

If a conflict arises between a Clinical Payment and Coding Policy and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. Blue Cross and Blue Shield of New Mexico may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSNM has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology, CPT® Assistant, Healthcare Common Procedure Coding System, ICD-10 CM and PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare and Medicaid Services National Correct Coding Initiative Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Vitamin B12 and Methylmalonic Acid Testing

Policy Number: CPCPLAB010

Version 1.0

Approval Date: January 23, 2025

Plan Effective Date: April 15, 2025

Description

The Plan has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information:

- 1) Total vitamin B12 (serum cobalamin) testing **may be reimbursable** once every three months for **any** of the following situations:
 - a) For individuals with the following signs and symptoms of vitamin B12 deficiency:
 - i) Cutaneous
 - (a) Hyperpigmentation
 - (b) Jaundice
 - (c) Vitiligo
 - ii) Gastrointestinal
 - (a) Glossitis
 - iii) Hematologic
 - (a) Anemia (macrocytic, megaloblastic)
 - (b) Leukopenia
 - (c) Pancytopenia
 - (d) Thrombocytopenia
 - (e) Thrombocytosis
 - iv) Neuropsychiatric
 - (a) Areflexia
 - (b) Cognitive impairment (including dementia-like symptoms and acute psychosis)
 - (c) Gait abnormalities
 - (d) Irritability
 - (e) Loss of proprioception and vibratory sense
 - (f) Olfactory impairment
 - (g) Peripheral neuropathy
 - b) For individuals undergoing treatment for vitamin B12 deficiency.
 - c) For individuals with one or more of the following risk factors for vitamin B12 deficiency:

- i) For individuals with decreased ileal absorption due to:
 - (a) Crohn's disease
 - (b) Ileal resection
 - (c) Tapeworm infection
 - (d) Having undergone, or for those who have been scheduled for, bariatric procedures such as Roux-en-Y gastric bypass, sleeve gastrectomy, or biliopancreatic diversion/duodenal switch.
 - ii) For individuals with decreased intrinsic factor due to:
 - (a) Atrophic gastritis
 - (b) Pernicious anemia
 - (c) Postgastrectomy syndrome
 - iii) For individuals with transcobalamin II deficiency
 - iv) For individuals with inadequate B12 intake:
 - (a) Due to alcohol abuse
 - (b) In individuals older than 75 years or elderly individuals being evaluated for dementia
 - (c) In vegans or strict vegetarians (including exclusively breastfed infants of vegetarian/vegan mothers)
 - (d) Due to an eating disorder
 - v) For individuals with prolonged medication use:
 - (a) Histamine H2 blocker use for more than 12 months
 - (b) Metformin use for more than 4 months
 - (c) Proton pump inhibitor use for more than 12 months
- 2) In asymptomatic high-risk individuals with low-normal levels of vitamin B12 or when vitamin B12 deficiency is suspected but the serum vitamin B12 level is normal or low-normal, methylmalonic acid testing to confirm vitamin B12 deficiency **may be reimbursable**.
 - 3) For the evaluation of inborn errors of metabolism, methylmalonic acid testing **may be reimbursable**.
 - 4) In healthy, asymptomatic individuals, screening for vitamin B12 deficiency **is not reimbursable**.
 - 5) For the confirmation of vitamin B12 deficiency, homocysteine testing **is not reimbursable**.
 - 6) For the screening, testing, or confirmation of vitamin B12 deficiency, holotranscobalamin testing **is not reimbursable**.

- 7) For all other situations not described above, total vitamin B12 (serum cobalamin) testing **is not reimbursable**.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Codes
82607, 83090, 83921, 84999

References:

