

Corporate Medical Policy

Folate Testing AHS – G2154

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Description of Procedure or Service

Folate, or vitamin B9, is a generic term for a water-soluble vitamin obtained from the diet that is involved in the transfer of methyl groups (i.e., single carbon-containing groups) in multiple biochemical metabolic pathways, including nucleic acid biosynthesis and methionine/homocysteine metabolism. Folate metabolism is closely linked to vitamin B12, cobalamin. Folate deficiency can be implicated in many disease states and processes; however, it is usually easily remedied with either a change in diet or a dietary supplement of the synthetic form, folic acid (Means Jr & Fairfield, 2023a; NIH, 2018).

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for measurement of serum folate concentration when it is determined the medical criteria or reimbursement guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When measurement of serum folate concentration is covered

Reimbursement for measurement of serum folate concentration is allowed for evaluation of patients when **all** the following criteria has been met:

- patients who have been diagnosed with megaloblastic or macrocytic anemia; **AND**
- megaloblastic anemia and/or macrocytosis does not resolve after folic acid treatment

When measurement of serum folate concentration is not covered

Reimbursement is not allowed for the measurement of serum folate concentration for any other indications not described above.

Reimbursement is not allowed for the measurement of red blood cell (RBC) folate for any indications.

Reimbursement is not allowed folate receptor autoantibody testing for all situations.

Policy Guidelines

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Folate, or vitamin B9, naturally occurs as polyglutamated compounds (pteroylpolyglutamates) in many plant and animal products. The synthetic form is a monoglutamate-containing compound called folic acid. Folic acid is more chemically stable for commercial production and storage, but it is less bioavailable than the naturally occurring folate (Means Jr & Fairfield, 2023a). Biochemically, folate is a coenzyme in single-carbon transfers *in vivo* and is directly linked to the cobalamin (vitamin B12) cycle, methionine metabolism, and nucleic acid biosynthesis. Dietary folates are hydrolyzed via γ -glutamyl hydrolase (or folate conjugase) prior to absorption in the intestinal mucosa (IOM, 1998). Both folate and vitamin B12 are required for formation of 5,10-methylene tetrahydrofolate, which is the cofactor involved in purine synthesis. Methylenetetrahydrofolate reductase (MTHFR) is the enzyme responsible in converting 5,10-methylene tetrahydrofolate to 5-methyl tetrahydrofolate, which is required for methionine synthase, the enzyme that converts homocysteine to methionine. The interlinked one-carbon cycle is depicted in the figure below with the metabolites assayed in clinical laboratories in bold (Finer et al., 2013).

