NG204
- 29 • [Shared decision making](#) (2021) NICE guideline NG197
- 30 • [Decision-making and mental capacity](#) (2018) NICE guideline NG108

- 1 • [Medicines optimisation](#) (2015) NICE guideline NG5
- 2 • [Patient experience in adult NHS services](#) (2012) NICE guideline CG138
- 3 • [Service user experience in adult mental health](#) (2011) NICE guideline
- 4 CG136
- 5 • [Medicines adherence](#) (2009) NICE guideline CG76

6 **3.4 Economic aspects**

7 We will take economic aspects into account when making recommendations.
8 We will develop an economic plan that states for each review question (or key
9 area in the scope) whether economic considerations are relevant, and if so
10 whether this is an area that should be prioritised for economic modelling and
11 analysis. We will review the economic evidence and carry out economic
12 analyses, using an NHS and personal social services (PSS) perspective, as
13 appropriate.

14 **3.5 Key issues and draft questions**

15 While writing this scope, we have identified the following key issues and draft
16 questions related to them:

17 1 Information and support for people with vitamin B12 deficiency, including
18 pernicious anaemia (and their families or carers)

19 1.1 What information and support is needed by people with
20 suspected or confirmed vitamin B12 deficiency caused by a lack of
21 vitamin B12 in their diet, and their families or carers?

22 1.2 What information and support is needed by people with
23 suspected or confirmed vitamin B12 deficiency (including
24 pernicious anaemia) caused by an inability to absorb vitamin B12,
25 and when should this be provided?

26 2 Initial identification and assessment of people with suspected vitamin
27 B12 deficiency

28 2.1 When should vitamin B12 deficiency be suspected (for
29 example, based on signs or symptoms, risk factors, comorbidities,
30 or abnormal findings on a full blood count)?

- 1 3 Diagnosing vitamin B12 deficiency
- 2 3.1 What is the diagnostic accuracy of individual tests (including the
- 3 serum cobalamin assay and holotranscobalamin, methylmalonic
- 4 acid and homocysteine tests) for diagnosing vitamin B12
- 5 deficiency?
- 6 3.2 What are the most clinically and cost-effective ways to
- 7 diagnose vitamin B12 deficiency, including the serum cobalamin
- 8 assay and holotranscobalamin, methylmalonic acid and
- 9 homocysteine tests?
- 10 4 Identifying the cause of vitamin B12 deficiency, including pernicious
- 11 anaemia
- 12 4.1 What is the diagnostic accuracy of individual tests and
- 13 investigations (including tests for serum intrinsic factor antibody
- 14 and gastric parietal cell antibody, and gastroscopy and
- 15 colonoscopy) for identifying the cause of vitamin B12 deficiency,
- 16 including pernicious anaemia?
- 17 4.2 What is the clinical and cost effectiveness of tests and
- 18 investigations (including tests for serum intrinsic factor antibody
- 19 and gastric parietal cell antibody, and gastroscopy and
- 20 colonoscopy) for identifying the cause of vitamin B12 deficiency
- 21 and pernicious anaemia?
- 22 5 Managing vitamin B12 deficiency, including pernicious anaemia
- 23 5.1 What is the clinical and cost effectiveness of vitamin B12
- 24 replacement, including the dose, frequency and route of
- 25 administration?
- 26 5.2 What is the clinical and cost effectiveness of self-administration
- 27 compared with healthcare professional administration of
- 28 intramuscular vitamin B12 replacement?
- 29 6 Ongoing care and monitoring

1 6.1 What is the optimal frequency of monitoring for people with
2 vitamin B12 deficiency, including pernicious anaemia?

3 6.2 What should be included in a monitoring review for people with
4 vitamin B12 deficiency, including pernicious anaemia?

5 7 Monitoring for gastric cancer (subject to discussion between NICE and
6 the UK National Screening Committee)

7 7.1 What monitoring should be offered to people with pernicious
8 anaemia to identify gastric cancer?

9 **3.6 Main outcomes**

10 The main outcomes that may be considered when searching for and
11 assessing the evidence are:

- 12 • quality of life
- 13 • patient-reported outcomes
- 14 • complications and adverse events
- 15 • adherence to treatment.

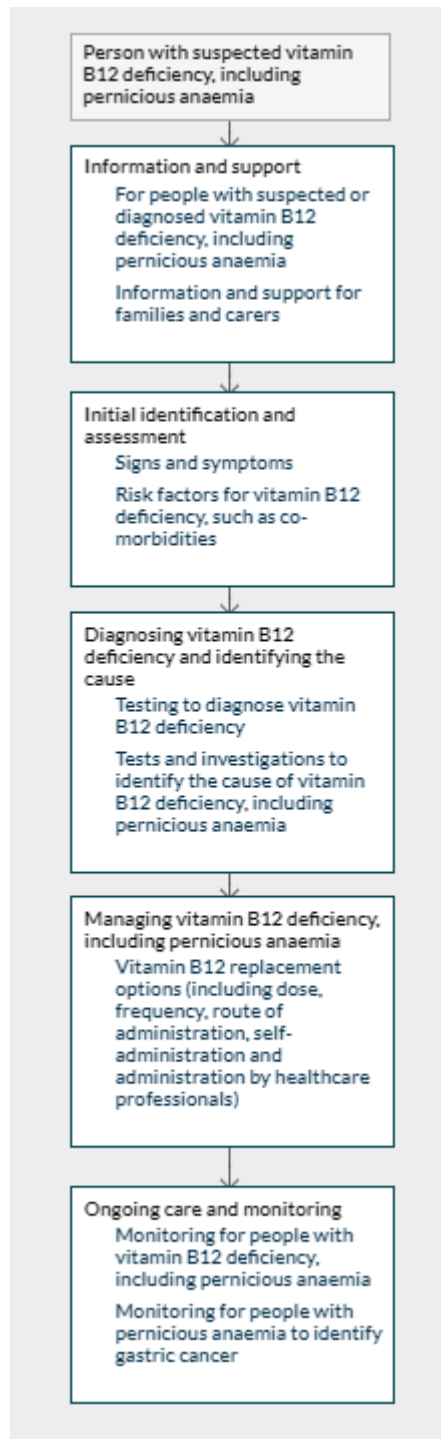
16 **4 NICE Pathways**

17 **4.1 NICE Pathways**

18 [NICE Pathways](#) bring together everything we have said on a topic in an
19 interactive flowchart. When this guideline is published, the recommendations
20 will be included in the NICE Pathway (in development).

21 Other relevant guidance and advice will also be added.

22 An outline based on this scope is included below. It will be adapted and more
23 detail added as the recommendations are written during guideline
24 development. Links will be added to relevant NICE Pathways.



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1 **5 Further information**

This is the draft scope for consultation with registered stakeholders. The consultation dates are 8 September to 6 October 2021.

The guideline is expected to be published in November 2023.

You can follow progress of the [guideline](#).

Our website has information about how [NICE guidelines](#) are developed.

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