- American Diabetes Association Professional Practice, C. (2023a). 3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes—2024. *Diabetes Care*, 47(Supplement_1), S43-S51. <https://doi.org/10.2337/dc24-S003>
- American Diabetes Association Professional Practice, C. (2023b). 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes—2024. *Diabetes Care*, 47(Supplement_1), S52-S76. <https://doi.org/10.2337/dc24-S004>
- APA. (2023). Practice Guideline for the Treatment of Patients With Eating Disorders. Fourth Edition. . <https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890424865>
- BCMA. (2023, May 1). *Cobalamin (vitamin B12) and Folate Deficiency*. British Columbia Medical Association. Retrieved October 26 from <https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/vitamin-b12>
- Berg, R. L., & Shaw, G. R. (2013). Laboratory evaluation for vitamin B12 deficiency: the case for cascade testing. *Clin Med Res*, 11(1), 7-15. <https://doi.org/10.3121/cmr.2012.1112>
- CDC. (2024). *Vitamin B12*. Retrieved 9/16/2024 from <https://www.cdc.gov/breastfeeding-special-circumstances/hcp/diet-micronutrients/vitamin-b12.html>
- Devalia, V., Hamilton, M. S., & Molloy, A. M. (2014). Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *Br J Haematol*, 166(4), 496-513. <https://doi.org/10.1111/bjh.12959>
- Fan, X., Zhang, L., Li, H., Chen, G., Qi, G., Ma, X., & Jin, Y. (2020). Role of homocysteine in the development and progression of Parkinson's disease. *Ann Clin Transl Neurol*. <https://doi.org/10.1002/acn3.51227>
- Garber, A. J., Handelsman, Y., Grunberger, G., Einhorn, D., Abrahamson, M. J., Barzilay, J. I., Blonde, L., Bush, M. A., DeFronzo, R. A., Garber, J. R., Garvey, W. T., Hirsch, I. B., Jellinger, P. S., McGill, J. B., Mechanick, J. I., Perreault, L., Rosenblit, P. D., Samson, S., & Umpierrez, G. E. (2020). Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology

- on the Comprehensive Type 2 Diabetes Management Algorithm - 2020 Executive Summary. *Endocr Pract*, 26(1), 107-139. <https://doi.org/10.4158/CS-2019-0472>
- Gebremicael, G., Alemayehu, M., Sileshi, M., Geto, Z., Gebreegziabxier, A., Tefera, H., Ashenafi, N., Tadese, C., Wolde, M., & Kassa, D. (2019). The serum concentration of vitamin B12 as a biomarker of therapeutic response in tuberculosis patients with and without human immunodeficiency virus (HIV) infection. *Int J Gen Med*, 12, 353-361. <https://doi.org/10.2147/ijgm.S218799>
