

Vitamin B12 for ME/CFS

Prepared by MECFS Canterbury (v31.10.2024)

www.mecfscanterbury.nz

Disclaimer:

The information in this leaflet is for informational purposes only. It does not substitute the need for professional medical advice or consultations with medical professionals. Always seek the advice of your doctor before starting a new medication or changing dosage.

Summary

- Vitamin B12, also known as cobalamin, is involved in cellular metabolism, brain and nervous system function, and the formation of red blood cells (RBCs). It is also a powerful scavenger of nitric oxide which is known to have a detrimental effect on brain function and pain sensitivity.
- Absorption of B12 from dietary sources requires an intrinsic factor (IF or GIF), i.e., a glycoprotein, synthesized in and secreted from parietal cells in the lining of the stomach.
- Vitamin B12 deficiency causes fatigue and other ME/CFS-like symptoms - so it should be excluded before a diagnosis of ME/CFS is made, especially in people where there is no clear infective onset for ME/CFS. B12 deficiency is linked to the potentially serious pernicious anaemia - where there are abnormally large red blood cells.
- The "normal" levels of B12 in blood tests have been set at those levels necessary to prevent pernicious anaemia - this may not be the same as the levels for optimal biochemical function. In addition, levels of B12 may be different and lower in the cerebrospinal fluid, than in the blood, which some experts consider is an issue in ME/CFS. Also, nitric oxide has been shown to be high in ME/CFS so may require higher levels of B12.
- There is no evidence that vitamin B12 deficiency occurs as part of the underlying disease process in ME/CFS.
- B12 is beneficial in patients with fatigue, including those with ME/CFS, and this suggests that there is a common mechanism of chronic fatigue which B12 is effective at alleviating, regardless of the cause of the fatigue.
- There is limited published research that vitamin B12 supplements or parenteral injections are of value in treating ME/CFS. However, a significant proportion of individuals with ME/CFS do report improvements that last longer than expected from a simple placebo effect.
- Some expert ME/CFS clinicians recommend B12 by parenteral injection as a foundation treatment before proceeding to other treatments, suggesting that 60% of patients may benefit.
- Vitamin B12 has no known toxicity and any B12 surplus to requirements is simply passed out in the urine (which may discolour pink).
- Dosage normally starts at 1 mg (1000 mcg) weekly over six weeks by subcutaneous injection, then frequency adjusted according to response. Many people end up injecting at least once a month, while others may inject 1-2 times per week in response to symptoms and stress.

Prescription Guidelines

Dose guidelines

- Vitamin B12 is usually delivered as hydroxocobalamin parenteral injections for ME/CFS and FM, at higher and more frequent doses than usual because of the amount needed to notice improvement. Sublingual (under the tongue) or oral forms of B12 are not considered to be as effective.
- IACFSME (International [Clinician] Association for CFS/ME) recommend a trial of a weekly injection of hydroxycobalamin 1000mcg for six weeks (or perhaps longer). Followed by monthly injections, if benefit found
- Some ME/CFS expert clinicians recommend daily injections of 500 mcg for six weeks.
- If parenteral B12 is not an option, Dr Lapp suggests sublingual B-12 from 1000 up to 5000 mcg day.
- Folic acid supplement may be required alongside.

Self-injection

Patients can learn to inject themselves, so that they can be independent of their medical centre and administer as their symptoms indicate.

Refer to guidance from The Health Centre at the University of Sussex (NHS) 'Self-administering a Vitamin B12 injection' handout www.unimed.co.uk/wp-content/uploads/2020/05/B12-self-injecting.pdf which includes a link to www.wikihow.com/Give-a-B12-Injection

Possible Side Effects

In rare cases, hydroxocobalamin can cause a serious allergic reaction (anaphylaxis).

As hydroxocobalamin contains cobalt, it can cause sensitivity reactions in people who have an allergy to cobalt. Symptoms can start straight away or up to 3 days after having a dose.

Pain, swelling or itchy skin may occur at the injection site. These symptoms are usually mild and should only last a few hours.

People with ME/CFS can be very sensitive to the fillers and other ingredients in medications.

Contraindications

There are dangers in taking vitamin B12 for those with pernicious anaemia.

Research and clinical guidelines

- **ME/CFS: A Primer for Clinical Practitioners**
International Association for CFS/ME, 2014, Retrieved from www.iacfsme.org
Extract from [pdf](#) on Page 25
"Vitamin B12 and B-Complex. Cerebrospinal fluid levels of vitamin B12 may be depleted in some patients with ME/CFS, and a trial of a weekly injection of hydroxycobalamin 1000µg for six weeks (or perhaps longer) may be helpful. There are no reports of serious

risk or side effects, despite the high blood levels achieved. A supplement of B complex will avoid concurrent B vitamin deficiency.”

- **Health Pathways – ME/CFS topic**

Health NZ. Retrieved 31/10/24.

canterbury.communityhealthpathways.org/44978.htm

“There is no evidence that supplements are useful for patients with healthy nutrition, however those commonly taken include:... B12 injections.”