Role of Folate in Anemia

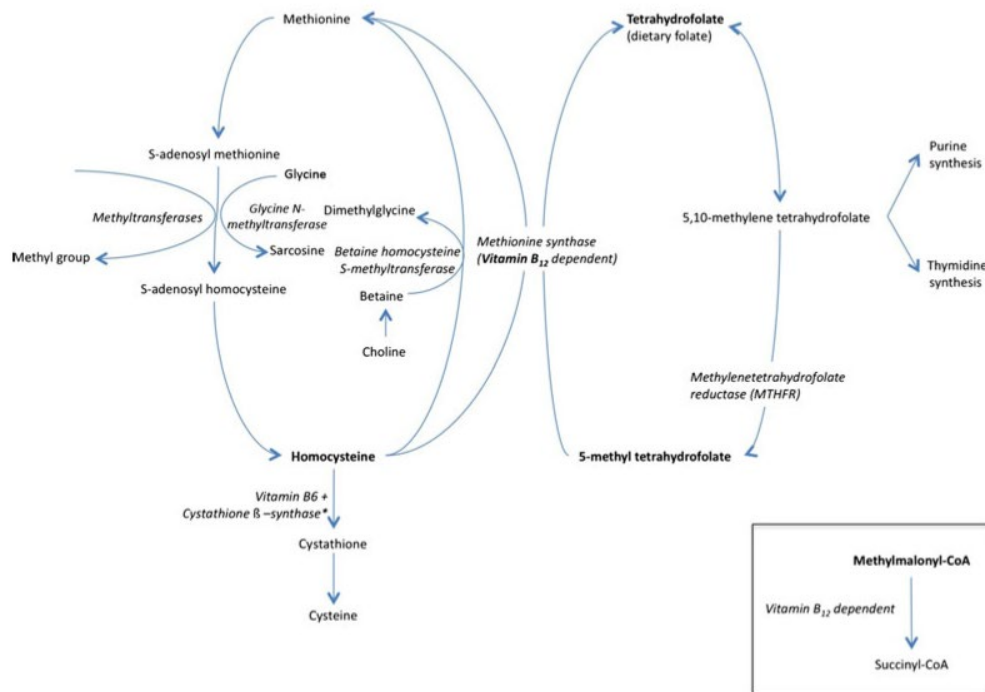


FIGURE 1 The one-carbon cycle. Metabolites readily assayed in clinical laboratories are highlighted in bold.

Anemia occurs when the body lacks healthy red blood cells (RBCs), leading to an insufficient amount of oxygen delivered to tissues. Typical symptoms of anemia include fatigue, weakness, pale skin, and lightheadedness.

Macrocytic anemia refers to anemias that have high mean corpuscular volume with large RBCs. Mean corpuscular volume, or mean cell volume, can be defined as the average volume of RBCs in an individual. Megaloblastic anemia is a specific macrocytic anemia due to nucleic acid metabolic defects that result in “nuclear-cytoplasmic dyssynchrony, reduced number of cell divisions in the bone marrow, and nuclear abnormalities in both myeloid and erythroid precursors” caused by folate and/or vitamin B12 deficiency (Means Jr & Fairfield, 2023b). These abnormal RBCs are the principle clinical manifestations of folate deficiency and symptoms “include weakness, fatigue, difficulty concentrating, irritability, headache, heart palpitations, and shortness of breath” (NIH, 2018).

Folate and Neural Tube Defects (NTDs)

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Neural tube defects (NTDs) develop early in pregnancy and are malformations of the brain and/or spine that include spina bifida and anencephaly. Folate deficiency is directly linked to NTDs. The role of folate in NTD development is not well-characterized. The role of folate in either the methylation cycle or nucleic acid synthesis has been suggested to play a part in NTD development during embryogenesis, and some studies have indicated that it is the bioavailability of specific folates in the pregnant individual that can increase the likelihood of NTDs (Imbard et al., 2013; Rothenberg et al., 2004). Individuals typically do not obtain enough folate from diet alone, so individuals of childbearing age are recommended to take a synthetic folic acid supplement to decrease the likelihood of NTDs in offspring (Bibbins-Domingo et al., 2017). To decrease the occurrence of NTDs and folate deficiency, the United States and Canada mandated folic acid supplementation to cereal grains in 1998, and as of March 2018 “92 countries have legislation to mandate fortification of at least one industrially milled cereal grain” (FFI, 2021).

It is notable that the prevalence of folate deficiency, and the prevalence of NTDs has declined in countries with routine folic acid supplementation (Crider et al., 2011). A review by Imbard et al. (2013) of 17 different studies on the impact of folic acid fortification of NTD rates show that 16 show a decrease in the rate of NTDs. Only one study of the rate of NTDs in California showed no decline since fortification. The reduction of the United States overall was 26-30% since folic acid fortification (Imbard et al., 2013).

Folate Receptor Antibody Testing (FRAT®)

Folate deficiency in the pregnant individual can “lead to pregnancy-related complications including neural tube defects (NTDs) in the fetus. Numerous studies have now established the benefits of folate supplementation in reducing the incidence of NTD pregnancy” (Sequeira, 2012). Fratnow's FRAT® measures the “presence of antibodies that interact by either blocking or binding with the activity of the Folate Receptor A. Data shows that folate is critical for the proper function of many tissues, including brain, placenta, and ovaries. FRAT® is not indicated for the diagnosis of any medical condition and thus has not been approved by the FDA. FRAT® can be useful as a research tool in the above disorders, as well as assessing the health of folate transport to the brain, placenta, and ovary” (Fratnow, 2016).