- Gonzalez-Campoy, J. M., St Jeor, S. T., Castorino, K., Ebrahim, A., Hurley, D., Jovanovic, L., Mechanick, J. I., Petak, S. M., Yu, Y. H., Harris, K. A., Kris-Etherton, P., Kushner, R., Molini-Blandford, M., Nguyen, Q. T., Plodkowski, R., Sarwer, D. B., & Thomas, K. T. (2013). Clinical practice guidelines for healthy eating for the prevention and treatment of metabolic and endocrine diseases in adults: cosponsored by the American Association of Clinical Endocrinologists/the American College of Endocrinology and the Obesity Society. *Endocr Pract*, 19 Suppl 3, 1-82. <https://doi.org/10.4158/ep13155.gl>
- Green, R. (2017). Vitamin B12 deficiency from the perspective of a practicing hematologist. *Blood*, 129(19), 2603-2611. <https://doi.org/10.1182/blood-2016-10-569186>
- Hama, Y., Hamano, T., Shirafuji, N., Hayashi, K., Ueno, A., Enomoto, S., Nagata, M., Kimura, H., Matsunaga, A., Ikawa, M., Yamamura, O., Ito, T., Kimura, Y., Kuriyama, M., & Nakamoto, Y. (2020). Influences of Folate Supplementation on Homocysteine and Cognition in Patients with Folate Deficiency and Cognitive Impairment. *Nutrients*, 12(10). <https://doi.org/10.3390/nu12103138>
- HQO. (2013). Vitamin B12 and cognitive function: an evidence-based analysis. *Ont Health Technol Assess Ser*, 13(23), 1-45. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3874776/>
- Huemer, M., Diodato, D., Schwahn, B., Schiff, M., Bandeira, A., Benoist, J. F., Burlina, A., Cerone, R., Couce, M. L., Garcia-Cazorla, A., la Marca, G., Pasquini, E., Vilarinho, L., Weisfeld-Adams, J. D., Kožich, V., Blom, H., Baumgartner, M. R., & Dionisi-Vici, C. (2017). Guidelines for diagnosis and management of the cobalamin-related remethylation disorders cblC, cblD, cblE, cblF, cblG, cblJ and MTHFR deficiency. *J Inherit Metab Dis*, 40(1), 21-48. <https://doi.org/10.1007/s10545-016-9991-4>
- Hunt, A., Harrington, D., & Robinson, S. (2014). Vitamin B12 deficiency. *Bmj*, 349, g5226. <https://doi.org/10.1136/bmj.g5226>
- Langan, R. C., & Goodbred, A. J. (2017). Vitamin B12 Deficiency: Recognition and Management. *Am Fam Physician*, 96(6), 384-389. <https://pubmed.ncbi.nlm.nih.gov/28925645/>
- Langan, R. C., & Zawistoski, K. J. (2011). Update on vitamin B12 deficiency. *Am Fam Physician*, 83(12), 1425-1430. <https://pubmed.ncbi.nlm.nih.gov/21671542/>
- Li, J., Li, B., Qi, J., & Shen, B. (2015). [Meta-analysis of clinical trials of folic acid, vitamin B12 and B6 supplementation on plasma homocysteine level and risk of cardiovascular disease]. *Zhonghua Xin Xue Guan Bing Za Zhi*, 43(6), 554-561.
- Mak, J., Peng, G., Le, A., Gandotra, N., Enns, G. M., Scharfe, C., & Cowan, T. M. (2023). Validation of a targeted metabolomics panel for improved second-tier newborn screening. *J Inherit Metab Dis*, 46(2), 194-205. <https://doi.org/10.1002/jimd.12591>
- Means Jr, R. T., & Fairfield, K. M. (2023, October 18, 2023). *Causes and pathophysiology of vitamin B12 and folate deficiencies*. Retrieved October 20 from