- **Clinical Article: Rationale for using vitamin B12 in CFS**

Dr Sarah Myhill (UK) , Retrieved 30/10/2024

[www.drmyhill.co.uk/wiki/B12 - rationale for using vitamin B12 in CFS](http://www.drmyhill.co.uk/wiki/B12_-_rationale_for_using_vitamin_B12_in_CFS)

“Introduction

Since 1982 a programme of treatment has evolved which I believe all Chronic Fatigue Syndrome patients must do as the foundation before proceeding to other treatments. Vitamin B12 by injection I see as an important part of this programme and it is effective for many, regardless of the cause of their Chronic Fatigue Syndrome.

”

Practical details

Vitamin B12 has no known toxicity and B12 surplus to requirement is simply passed out in the urine (which may discolour pink). It is theoretically possible to be allergic to B12 but in the thousands of injections that I have sanctioned this has only ever occurred after several injections and caused local itching, redness and swelling (although the commonest cause of redness and swelling is poor injection technique) in a handful of patients. I usually start with 1/2 mg (500 mcg) daily by subcutaneous injection, then adjust the frequency according to response - some patients will respond straight away, some need several doses before they see improvement. I would do at least two months of daily injections (i.e. 60) before giving up. If there is improvement then adjust the frequency of the dose to maintain that. Many people end up injecting at least once a month, often 1-2 times per week, more if stressed, less often if well. ... There is some evidence that vitamin B12 is anti-viral and this may explain its wide application and why so many see benefit.

...

Nearly all of my patients learn to inject themselves - this means they can be independent of their doctors. If self-injecting is not feasible and your own doctor is willing to prescribe and authorise administration of B12 injections, then I would recommend a weekly injection of 2 ml hydroxocobalamin and assess clinical response after 2 months.

...”

- **Response to vitamin B12 and folic acid in myalgic encephalomyelitis and fibromyalgia**

Björn Regland et al, 2015, PLOS One

doi.org/10.1371/journal.pone.0124648

A survey of 38 ME/CFS patients who had been receiving vitamin B12 injections in combination with folic acid at least once a week for six months, 15 reported a good response and 23 reported a mild response.

“Conclusions: Dose-response relationship and long-lasting effects of B12/folic acid support a true positive response in the studied group of patients with ME/fibromyalgia. It's important to be alert on co-existing thyroid dysfunction, and we suspect a risk of counteracting interference between B12/folic acid and certain opioid analgesics and other drugs that have to be demethylated as part of their metabolism.”

- **Clinical Article: Are supplements important in ME/CFS?**

Dr Ros Vallings (NZ) , Retrieved 30/10/2024

www.drvallings.co.nz/uploads/5/0/8/0/50805589/are_supplements_important_in_me.pdf

“... Certainly a number of people with CFS do seem to improve with a course of B12 injections, and the benefits seem to last far longer than we would expect from a simple placebo effect. Some Scandinavian research has indicated that the levels of B12 maybe low in the cerebro-spinal fluid, while the blood levels appear normal. This is the fluid surrounding the brain and spinal cord. B12 is needed by brain cells for efficient function.

Having B12 by mouth has very little benefit as you only absorb it minimally and probably not at all if your blood levels are normal. So, having it by injection maybe useful for possibly about 60% of CFS people. The benefit may not be apparent immediately, some people find it takes about a month of weekly injections before they feel any better. B12 is a water soluble vitamin, and the body can therefore easily rid itself of any excess. In quite big dose trials being done overseas, there seems little risk of side effects or long term ill effects.

If you are having B12, it is important to also take a mixed B complex tablet daily as the other B vitamins (particularly folic acid) can get out of kilter. Some women with CFS, who may have a worsening of symptoms premenstrually do find vitamin B6 (pyridoxine) can be helpful, but it is of no use taking it just around period time, as it needs to build up to be of benefit and taken daily regularly.”

- **Clinical Article: Dr Lapp’s Recommendations on Supplements**

Bruce Campbell, Retrieved 30/10/2024

cfsselfhelp.org/library/dr-lapp%27s-recommedations-supplements

“2) B12

He [Dr Lapp] recommends the injectible form and says that up to 80% of people with CFS/FM who use it experience a 10% to 15% energy boost. If parenteral B12 is not an option, consider oral methyl-cobalamin at 1000 to 5000 mcg daily.”