Causes of Folate Deficiency

Folate deficiency can be caused by dietary intake. Nutritional deficits may occur due to diet, alcoholism, depression, and even overcooked foods. Many malabsorptive disorders, such as celiac disease and ulcerative colitis, can also result in a decrease in folate uptake. Further, bariatric procedures may result in decreased absorption, and drugs, including methotrexate and trimethoprim that inhibit dihydrofolate reductase (DHFR), can also cause a folate deficiency. It is also important to note that an increased need of folate for DNA synthesis during pregnancy and lactation, chronic hemolytic anemias, exfoliative skin diseases, and hemodialysis cause folic acid deficiency. Folate deficiency is also more prevalent in older adults than younger (Means Jr & Fairfield, 2023b).

Methodology of Folate Testing

Folate concentrations have been measured from serum, erythrocytes (RBC), and urine. Serum folate levels may not “differentiate between what may be a transitory reduction in folate intake or chronic folate deficiency accompanied by depleted folate stores and functional changes” (IOM, 1998). RBCs have a lifespan of approximately 120 days, and folate is only taken in during initial erythropoiesis (red blood cell production); consequently, RBC folate concentrations are less likely to be affected by transitory dietary fluctuations. However, Wu et al. (1975) show that both RBC folate and serum folate levels correlate to hepatocyte folate levels (IOM, 1998; Wu et al., 1975). Galloway and Rushworth (2003) released a study in conjunction with the National Pathology Alliance review in the United Kingdom comparing data of laboratories of the National Health Service that routinely use serum folate testing only, RBC folate testing only, or both serum and RBC folate testing together. The researchers conclude that there is no need to use both tests to determine folate concentration as an initial screen. “The serum folate assay provided equivalent information to the measurement of red cell folate and evidence from the literatures [sic] suggest that the serum folate assay should be the method of choice” (Galloway & Rushworth, 2003).

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Clinical Utility and Validity

A study by Shojania and von Kuster (2010) investigated the use of serum folate testing (Trompeter et al.) and RBC folate testing (RF) in cases of anemia in a country that has mandated folic acid supplementation in grain products. By examining the data for folate testing in anemia at two different teaching hospitals in Canada, they report that in one hospital in 2001 “11 out of 2154 (0.5%) SF were low (<7.0 nmol/L) and 4 out of 560 (0.7%) RF were low (<417 nmol/L). In no subject with low SF or RF could the anemia be attributed to folate deficiency.” For the other hospital, the data from 1999-2001 shows that “19 out of 991 (1.9%) had low RF (<225 nmol/L) but in only 2 patients (0.2%) the low RF was in folate deficiency anemia range” (Shojania & von Kuster, 2010). The authors conclude that neither serum folate testing, nor RBC folate testing is justified in cases of anemia for folic acid fortified countries due to such low incidence rates of folate deficiency anemia.

A study by Joelson et al. (2007) examined the records of three different hospitals in the U.S. that service a high number of indigent patients. The researchers reported the data from three non-consecutive years (1997, 2000, and 2004) to examine the impact of folate fortification in food products. Using the RBC folate levels only with a RBC folate cutoff value of 160 ng/mL (363.6 nmol/L), “the combined incidence of folate deficiency decreased from 4.8% in 1997 to 0.6% in 2004...Even when the folate concentration was found to be low, the majority of these subjects did not have macrocytosis.” This study included a total of 4134 RBC folate tests performed over the course of three years. It is of interest to note that the number of tests performed increased from 813 in 1997 to 1759 in 2004. The authors do note of a potential limitation of the study since the data of the patients cannot be separated into specific groups (pregnant individuals, alcoholics, socioeconomic classes, and so on). The authors conclude “that folate deficiency has become a rare event in the United States, and the utility of routine folate measurements for patients with anemia and/or increased mean corpuscular volume are difficult to justify” (Joelson et al., 2007).