https://www.uptodate.com/contents/causes-and-pathophysiology-of-vitamin-b12-and-folate-deficiencies?source=see_link

- Mechanick, J. I., Apovian, C., Brethauer, S., Garvey, W. T., Joffe, A. M., Kim, J., Kushner, R. F., Lindquist, R., Pessah-Pollack, R., Seger, J., Urman, R. D., Adams, S., Cleek, J. B., Correa, R., Figaro, M. K., Flanders, K., Grams, J., Hurley, D. L., Kothari, S., . . . Still, C. D. (2019). CLINICAL PRACTICE GUIDELINES FOR THE PERIOPERATIVE NUTRITION, METABOLIC, AND NONSURGICAL SUPPORT OF PATIENTS UNDERGOING BARIATRIC PROCEDURES - 2019 UPDATE: COSPONSORED BY AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY, THE OBESITY SOCIETY, AMERICAN SOCIETY FOR METABOLIC & BARIATRIC SURGERY, OBESITY MEDICINE ASSOCIATION, AND AMERICAN SOCIETY OF ANESTHESIOLOGISTS - EXECUTIVE SUMMARY. *Endocr Pract*, 25(12), 1346-1359. <https://doi.org/10.4158/gl-2019-0406>
- NICE. (2024). *Vitamin B12 deficiency: Diagnosis and management*. <https://www.nice.org.uk/guidance/ng239>
- O'Kane, M., Parretti, H. M., Pinkney, J., Welbourn, R., Hughes, C. A., Mok, J., Walker, N., Thomas, D., Devin, J., Coulman, K. D., Pinnock, G., Batterham, R. L., Mahawar, K. K., Sharma, M., Blakemore, A. I., McMillan, I., & Barth, J. H. (2020). British Obesity and Metabolic Surgery Society Guidelines on perioperative and postoperative biochemical monitoring and micronutrient replacement for patients undergoing bariatric surgery—2020 update. *Obesity Reviews*, 21(11), e13087. <https://doi.org/10.1111/obr.13087>
- Obeid, R., Andr s, E.,  eřka, R., Hooshmand, B., Gu ant-Rodr guez, R. M., Prada, G. I., S lawek, J., Traykov, L., Ta Van, B., V rkonyi, T., Reiners, K., & The Vitamin, B. C. P. G. (2024). Diagnosis, Treatment and Long-Term Management of Vitamin B12 Deficiency in Adults: A Delphi Expert Consensus. *J Clin Med*, 13(8). <https://doi.org/10.3390/jcm13082176>
- Oberley, M. J., & Yang, D. T. (2013). Laboratory testing for cobalamin deficiency in megaloblastic anemia. *Am J Hematol*, 88(6), 522-526. <https://doi.org/10.1002/ajh.23421>
- Oh, R., & Brown, D. L. (2003). Vitamin B12 deficiency. *Am Fam Physician*, 67(5), 979-986. <https://pubmed.ncbi.nlm.nih.gov/12643357/>
- Parrott, J., Frank, L., Rabena, R., Craggs-Dino, L., Isom, K. A., & Greiman, L. (2017). American Society for Metabolic and Bariatric Surgery Integrated Health Nutritional Guidelines for the Surgical Weight Loss Patient 2016 Update: Micronutrients. *Surg Obes Relat Dis*, 13(5), 727-741. <https://doi.org/10.1016/j.soard.2016.12.018>
- Pratt, J. S. A., Browne, A., Browne, N. T., Bruzoni, M., Cohen, M., Desai, A., Inge, T., Linden, B. C., Mattar, S. G., Michalsky, M., Podkameni, D., Reichard, K. W., Stanford, F. C., Zeller, M. H., & Zitsman, J. (2018). ASMBS pediatric metabolic and bariatric surgery guidelines, 2018. *Surg Obes Relat Dis*, 14(7), 882-901. <https://doi.org/10.1016/j.soard.2018.03.019>
- Rogne, T., Tielemans, M. J., Chong, M. F., Yajnik, C. S., Krishnaveni, G. V., Poston, L., Jaddoe, V. W., Steegers, E. A., Joshi, S., Chong, Y. S., Godfrey, K. M., Yap, F., Yahyaoui, R., Thomas, T., Hay, G., Hogeveen, M., Demir, A., Saravanan, P., Skovlund, E., . . . Risnes, K. R. (2017). Associations of Maternal Vitamin B12 Concentration in Pregnancy With the Risks of Preterm Birth and Low Birth

