

Vitamin B12

Cobalamin — supplemented as cyanocobalamin, methylcobalamin or hydroxocobalamin

B12 is essential, cheap, effectively non-toxic, and sold overwhelmingly to people who do not need it. The genuine issue is diagnostic rather than therapeutic: total serum B12 is an unreliable test, the indeterminate band is wide, and the NICE guideline published in 2024 reorganized how deficiency should be identified. It is also the supplement whose delayed treatment causes the most permanent damage.

SUMMARY TABLE

Attribute	Summary
Primary uses	Treating/preventing deficiency and pernicious anemia; reversing megaloblastic anemia and deficiency-related neuropathy; prevention in vegans, post-bariatric/gastrectomy patients, older adults, long-term metformin or PPI users.
Evidence strength	Very high for treating deficiency. Moderate for high-dose oral matching intramuscular injection. High for the metformin-depletion association. No credible support for energy, mood or cognition in people who are not deficient.
Effective dose	RDA 2.4 mcg/day. No tolerable upper intake level. Maintenance supplementation 250–1,000 mcg/day; NICE specifies a minimum of 1,000 mcg/day for malabsorption-related deficiency.
How to take	Plain swallowed cyanocobalamin tablet, daily. Sublingual, lozenge and spray formats carry a price premium without demonstrated advantage — a 2025 meta-analysis found sublingual produced the smallest serum rise of the three routes.
Time to effect	Reticulocytosis peaks ~1 week after starting; blood counts normalize ~8 weeks. Neurological improvement begins in the first week, typically complete between 6 weeks and 3 months.
Serious risks	Hypokalemia during treatment of severe megaloblastic anemia (monitor and correct). A large observational cohort found high-dose B12 (>55 mcg/day) associated with roughly doubled lung-cancer risk in male current smokers only.
Who should avoid it	Essentially no one at nutritional doses. Cyanocobalamin specifically is contraindicated in Leber hereditary optic neuropathy (use hydroxocobalamin); male current smokers should avoid chronic high-dose B12 without documented deficiency.
Quality markers	USP Verified or NSF Certified; cyanocobalamin unless a specific exception applies; 250–1,000 mcg dose (5,000 mcg products offer nothing extra, since absorption fraction falls as dose rises).

TWO ENZYMES, AND WHY THE DOSES LOOK ABSURD

B12 is a cofactor for exactly two human enzymes; deficiency raises both homocysteine and methylmalonic acid (MMA), while folate deficiency raises homocysteine only — making MMA the more discriminating test. A 1,000 mcg tablet against a 2.4 mcg requirement looks absurd, but intrinsic-factor-mediated absorption saturates at ~1.5–2 mcg per dose, so a separate passive-diffusion route (a fixed ~1.2% of any oral dose) is what makes 1,000–2,000 mcg oral therapy work even in pernicious anemia, where intrinsic factor is destroyed.

NICE 2024 AND THE DIAGNOSTIC TRAPS

NICE guideline NG239 (March 2024) recommends testing anyone with a common symptom plus a risk factor (explicitly including metformin, PPIs, H2 antagonists, nitrous oxide use), retires the old 30 ng/mL target, and defines an indeterminate band of 180–350 ng/L where methylmalonic acid or empiric treatment is advised. It is folic acid that masks B12 deficiency — correcting the anemia while neurological degeneration continues — and any supplementation invalidates subsequent serum B12 testing, so test first or use MMA.

DELAY CAUSES THE PERMANENT DAMAGE

Roughly 6% of patients with neurological involvement retain permanent disability, concentrated among those whose treatment was delayed beyond six months — the central reason NICE advises empiric treatment of indeterminate results when neurological signs are present. Metformin roughly triples the odds of deficiency (pooled OR 2.95), and the resulting neuropathy is routinely misattributed to diabetes itself.

BOTTOM LINE

B12 is worth supplementing if you are vegan/vegetarian, over about 60, on metformin or a long-term PPI, post-bariatric/gastric surgery, or use nitrous oxide — for those groups, 250–1,000 mcg of plain cyanocobalamin daily is cheap, effective and effectively risk-free. Buy the cheap cyanocobalamin form; skip sublingual and 5,000 mcg tablets. If investigating symptoms, get tested before supplementing, since treatment makes the test uninterpretable for months.

SOURCES

1. NICE. "Vitamin B12 deficiency in over 16s: diagnosis and management." Guideline NG239, March 2024.
2. "Comparative efficacy of sublingual, oral and intramuscular vitamin B12: meta-analysis." *Frontiers in Pharmacology*, 2025.
3. Carmel R. "How I treat cobalamin (vitamin B12) deficiency." *Blood*, 2008;112(6):2214.
4. "Effect of Metformin on Vitamin B12 Deficiency in T2D: Meta-Analysis." *Cureus*, 2022.
5. NIH Office of Dietary Supplements. "Vitamin B12 — Fact Sheet for Health Professionals."

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