



**STATEMENT FROM THE B12-ALLIANCE ON THE PUBLICATION OF THE NICE GUIDELINES
Vitamin B12 deficiency in over 16s: diagnosis and management
6TH March 2024**

THE B12 ALLIANCE

cluB-12 is a not-for profit organisation of scientists and healthcare professionals which facilitates the sharing of knowledge and co-ordination of research into Vitamin B12. Within cluB-12, the B12-Alliance is the community of patient advocacy groups with relevant expertise and experience. The purpose of the B12-Alliance is to use their shared resources and combined expertise to raise awareness, share evidenced based research and inform the healthcare profession and public about B12 deficiency and about conditions where B12 deficiency is a consequence or risk factor.

The current members of the B12-Alliance are:

Pernicious Anaemia Society
The B12 Society
B12 Deficiency Support Group
HCU Network America
B12 Institute Netherlands
cluB-12

The B12-Alliance through cluB-12 and its individual members, contributed as stakeholders to the NICE Guidelines on Vitamin B12 Deficiency in over 16s.

The B12-Alliance endorses many of the recommendations in the Guideline and welcomes the opportunity that the publication of these guidelines creates to raise awareness, increase knowledge and education for patients and health care professionals and improve the diagnosis and treatment of individuals who have a B12 Deficiency for dietary or non-dietary reasons.

As our constituent groups, we very much appreciated the opportunity to be involved in the development of, and then feedback on, the draft document. The committee's respect for the stakeholders' views being evidenced by the many updates to the final version. We appreciate that there are still areas which the guidelines committee was unable to address due to lack of robust evidence.

As the B12-Alliance we will continue to advocate for guidelines for the under 16s, the need to address Pernicious Anaemia as a condition specifically, and the need to replenish related vitamin and mineral deficiencies (often referred to as co-factors) such as folate and iron, which frequently coexist in those with B12 deficiency.

The symptoms and risk factors for B12 Deficiency are many and the consequences of severe deficiency are debilitating and life changing. We retain concerns our members expressed during the consultation process that by limiting in the guideline the list of "common" symptoms and "common" risk factors, patients remain at risk. Knowledge and awareness of

symptoms and risks remains low within the healthcare profession, particularly primary care. We urge health care professionals and patients alike to use reputable resources like those of the British Medical Journal and resources of members of the B12-Alliance, to ensure they have a full understanding of both symptoms and risks.

The B12-Alliance believes that there are many positive recommendations in the guidelines which, with appropriate levels of communication throughout primary and secondary care in the NHS, through better education on nutrition in the medical curriculum and improved patient awareness, will help contribute to better diagnosis and treatment of B12 Deficiency.

Vitamin B12 deficiency can be caused by dietary and lifestyle choices; by non-dietary causes including medical conditions such as autoimmune gastritis, low stomach acid, damage to parietal cells, lack of intrinsic factor, intrinsic factor antibodies, malabsorption issues including the term pernicious anaemia as it is currently used, and as a side effect of certain prescribed medicines or recreational drugs and substances and environmental chemicals.

The B12-Alliance welcomes the following from the guidelines:

- Vitamin B12 replacement dose, frequency and method of delivery may need to be adjusted or changed for it to work properly.
- The importance of continuing with treatment so symptoms do not return or get worse and, for those with autoimmune gastritis including those with a diagnosis of Pernicious Anaemia, is lifelong.
- The recommendation¹ that diagnostic testing for B12 Deficiency should be based on 1 common symptom and 1 risk factor. However, we have serious concerns about the application of this in practice in primary care. Delays and misdiagnosis frequently occur when a risk factor is not present. We are aware of many instances of misdiagnoses, with fibromyalgia, functional neurological disorder (FND), multiple sclerosis (MS) or myalgic encephalomyelitis, also known as chronic fatigue syndrome or ME/CFS and of long delays to a B12 deficiency diagnosis. Better awareness and knowledge in the health care profession is necessary to ensure that patients are quickly and properly treated. The B12-Alliance remains willing to work on better education in this area.
- The inclusion of Active B12 (serum holotranscobalamin) to the initial test for diagnosis as routine. We also support the advice to test before and take into account B12 replacement by the patient which can skew test results. We remain concerned by the limitations to Serum and Active B12 tests and IFA tests in terms of accuracy.
- We appreciate the table simplification² of thresholds for interpreting B12 deficiency results but we remain concerned that healthcare professionals over-rely on cut-off points and ranges when flexibility and focus on symptoms is more important. A significant improvement in these guidelines is the recognition that even with a B12 concentration of more than 350 nanograms per litre (258 pmol) (70pmol Active B12) the test results do not rule out a vitamin B12 deficiency.

¹ 1.2.5

² 1.3.9

- The acknowledgement³ that symptoms can take a long time to improve and may get worse initially.
- The recommendation for treatment for malabsorption as a confirmed or suspected cause⁴ is lifelong intramuscular B12 replacement for those with autoimmune gastritis/pernicious anaemia.
- The recommendation that other causes of malabsorption should offer the option of both high dose (1mg) oral replacement and injections, but we urge the healthcare profession to focus on resolving severe B12 deficiency symptoms with injections and note that it is specifically acknowledged that the cost efficiency of this is already proven.
- We also are grateful for the acknowledgement throughout the process of preparing these guidelines that there is no evidence that oral doses are as effective as intramuscular injections.
- The recommendations for research about self-administration⁵ either intramuscular or sub-cutaneous. This is an important step, giving people with B12 deficiency control back and relief from their symptoms. Their lives have already been upturned and many are happy and confident to self-inject.
- The recommendation that stopping treatment is only an option if symptoms have resolved **and** the cause has been addressed.
- The very clear statement⁶ about not repeating initial diagnostic testing for people on Vitamin B12 replacement.
- The clarity from these guidelines⁷ that the best way forward is to increase frequency of injections until symptoms are resolved.

We support the calls for further research into B12 Deficiency particularly for better diagnostic tests, self-administration options, delivery methods.

We remain concerned by the lack of evidence or adequate research in many areas of vitamin B12 deficiency as a symptom and into conditions which result in B12 Deficiency as a symptom. We hope that these guidelines focus funding and research grants in these areas.

Whilst we believe that these guidelines are helpful for both healthcare professionals and patients alike, we know that not all healthcare practitioners are aware of the existing guidelines and, therefore, these are not always followed in everyday practice. We trust that these guidelines will be communicated effectively to ensure increased knowledge and awareness about B12 deficiency in the healthcare profession.

We are keen to point out that whilst for some, lifestyle choices have a role in the evolution of their B12 deficiency, for the majority the aetiology (the cause due to medical conditions or environmental) remains outside of their control. We're delighted that the publication of these guidelines will lead to more constructive conversations about B12 deficiency between patients, support groups and the healthcare profession.

³ 1.5

⁴ 1.5.3

⁵ Page 12 Self-Administration and page 23 (5)

⁶ 1.6.10

⁷ 1.6.11