- Weight: A Systematic Review and Meta-Analysis of Individual Participant Data. *Am J Epidemiol*, 185(3), 212-223. <https://doi.org/10.1093/aje/kww212>
- Rozmarič, T., Mitulović, G., Konstantopoulou, V., Goeschl, B., Huemer, M., Plecko, B., Spenger, J., Wortmann, S. B., Scholl-Bürgi, S., Karall, D., Greber-Platzer, S., & Zeyda, M. (2020). Elevated Homocysteine after Elevated Propionylcarnitine or Low Methionine in Newborn Screening Is Highly Predictive for Low Vitamin B12 and Holo-Transcobalamin Levels in Newborns. *Diagnostics (Basel)*, 10(9). <https://doi.org/10.3390/diagnostics10090626>
- Rubio-Tapia, A., Hill, I. D., Kelly, C. P., Calderwood, A. H., & Murray, J. A. (2013). ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol*, 108(5), 656-676; quiz 677. <https://doi.org/10.1038/ajg.2013.79>
- Sands, T., Jawed, A., Stevenson, E., Smith, M., & Jawaid, I. (2024). Vitamin B12 deficiency: NICE guideline summary. *Bmj*, 385, q1019. <https://doi.org/10.1136/bmj.q1019>
- Sangle, P., Sandhu, O., Aftab, Z., Anthony, A. T., & Khan, S. (2020). Vitamin B12 Supplementation: Preventing Onset and Improving Prognosis of Depression. *Cureus*, 12(10), e11169. <https://doi.org/10.7759/cureus.11169>
- Sasaki, Y., Sato, T., Maeda, T., Komatsu, F., Kawagoe, N., Imai, T., Shigeta, T., Kashima, N., & Urita, Y. (2023). Evaluation of the One-Hour ¹³C-Propionate Breath Test in 49 Patients from a Single Center in Japan to Detect Vitamin B₁₂ Deficiency. *Med Sci Monit*, 29, e940238. <https://doi.org/10.12659/msm.940238>
- Schroder, T. H., Tan, A., Mattman, A., Sinclair, G., Barr, S. I., Vallance, H. D., & Lamers, Y. (2019). Reference intervals for serum total vitamin B12 and holotranscobalamin concentrations and their change points with methylmalonic acid concentration to assess vitamin B12 status during early and mid-pregnancy. *Clin Chem Lab Med*. <https://doi.org/10.1515/ccim-2018-1337>
- Sobczynska-Malefora, A., Gorska, R., Pelisser, M., Ruwona, P., Witchlow, B., & Harrington, D. J. (2014). An audit of holotranscobalamin ("Active" B12) and methylmalonic acid assays for the assessment of vitamin B12 status: application in a mixed patient population. *Clin Biochem*, 47(1-2), 82-86. <https://doi.org/10.1016/j.clinbiochem.2013.08.006>
- Stabler, S. P. (2013). Clinical practice. Vitamin B12 deficiency. *N Engl J Med*, 368(2), 149-160. <https://doi.org/10.1056/NEJMcp1113996>
- Willis, C. D., Elshaug, A. G., Milverton, J. L., Watt, A. M., Metz, M. P., & Hiller, J. E. (2011). Diagnostic performance of serum cobalamin tests: a systematic review and meta-analysis. *Pathology*, 43(5), 472-481. <https://doi.org/10.1097/PAT.0b013e3283486435>
- Wolffenbuttel, B. H., Owen, P. J., Ward, M., & Green, R. (2023). Vitamin B12. *Bmj*, 383, e071725. <https://doi.org/10.1136/bmj-2022-071725>
- Wolffenbuttel, B. H. R., Heiner-Fokkema, M. R., Green, R., & Gans, R. O. B. (2020). Relationship between serum B12 concentrations and mortality: experience in NHANES. *BMC Medicine*, 18(1), 307. <https://doi.org/10.1186/s12916-020-01771-y>
- Yetim, A., Aygun, E., Yetim, C., Ucar, A., Karakas, Z., Gokcay, G., Demirkol, M., Omer, B., Gokcay, G., Bas, F., Erginoz, E., & Dagoglu, T. (2019). Measurement of serum vitamin B12-related metabolites in newborns: implications for new cutoff values to detect B12 deficiency. *J Matern Fetal Neonatal Med*, 1-9. <https://doi.org/10.1080/14767058.2019.1633301>

Zeuschner, C. L., Hokin, B. D., Marsh, K. A., Saunders, A. V., Reid, M. A., & Ramsay, M. R. (2013). Vitamin B(1)(2) and vegetarian diets. *Med J Aust*, 199(4 Suppl), S27-32. <https://pubmed.ncbi.nlm.nih.gov/25369926/>

Policy Update History:

Approval Date	Effective Date; Summary of Revisions
01/23/2025	04/15/2025; Document updated with literature review. The following changes were made to Reimbursement Information: Added a three month testing frequency for all vitamin B testing/screening, resulting in a new main criterion 1 which reads: "Total vitamin B12 (serum cobalamin) testing may be reimbursable once every three months for any of the following situations:" Former statements 1, 2, 3 are now included in this main criterion. Added new #7: For all other situations not described above, total vitamin B12 (serum cobalamin) testing is not reimbursable. References revised.
04/29/2024	01/15/2025; Document updated. Added #8: For the screening, testing, or confirmation of vitamin B12 deficiency, holotranscobalamin testing is not reimbursable. No references added.
03/15/2024	03/15/2024: Document updated with literature review. Reimbursement Information unchanged. References revised; some added; others updated. Added code 84999.
11/01/2023	11/01/2023: Document updated with literature review. The following changes were made to Reimbursement Information: revised #3aiv to include "or for those who have been scheduled for" regarding bariatric procedures; removed not reimbursable statement on holotranscobalamin testing for screening, testing or confirmation of vitamin B12 deficiency. Other changes made for clarity. References revised.
11/1/2022	11/01/2022: New policy