Urinary folate levels do not reflect either the stored folate concentrations or the fluctuations in folate concentration due to transitory dietary changes. Only about 1-2% of the folate excreted in the urine is unmetabolized and “excretion continued in the face of advanced folate depletion” (IOM, 1998). One study of ten postmenopausal individuals on a low folate diet measured folate turnover using urinary testing of folate and folate metabolites. “Folate intake did not significantly influence ApABG (*para*-acetamidobenzoylglutamate) or pABG (*para*-aminobenzoylglutamate) excretion.” ApABG and pABG along with pterins are the major folate catabolites. The authors conclude that “the rate of folate catabolite excretion is related mainly to masses of slow-turnover folate pools governed by long-term folate intake” (Gregory et al., 2000).

Epstein-Peterson et al. (2020) collected and analyzed all folate tests performed in 2017 at an academic cancer center. In total, 937 patients were tested 1065 times; approximately 7% of tests indicated a folate deficiency, and folate deficiency was significantly associated with a higher risk of death (P=0.01) (Epstein-Peterson et al., 2020).

Tran et al. (2022) performed a literature review on the diagnostic accuracy, clinical utility, cost-effectiveness, and evidence-based guidelines regarding the use of serum folate testing in people with suspected folate deficiency. An information specialist completed a literature search using the search concepts “folate deficiency AND testing” and only limiting results to the human population for publications between January 1, 2012, and February 15, 2022. The authors were not able to identify any relevant literature regarding diagnostic test accuracy, clinical utility, cost-effectiveness, or evidence-based guidelines (Tran et al., 2022).

Guidelines and Recommendations

Centers for Disease Control and Prevention (CDC)

The CDC urges all individuals who are capable of becoming pregnant and who are also of reproductive age to “take 400 micrograms (Handelsman et al.) of folic acid each day, in addition to consuming food with folate from a varied diet, to help prevent some major birth defects of the baby’s brain (anencephaly) and

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spine (spina bifida)” (CDC, 2022). This was reviewed in 2021. This recommendation includes all individuals of reproductive age planning to become pregnant or not, as about half of U.S. pregnancies are unplanned.

American Society for Clinical Pathology (ASCP)/Choosing Wisely

The ASCP published a recommendation in 2017 in *Choosing Wisely*, an American Board of Internal Medicine (ABIM) initiative, where they clearly state the following: “Do not order red blood cell folate levels at all. In adults, consider folate supplementation instead of serum folate testing in patients with macrocytic anemia.” They indicate that the drastic decrease in folic deficiency in both the U.S. and Canada after mandated folic acid supplementation in foods no longer requires for either serum folate or red blood cell folate concentrations be tested. “While red blood cell folate levels have been used in the past as a surrogate for tissue folate levels or a marker for folate status over the lifetime of red blood cells, the result of this testing does not, in general, add to the clinical diagnosis or therapeutic plan” (ASCP, 2017).

National Pathology Alliance (of the United Kingdom)

The National Pathology Alliance of the United Kingdom in 2003 published in the *Journal of Clinical Pathology* their recommendation “that serum folate measurements provide equivalent information to red cell folate measurements” (Galloway & Rushworth, 2003).