- **Clinical Practice Article: Vitamin B12**

B Wolfeenbittel et al, BMJ 2023;383:e071725,

doi.org/10.1136/bmj-2022-071725

Comprehensive guidance for use of B12 that is not specific to ME/CFS

- **NZ Data Sheet – Neo-B12 Injection Hydroxocobalamin 1000 microgram/1 mL**

www.medsafe.govt.nz/profs/datasheet/n/Neo-B12inj.pdf

- **NZ Medicine Formulary – ‘hydroxocobalamin (systemic)’ topic**

nzf.org.nz/nzf_4943

- **Healthify – ‘Vitamin B12 injection’ topic**

healthify.nz/medicines-a-z/h/hydroxocobalamin/

Other Information

- **Article: Supplements**

Massachusetts ME/CFS and FM Association. , Retrieved 30/10/2024

massmecfs.org/more-resources-for-me-cfs/19-supplements?showall=1

Extract in section “Improve energy, strength and/or mitochondrial function
...Vitamin B-12 is a water-soluble vitamin found naturally in animal foods, fish, and dairy products. It is vital to red blood cell formation, absorption of foods, metabolic regulation, growth, and protection of nerve cells and function. Deficiency often presents as chronic fatigue, digestive disorders, pernicious anemia, various memory, mood or neurologic problems. B-12 deficiency may also be present in some individuals who consume a very limited vegan-type diet. Long-term use of proton pump inhibitor medications which reduce stomach acid (like those controlling GERD) may also interfere with the absorption of B-12.

Therapeutic treatment with this vitamin is often delivered as hydroxocobalamin injections and for ME/CFS and FM, at higher and more frequent doses than usual because of the amount needed to notice improvement. Not only does B-12 help to promote energy and overall better function, but also it works at a deeper level to reduce nitric oxide and peroxynitrite levels regarded by some researchers to be the main culprit in causing the ME/CFS process.

It is generally not found to be toxic or problematic in the majority of people, unless they are sensitive to the compounds that make up the vitamin, an ingredient in the injection material and/or have an unusual optic neuropathy. Vitamin B-12 injections, when used for ME/CFS, are often started at a high-dose of approximately 3000 mcg, several times per week, for 15 doses and then it is tapered down. Sublingual B-12 is the preferred oral form, from 1000 up to 5000 mcg day.”

Also

Extract in section “Miscellaneous Treatments

Methylation protocol — Based on a hypothesis that insufficient methylation drives ME/CFS, the methylation protocol uses a supplement regimen to boost methylation. The daily regimen includes: vitamin B12 hydroxocobalamin 2000 mcg sublingual, methylfolate 200 mcg, folic acid 200 mcg, lecithin 1200 mg, and a multivitamin/multimineral tablet. Search PR for the methylation protocol.”

• **Article: Potential Treatments for ME/CFS**

Phoenix Rising ME/CFS Community Forum, Retrieved 30/10/2024.

phoenixrising.me/treatment/potential-treatments/

“Vitamin B12 Injections

Some ME/CFS patients find vitamin B12 injections reduce brain fog and fatigue. Injected doses of around 500 to 1000 mcg are used; the forms of vitamin B12 typically employed are methylcobalamin or hydroxocobalamin. A more convenient alternative to injections is the transdermal B12 oil developed by Dr Greg Russell-Jones, which use a micro-emulsion permeation enhancer to draw B12 through the skin in amounts similar to injected doses. High dose B12 can cause transient low blood potassium (hypokalaemia) a few hours after injecting the B12, which may manifest as tiredness. This can be prevented by taking around 300 mg of oral potassium.”

• **ME-pedia – ‘Methylation cycle hypothesis’ topic**

Curated information from the ME/CFS community, Retrieved 30/10/2024.

me-pedia.org/wiki/Methylation_cycle_hypothesis

“The methylation cycle hypothesis posits that a core component of the pathophysiology of chronic fatigue syndrome involves a partial block in the methylation cycle.

...

The methylation cycle hypothesis states that many if not all of the symptoms of CFS are caused by errors in the genes that regulate or have a strong impact on one-carbon metabolism, such as MTHFR, CBS, DHPR, MTRR, or MAO-A. Through knowledge obtained by their genetic SNPs, patients can address inconsistencies in their one-carbon

metabolism by supplementing nutrients in which they are deficient, or that encourage bypassing problematic aspects of the cycle, such as folinic acid, in order to optimize the efficiency of the methylation and related cycles.

...

There is little direct evidence to support the popular methylation protocols. However, numerous patients have reported benefit while others have reported no benefit.

...

Indirect evidence supporting a possible benefit of methylation cycle supplements include findings of increased homocysteine in the cerebrospinal fluid of CFS and fibromyalgia patients.

...

There is compelling evidence that some ME/CFS patients are low in methylation cycle metabolites, and there are some studies that provide direct evidence of methylation cycle dysregulation in ME/CFS. However, it is important to note that there are limited studies on either protocol's effect on methylation, and no studies on Yasko's utilization of SNP data to drive decision-making about supplements.

..."

- **Booklet: Vitamin B12 and ME/CFS**

ME Association (UK)

meassociation.org.uk/wp-content/uploads/2024/09/Vitamin-B12-September-2024.pdf

- **Patient Discussion: 'Methylation, B12, Glutathione'**

Phoenix Rising ME/CFS Community Forum

forums.phoenixrising.me/forums/methylation-b12-glutathione-etc.6/

- **ME-pedia – 'Cobalamin' topic:**

Curated information from the ME/CFS community.

me-pedia.org/wiki/Cobalamin