



If a conflict arises between a Clinical Payment and Coding Policy (“CPCP”) 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. BCBSNM 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 (“HIPAA”) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (“UB”) Editor, American Medical Association (“AMA”), Current Procedural Terminology (“CPT®”), CPT® Assistant, Healthcare Common Procedure Coding System (“HCPCS”), ICD-10 CM and PCS, National Drug Codes (“NDC”), Diagnosis Related Group (“DRG”) guidelines, Centers for Medicare and Medicaid Services (“CMS”) National Correct Coding Initiative (“NCCI”) 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

Enterprise Medical Policy Committee Approval Date: 1/25/2022

Plan Effective Date: May 1, 2022

Description

BCBSNM 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. Vitamin B12 testing **may be reimbursable** in individuals being evaluated for clinical manifestations of Vitamin B12 deficiency including:
 - a. Cutaneous
 - i. Hyperpigmentation
 - ii. Jaundice
 - iii. Vitiligo

- b. Gastrointestinal
 - i. Glossitis
 - c. Hematologic
 - i. Anemia (macrocytic, megaloblastic)
 - ii. Leukopenia
 - iii. Pancytopenia
 - iv. Thrombocytopenia
 - v. Thrombocytosis
 - d. Neuropsychiatric
 - i. Areflexia
 - ii. Cognitive impairment (including dementia-like symptoms and acute psychosis)
 - iii. Gait abnormalities
 - iv. Irritability
 - v. Loss of proprioception and vibratory sense
 - vi. Olfactory impairment
 - vii. Peripheral neuropathy
2. Vitamin B12 testing **may be reimbursable** when performed no sooner than 3 months after initiation of therapy for individuals undergoing treatment for vitamin B12 deficiency.
 3. Screening for Vitamin B12 deficiency **may be reimbursable** for individuals with one or more of the following risk factors:
 - a. Decreased ileal absorption
 - i. Crohn disease
 - ii. Ileal resection
 - iii. Tapeworm infection
 - iv. Patients that have undergone bariatric procedures such as Roux-en-Y gastric bypass, sleeve gastrectomy, or biliopancreatic diversion/duodenal switch
 - b. Decreased intrinsic factor
 - i. Atrophic gastritis
 - ii. Pernicious anemia
 - iii. Post-gastrectomy syndrome
 - c. Genetic
 - i. Transcobalamin II deficiency
 - d. Inadequate intake
 - i. Alcohol abuse
 - ii. Patients older than 75 years or elderly individuals being evaluated for dementia
 - iii. Vegans or strict vegetarians (including exclusively breastfed infants of vegetarian/vegan mothers)
 - iv. Eating disorders
 - e. Prolonged medication use
 - i. Histamine H2 blocker use for more than 12 months
 - ii. Metformin use for more than four months
 - iii. Proton pump inhibitor use for more than 12 months
 4. Methylmalonic acid testing **may be reimbursable** to confirm vitamin B12 deficiency in asymptomatic high-risk patients 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.

5. Methylmalonic acid **may be reimbursable** for the evaluation of inborn errors of metabolism, which is out of scope for this policy.

The following criteria for Vitamin B12 deficiency **are not reimbursable**:

- Screening for Vitamin B12 deficiency in healthy, asymptomatic individuals; or
- Homocysteine testing for the confirmation of vitamin B12 deficiency; or
- Holotranscobalamin testing for the screening, testing or confirmation of vitamin B12 deficiency.

Procedure Codes

Codes
82607, 83090, 83921, 84999

References:

ADA. (2020a). 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes—2020. *Diabetes Care*, 43(Supplement 1), S32-S36. <https://doi.org/10.2337/dc20-S003>

ADA. (2020b). 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes—2020. *Diabetes Care*, 43(Supplement 1), S37-S47. <https://doi.org/10.2337/dc20-S004>

ADA. (2021). 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes-2021. *Diabetes Care*, 44(Suppl 1), S34-S39. <https://doi.org/10.2337/dc21-S003>

BCMA. (2013, May 1). Cobalamin (vitamin B12) Deficiency - Investigation & Management - Province of British Columbia. 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. (n.d., August 26, 2021). Vitamin B12. Retrieved October 25 from <https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/diet-and-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.g1>

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 Inher 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>

IOM. (1998). In *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. <https://doi.org/10.17226/6015>

Knopman, D. S., DeKosky, S. T., Cummings, J. L., Chui, H., Corey-Bloom, J., Relkin, N., Small, G. W., Miller, B., & Stevens, J. C. (2001). Practice parameter: Diagnosis of dementia (an evidence-based review). *Neruology*, 56(9), 1143-1153. <https://doi.org/10.1212/WNL.56.9.1143>

Langan, R. C., & Goodbred, A. J. (2017). Vitamin B12 Deficiency: Recognition and Management. *Am Fam Physician*, 96(6), 384-389. <http://dx.doi.org/>

- Langan, R. C., & Zawistoski, K. J. (2011). Update on vitamin B12 deficiency. *Am Fam Physician*, 83(12), 1425-1430.
- 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.
- Means Jr, R. T., & Fairfield, K. M. (2019, October 22). 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., Seger, M. V., & 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>
- Mechanick, J. I., Youdim, A., Jones, D. B., Garvey, W. T., Hurley, D. L., McMahon, M. M., Heinberg, L. J., Kushner, R., Adams, T. D., Shikora, S., Dixon, J. B., & Brethauer, S. (2013). Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient--2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Endocr Pract*, 19(2), 337-372. <https://doi.org/10.4158/ep12437.gl>
- 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>
- 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. <http://dx.doi.org/>
- 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., Podkamieni, 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., Martinussen, M. P., Jacobsen, G. W., Franco, O. H., Bracken, M. B., & 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>
- 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>
- 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/cclm-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. 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>
- Yager, J., Devlin, M., Halmi, K., Herzog, D., Mitchell, J., Powers, P., & Zerbe, K. (2006). Treatment of patients with eating disorders, third edition. American Psychiatric Association. *Am J Psychiatry*, 163(7 Suppl), 4-54. <https://www.ncbi.nlm.nih.gov/pubmed/?term=PRACTICE+GUIDELINE+FOR+THE+Treatment+of+Patients+With+Eating+Disorders+Third+Edition>
- 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. <http://dx.doi.org/>

Policy Update History:

5/1/2022	New policy
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