American Association of Clinical Endocrinologists (AACE)/The American College of Endocrinology (ACE), The Obesity Society (TOS), American Society for Metabolic and Bariatric Surgery (ASMBS), Obesity Medicine Association (OMA), and American Society of Anesthesiologists (ASA)

In 2013, the AACE, ACE, and TOS issued joint guidelines regarding healthy eating for the prevention and treatment of metabolic and endocrine diseases in adults (Gonzalez-Campoy et al., 2013). Based on the data from the National Health and Nutrition Examination Survey (NHANES), they state “that patients with vitamin B₁₂ deficiency had higher folate levels, were more likely to be anemic, and had more cognitive impairment than those with normal serum folate levels” [evidence level (EL) 2]. They evaluate the evidence concerning the link between folate and cardiovascular disease as EL4 and the link between NTDs and folate as EL1. With respect to pregnancy nutritional needs, they “should be assessed prior to conception to improve pregnancy outcome.” All individuals of childbearing age “should consume at least 400 µg dietary equivalents of folate per day” [EL4] and that during pregnancy the daily amount should be increased to 600 µg [EL3].

The AACE and ACE in 2015 released their *Clinical Practice Guidelines for Developing a Diabetes Mellitus Comprehensive Care Plan* (Handelsman et al., 2015). Concerning patients with diabetic nephropathy, they suggest that they “undergo annual or more frequent assessment of electrolytes.” For those with anemia, iron, transferrin saturation (TSAT), ferritin, vitamin B₁₂, and folate levels “should be further investigated” [EL4].

In 2017, the AACE and ACE released their guidelines for management of dyslipidemia and prevention of cardiovascular disease (Jellinger et al., 2017). Since bile acid sequestrant treatments such as cholestyramine can cause folate depletion in children, they recommend that children on such treatments supplement their diet with a multivitamin. They also note that folate, B₆, and B₁₂ supplementation can help mediate hyperhomocysteinemia, but that the supplements do not reduce risk of atherosclerotic cardiovascular disease.

In 2019, the AACE/ACE, TOS, ASMBS, OMA, and ASA issued joint guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient (Mechanick et al., 2019). Here, as part of a pre-operative bariatric surgery checklist that has a “Grade A” recommendation, they include “nutrient screening with iron studies, B₁₂ and folic acid (RBC folate, homocysteine, methylmalonic acid optional) ...consider more extensive testing in patients undergoing malabsorptive procedures based on symptoms and risks.” With regards to patients who become pregnant after having a bariatric procedure, they recommend (with Grade D) having nutritional surveillance laboratory screenings done each trimester for folate deficiency along with iron, calcium, B₁₂, and vitamin D, and if after a malabsorptive procedure, fat-soluble vitamins, zinc, and copper. With a Grade C, they state that “nutritional anemias resulting from malabsorptive bariatric surgical procedures can involve deficiencies in vitamin B₁₂, folate, protein, copper,

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selenium, and zinc and may be evaluated when routine aggressive case finding for iron-deficiency anemia is negative.” Additionally, findings of folate deficiency in patients with obesity prior to bariatric surgery by the ASMBS “justifies aggressive case finding preoperatively with biochemical testing, specifically using sensitive markers, such as red-blood-cell folate and homocysteine (methylmalonic acid is normal with folate deficiency and normal B12 status)” and they note that particular attention should be given to individuals of childbearing age.

National Institute for Health and Care Excellence (NICE)

The National Institute for Health and Care Excellence (NICE) of the Department of Health in the United Kingdom published their extensive guidelines concerning bladder cancer on February 25, 2015. Within the section concerning the follow-up treatment for muscle-invasive bladder cancer, they recommend a protocol after radical cystectomy that includes “monitoring for metabolic acidosis and B12 and folate deficiency at least annually” (NICE, 2015). This guideline was reaffirmed in 2019.

American Academy of Family Physicians (AAFP)

The AAFP released the recommendations concerning macrocytosis and macrocytic anemia in 2009. Of note, they state that “serum folate levels are not useful because they fluctuate rapidly with dietary intake and are not cost effective. RBC folate levels more accurately correlate with folate stores and should be performed if folate deficiency is suspected.” They give the following key recommendation (with evidence rating of “C” or “consensus, disease-oriented evidence, usual practice, expert opinion, or case series”) to “obtain red blood cell folate level if other etiologies are not found (serum folate levels may be misleading).” In the evaluation of macrocytic anemia, they included a flowchart outlining the order of steps and tests to be taken, including when the RBC folate level should be checked. For a patient exhibiting a mean corpuscular volume 100 fL and an abnormal peripheral smear showing megaloblastic features and a reticulocyte count under 2%, they should have their RBC folate level measured only if the vitamin B₁₂ level is >400 pg. The flowchart is included below (Kaferle & Strzoda, 2009).

