

Fact Sheet

Vitamin B12 tests



Vitamin B12 and folate testing have increased rapidly in the last decade. Vitamin B12 deficiency is rare, and testing should only be ordered in a selected group of patients.

Key points

- ▶ An MBS review identified a rapid increase in vitamin B12 and folate testing over the last decade.
 - Item 66602 (serum B12 and red cell folate and, if required, serum folate) increased by 307%.¹
 - Item 66599 (serum B12 or red cell folate and, if required, serum folate) more than doubled (119% increase).¹
- ▶ These previous MBS items link vitamin B12 and serum folate/red cell folate testing. This made it difficult to identify which test or tests are being ordered at an individual patient level and may have led to over-ordering.
- ▶ In order to encourage the quality use of testing under Medicare, and to improve transparency, vitamin B12 and serum folate/red cell folate testing are now listed under separate items. This decision is evidence-based and supported by the Medical Services Advisory Committee (MSAC; www.msac.gov.au).

Requesting vitamin B12 tests

While folate and vitamin B12 tests may be used singularly or together to find vitamin deficiency, linking these tests in the same MBS item has resulted in difficulty identifying which test or tests were being ordered at an individual patient level and may have led to over-ordering.¹

As a result of a review of MBS items for B12 and folate, these individual tests will now be separated and the following item numbers will need to be used when investigating B12 levels:¹

ITEM	ITEM DESCRIPTION	SCHEDULE FEE	BENEFIT PAID
66838	Serum vitamin B12 test (Item is subject to Rule 25)*	\$23.60	75% = \$17.70 85% = \$20.10
66839	Quantification of vitamin B12 markers such as holotranscobalamin or methylmalonic acid, where initial serum vitamin B12 result is low or equivocal†	\$42.95	75% = \$32.25 85% = \$36.55

* Rule 25: For any particular patient, this item is applicable not more than once in a 12 month period.

† Check with laboratory pathologist to determine if this test is clinically warranted. Laboratories will perform serum B12 where indicated and when the result is 'low' or 'equivocal' (i.e. not clearly replete and not clearly deficient) the laboratory pathologist can determine if holotranscobalamin or methylmalonic acid is required as a reflex test.

What is the role of vitamin B12?

Vitamin B12 and folate are linked by two enzymatic reactions where they function as co-factors.² Deficiency of either vitamin can interrupt key pathways, with consequent disruption of DNA synthesis resulting in megaloblastic anaemia and other adverse effects on the nervous system and other organs.²

What does vitamin B12 testing involve?

Tests covered by the MBS for vitamin B12 measurement include serum B12 and, when required, evaluation of specific markers (e.g. holotranscobalamin or methylmalonic acid).³

Serum B12 tests have poor discriminative ability for determining tissue concentrations of vitamin B12.⁴ This is demonstrated in conditions where the serum concentrations are low without tissue deficiency, i.e. pregnancy, simple atrophic gastritis.⁵ The test is therefore limited and may misrepresent tissue stores of vitamin B12.

The diagnostic accuracy of serum B12 tests is low due to:

- ▶ Lack of a gold standard.⁶
- ▶ Inconsistent cutoff values used to define deficiency
 - differences in methods
 - differences in approaches to define deficiency.⁴
- ▶ The fraction of vitamin B12 bound to haptocorrin, an inactive carrier protein.⁷

Newer tests such as the measurement of holotranscobalamin or methylmalonic acid have comparable or better diagnostic accuracy.⁷

However, there is insufficient evidence to establish these tests as an alternative first-line test.^{1,7}

Holotranscobalamin, the metabolically active form of vitamin B12, also relies on poorly defined reflex serum B12 reference limits (Table 1).⁴

Table 1. Vitamin B12 test reference values^{*3,8,9}

	SERUM VITAMIN B12 (PMOL/L)	METHYLMALONIC ACID (NMOL/L)	HOLO- TRANSCOBALAMIN (PMOL/L)
Normal	120–680	70–270	> 35
Low	< 120	> 270	< 35

^{*} Reference values may vary between laboratories.

Who requires vitamin B12 testing?