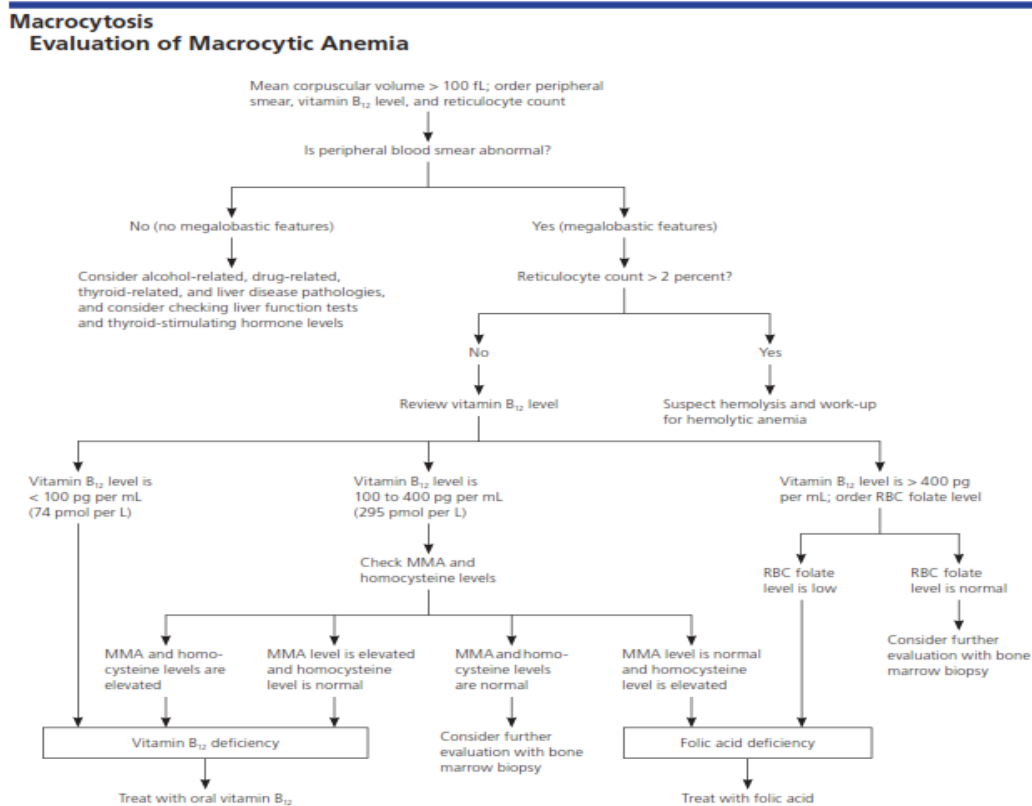


Figure 3. Algorithm for the evaluation of macrocytic anemia. (RBC = red blood cell; MMA = methylmalonic acid.)

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American Academy of Neurology (AAN)

In 2001, the AAN updated their practice parameters for the diagnosis of dementia. Within the section concerning the comorbidities that should be screened in an initial assessment for dementia, they recommend folate testing along with complete blood count, serum electrolytes, B₁₂, blood urea nitrogen/creatinine, syphilis serology, thyroid function, and glucose. They did note that as of that time “no studies were identified that evaluated these recommendations” since the last practice parameters released in 1994 (Knopman et al., 2001).

Kidney Disease Improving Global Outcomes (KDIGO)

KDIGO released their updated *KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease* in 2012. They gave a “not graded” recommendation for “in patients with CKD [chronic kidney disease] and anemia (regardless of age and CKD stage), include the following tests in initial evaluation of the anemia (*Not Graded*):

- Complete blood count (CBC), which should include Hb concentration, red cell indices, white blood cell count and differential, and platelet count
- Absolute reticulocyte count
- Serum ferritin level
- Serum transferrin saturation (TSAT)
- Serum vitamin B₁₂ and folate levels”

They also state that “RBC folate levels can be measured when serum folate levels are equivocal or when there is concern that recent dietary intake may obscure underlying folate deficiency using serum levels alone” (McMurray et al., 2012).

American Society for Parenteral and Enteral Nutrition (ASPEN) & Society of Critical Care Medicine (SSCM)

In 2013, ASPEN and SSCM issued joint clinical guidelines concerning the nutrition support of hospitalized obese adults. With a “Recommendation: Weak” status, they recommended “in acutely ill hospitalized patients with history of these procedures [sleeve gastrectomy, gastric bypass, or biliopancreatic diversion ± duodenal switch], evaluation for evidence of depletion of iron, copper, zinc, selenium, thiamine, folate, and vitamins B₁₂ and D is suggested as well as repletion of deficiency states” (Choban et al., 2013).

In 2016, ASPEN and SSCM issued their *Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient*. The committee recommended that “evaluation for and treatment of micronutrient deficiencies such as calcium, thiamin, vitamin B₁₂, fat-soluble vitamins (A, D, E, K), and folate, along with the trace minerals iron, selenium, zinc, and copper, should be considered” (McClave et al., 2016). In 2021, the ASPEN and SSCM updated their *Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient*; the guidelines do not mention folate testing (Compher et al., 2022). In 2017, ASPEN and SSCM updated their *Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient*. These guidelines do not mention folate testing (Mehta et al., 2017).

Academy of Nutrition and Dietetics (AND)

The AND released their *Oncology evidence-based nutrition practice guideline* in 2013 and reaffirmed the guideline in a 2017 publication. On the “Assessment of Biochemical Data Medical Tests, and Procedures on Adult Oncology Patients” portion, the committee recommended with “Consensus, Imperative” that “the RDN [Registered Dietitian Nutritionist] should evaluate available data and recommend as indicated: biochemical data, medical tests and procedures of adult oncology patients” and included on their list is “Nutritional anemia profile (hemoglobin, hematocrit, folate, B₁₂, iron).” “Assessment of these factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions” (Thompson et al., 2017).

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European Crohn’s and Colitis Organisation (ECCO)

ECCO’s guidelines concerning irritable bowel disorders (IBD) included an extensive discussion on causes and treatments of anemia in IBD—both iron deficiency anemia and non-iron deficiency anemia. With an [EL 5], they state that “deficiencies of Vitamin B₁₂ and folate should be treated to avoid anaemia. Serum levels of vitamin B₁₂ and folic acid should be measured at least annually, or if macrocytosis is present. Patients at risk for vitamin B₁₂ or folic acid deficiency [eg small bowel disease or resection] need closer surveillance. The recommended timelines are based on expert opinions and reflect common clinical practice, but do not apply to patients with extensive small bowel resection, extensive ileal Crohn’s disease, or ileal-anal pouch” (Dignass et al., 2015).

American College of Gastroenterology (ACG)

In their guidelines and recommendations concerning the diagnosis and management of celiac disease (CDC) in 2013, the ACG recommended the following statement with *Conditional recommendation, low level of evidence*: “People with newly diagnosed CD should undergo testing and treatment for micronutrient deficiencies. Deficiencies to be considered for testing should include, but not be limited to, iron, folic acid, vitamin D, and vitamin B₁₂” (Rubio-Tapia et al., 2013). This guideline was reaffirmed in 2016.