The MBS review did not identify any prospective studies that evaluated the clinical indications for vitamin B12 testing.¹

However, several guidelines recommend testing vitamin B12 levels to investigate the following clinical indications:

- ▶ In the initial evaluation of anaemia in chronic kidney disease.¹⁰
- ▶ In the initial evaluation of mild cognitive impairment or dementia in elderly patients.^{11,12} The incidence of low vitamin B12 levels in Australia appears to increase with age (> 65 years).^{13,14}
- ▶ Patients with polyneuropathy.¹⁵
- ▶ Patients with Crohn's disease with macrocytic anaemia or who do not respond to iron treatment.
- ▶ Patients with symptoms or signs of macrocytic anaemia.¹⁶
- ▶ Patients with chronic fatigue syndrome or myalgic encephalopathy, if they have already undergone pre-test investigations (such as full blood examinations).^{4,17}
- ▶ It is unclear whether other special populations should be tested for B12 deficiency (e.g. patients with suspect neuropsychiatric abnormalities).¹⁶

Practice points

Assess patients for:

- ▶ Signs and symptoms to suggest deficiency including:
 - Neuromotor (paraesthesia, ataxia, decreased reflexes, restless leg syndrome, peripheral neuropathy).^{1,18}
 - Neuropsychiatric (dementia, depression, psychosis, personality changes).^{1,18}
 - Haematological symptoms (anaemia, macrocytic anaemia, macrocytosis, pernicious anaemia).^{1,18}Note that some symptoms are non-specific i.e. fatigue, mild neurological features and some features may manifest without anaemia or low serum vitamin B12 levels.⁷
 - ▶ Risk factors associated with deficiency (check patient's medical history, medicines for *Helicobacter pylori* eradication therapy, vegetarian diet).^{18,19}
- There is no need to repeat testing unless there is a lack of patient response to treatment (i.e. patient remains symptomatic) or if anaemia re-occurs.²⁰

Further information

See the MBS review, Vitamin B12 testing report (at: www.msac.gov.au/internet/msac/publishing.nsf/Content/0013r-public).

1. Australian Government Department of Health. MBS reviews, Vitamin B12 testing report. February 2014. [http://www.msac.gov.au/internet/msac/publishing.nsf/Content/97032EDF3C9B07F4CA257D77007FD B37/\\$File/Vitamin%20B12%20testing%20Review%20Report-accessible.pdf](http://www.msac.gov.au/internet/msac/publishing.nsf/Content/97032EDF3C9B07F4CA257D77007FD B37/$File/Vitamin%20B12%20testing%20Review%20Report-accessible.pdf) (accessed 28 October 2014).
2. Oh R, Brown DL. Am Fam Physician 2003;67:979–86.
3. Schrier SL. UpToDate: Diagnosis and treatment of vitamin B12 and folate deficiency. 2014. <http://www.uptodate.com/contents/diagnosis-and-treatment-of-vitamin-b12-and-folate-deficiency> (accessed 20 September 2014).
4. Willis CD, et al. Med J Aust 2013;198:586–8.
5. Metz J. Aust Prescr 1999;22:16–8.
6. Willis CD, et al. Pathology 2011;43:472–81.
7. Hunt A, et al. BMJ 2014;349:g5226.
8. The Royal College of Pathologists of Australasia. Vitamin B12 - serum. March 2004. http://rcpamanual.edu.au/index.php?option=com_pttests&task=show_test&id=322&Itemid=77 (accessed 28 October 2014).
9. Alfred Health. Pathology search: holotranscobalamin. 2013. <http://pathology.alfred.org.au/handbook/index.php?testid=413> (accessed 6 October 2014).
10. Anemia Work Group. Kidney inter Suppl 2012;2:279–335.
11. Galvin JE, et al. J Am Board Fam Med 2012;25:367–82.
12. British Columbia Ministry of Health. Cognitive impairment in the elderly: recognition, diagnosis and management. 2007. http://www.bcguidelines.ca/guideline_cognitive.html (accessed 23 September 2014).
13. Flood VM, et al. Aust N Z J Public Health 2006;30:38–41.
14. Mirkazemi C, et al. J Nutr Health Aging 2012;16:277–80.
15. England JD, et al. PM R 2009;1:5–13.
16. Health Quality Ontario. Serum vitamin B12 testing: a rapid review. December 2012. <http://www.hqontario.ca/Portals/0/Documents/eds/rapid-reviews/vitamin-b12-121212-en.pdf> (accessed 22 September 2014).
17. Turnbull N, et al. Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children. London: Royal College of General Practitioners. 2007. <http://www.ncbi.nlm.nih.gov/books/NBK53577/> (accessed 23 September 2014).
18. Schrier SL. UpToDate: Etiology and clinical manifestations of vitamin B12 and folate deficiency. 2014. <http://www.uptodate.com/contents/etiology-and-clinical-manifestations-of-vitamin-b12-and-folate-deficiency> (accessed 20 September 2014).
19. British Columbia Medical Association. Cobalamin (vitamin B12) deficiency - investigation & management. May 2013. <http://www.bcguidelines.ca/pdf/cobalamin.pdf> (accessed 22 September 2014).
20. Smellie WS, et al. J Clin Pathol 2005;58:1016–24.

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