British Committee for Standards in Haematology (BCSH)

In 2014, the BCSH released guidelines on folate deficiencies. They noted that “routine red cell folate testing is not necessary because serum folate alone is sufficient in most cases.” However, they also acknowledged that “in the presence of strong clinical suspicion of folate deficiency, despite a normal serum level, a red cell folate assay may be undertaken, having ruled out cobalamin deficiency.” The BCSH also noted that “folate status is generally checked in clinical situations similar to those of cobalamin deficiency (Grade 1A)” (Devalia et al., 2014).

In 2016, the BCSH recommended that a “documented vitamin B₁₂ or folate deficiency should be corrected before a final diagnosis of AA is confirmed. Bone marrow aplasia due to vitamin deficiency is exceedingly rare” (Killick et al., 2016).

In the 2021 BCSH *Guidelines for the Investigation and Management of Vitamin B₁₂ and Folate Deficiency* list the following four indications for folate testing: “unexplained anaemia/macrocytic anaemia/megaloblastic anaemia, excess alcohol intake especially with coexisting liver disease, exfoliative skin diseases, post gastric and bariatric surgery.” Alternatively, the guidelines list the following two indications when folate supplementation should occur without folate testing: “pregnancy, haemolytic anaemia – autoimmune haemolysis, red cell membrane disorders and haemoglobinopathies.” The guidelines also state that folate and B₁₂ should always be tested together, but notes that “once a patient has commenced B₁₂ replacement there is no further need for it to be measured again” (BCSH, 2021).

Renal Association Clinical Practice Guideline

The Renal Association recommends measuring serum folate concentration for evaluation of anemia in CKD (Mikhail et al., 2017).

National Comprehensive Cancer Network (NCCN)

The NCCN recommends measurement of RBC folate as part of the initial evaluation for myelodysplastic syndromes. Serum folate may be considered as an alternative, but is not preferable to RBC folate. “RBC folate is a more representative measure of folate stores and is the preferred test to serum folate” (NCCN, 2023).

Applicable Federal Regulations

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA ’88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

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Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 82746, 82747, and 0399U

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Specialty Matched Consultant Advisory Panel review 2/2020

Medical Director review 7/2021

Medical Director review 7/2022

Medical Director review 7/2023

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Policy Implementation/Update Information

- 1/1/19 New policy developed. BCBSNC will provide coverage for measurement of serum folate concentration when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (an)
- 8/27/19 References updated. No change in policy statement. (eel)
- 10/1/19 Reviewed by Avalon 2nd Quarter 2019 CAB. Medical Director review 8/2019. (eel)
- 10/29/19 Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed. (gm)
- 03/10/20 Specialty Matched Consultant Advisory Panel review 2/19/2020. No change to policy statement. (eel)
- 7/28/20 Updated Description, Policy Guidelines and Reference sections. Reviewed by Avalon 2nd Quarter CAB. Medical Director review 7/2020. No change to policy statement. (eel)
- 3/9/21 Specialty Matched Consultant Advisory Panel 2/17/2021. No changes to policy. (bb)
- 8/10/21 Reviewed by Avalon 2nd Quarter 2021 CAB. Updated Description and policy guidelines. Added references. Medical Director review 7/2021. (lpr)
- 9/13/22 Reviewed by Avalon 2nd Quarter 2022 CAB. Description, Policy Guidelines, and References updated. Updated When Covered section to reflect: “Reimbursement for measurement of serum folate concentration is allowed for evaluation of patients when **all** of the following criteria have been met, patients who have been diagnosed with megaloblastic or macrocytic anemia; **AND** megaloblastic anemia and/or macrocytosis does not resolve after folic acid. When Not Covered section updated for clarity. Medical Director review 7/2022. (tt)
- 6/30/23 Added CPT code 0399U to Billing/Coding section, effective 7/1/2023. (tt)
- 8/15/23 Reviewed by Avalon 2nd Quarter 2023 CAB. Updated Description and policy guidelines. Added references. Added the following statement to When Not Covered section: “Reimbursement is not allowed folate receptor autoantibody testing for all situations.” Medical Director review 7/2023. (tt)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.