



Medical Coverage Policy

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Serum Folate and Red Blood Cell Folate Testing

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Related Coverage Resources

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers

must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses serum folate and red blood cell (RBC) folate testing which are two methods of folate testing (folic acid test, Vitamin B9 test).

Coverage Policy

CPT® code 82746

Serum folate testing (Current Procedural Terminology [CPT®] code 82746) is considered medically necessary for EITHER of the following:

- Suspected diagnosis of folate deficiency associated with ANY of the following:
 - Anemia, where folate deficiency is in the differential diagnosis (e.g., megaloblastic anemia with or without other associated cytopenias).
 - Neural tube defects and neurologic disorders where folate deficiency is known to be a potential underlying cause.
 - Diseases of the digestive system associated with malabsorption.
 - Eating disorders.
- Monitoring treatment of folate deficiency.

Serum folate testing is not covered or reimbursable for ANY other indication.

CPT® code 82747

Red blood cell (RBC) folic acid testing (Current Procedural Terminology [CPT®] code 82747) is considered medically necessary in the initial evaluation of cytopenia(s) when myelodysplasia is suspected.

Red blood cell (RBC) folic acid testing (Current Procedural Terminology [CPT®] code 82747) is not covered or reimbursable for ANY other indication.

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
82746	Folic acid; serum

ICD-10-CM Diagnosis Codes	Description
C92.00	Acute myeloblastic leukemia, not having achieved remission
C92.01	Acute myeloblastic leukemia, in remission
C92.02	Acute myeloblastic leukemia, in relapse
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C92.20	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
C92.21	Atypical chronic myeloid leukemia, BCR/ABL-negative, in remission
C92.22	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse
C92.30	Myeloid sarcoma, not having achieved remission
C92.31	Myeloid sarcoma, in remission
C92.32	Myeloid sarcoma, in relapse
C92.40	Acute promyelocytic leukemia, not having achieved remission
C92.41	Acute promyelocytic leukemia, in remission
C92.42	Acute promyelocytic leukemia, in relapse
C92.50	Acute myelomonocytic leukemia, not having achieved remission
C92.51	Acute myelomonocytic leukemia, in remission
C92.52	Acute myelomonocytic leukemia, in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.90	Myeloid leukemia, unspecified, not having achieved remission
C92.91	Myeloid leukemia, unspecified in remission
C92.92	Myeloid leukemia, unspecified in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia, not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia, in remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia, in relapse
C92.Z0	Other myeloid leukemia not having achieved remission
C92.Z1	Other myeloid leukemia, in remission
C92.Z2	Other myeloid leukemia, in relapse
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.22	Refractory anemia with excess of blasts 2
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia

ICD-10-CM Diagnosis Codes	Description
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
D46.Z	Other myelodysplastic syndromes
D50.8	Other iron deficiency anemias
D50.9	Iron deficiency anemia, unspecified
D51.0	Vitamin B12 deficiency anemia due to intrinsic factor deficiency
D51.1	Vitamin B12 deficiency anemia due to selective vitamin B12 malabsorption with proteinuria
D51.2	Transcobalamin II deficiency
D51.3	Other dietary vitamin B12 deficiency anemia
D51.8	Other vitamin B12 deficiency anemias
D51.9	Vitamin B12 deficiency anemia, unspecified
D52.0	Dietary folate deficiency anemia
D52.1	Drug-induced folate deficiency anemia
D52.8	Other folate deficiency anemias
D52.9	Folate deficiency anemia, unspecified
D53.0	Protein deficiency anemia
D53.1	Other megaloblastic anemias, not elsewhere classified
D53.2	Scorbutic anemia
D53.8	Other specified nutritional anemias
D53.9	Nutritional anemia, unspecified
D56.1	Beta thalassemia
D58.2	Other hemoglobinopathies
D59.4	Other nonautoimmune hemolytic anemias
D59.8	Other acquired hemolytic anemias
D59.9	Acquired hemolytic anemia, unspecified
D61.818	Other pancytopenia
D61.89	Other specified aplastic anemias and other bone marrow failure syndromes
D61.9	Aplastic anemia, unspecified
D69.3	Immune thrombocytopenic purpura
D69.49	Other primary thrombocytopenia
D69.59	Other secondary thrombocytopenia
D69.6	Thrombocytopenia, unspecified
D70.8	Other neutropenia
D70.9	Neutropenia, unspecified
D72.819	Decreased white blood cell count, unspecified
E40	Kwashiorkor
E42	Marasmic kwashiorkor
E43	Unspecified severe protein-calorie malnutrition
E44.0	Moderate protein-calorie malnutrition
F02.80	Dementia in other diseases classified elsewhere, unspecified severity, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F02.811	Dementia in other diseases classified elsewhere, unspecified severity, with agitation
F02.818	Dementia in other diseases classified elsewhere, unspecified severity, with other behavioral disturbance
F02.82	Dementia in other diseases classified elsewhere, unspecified severity, with psychotic disturbance

ICD-10-CM Diagnosis Codes	Description
F02.83	Dementia in other diseases classified elsewhere, unspecified severity, with mood disturbance
F02.84	Dementia in other diseases classified elsewhere, unspecified severity, with anxiety
F02.A0	Dementia in other diseases classified elsewhere, mild, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F02.A11	Dementia in other diseases classified elsewhere, mild, with agitation
F02.A18	Dementia in other diseases classified elsewhere, mild, with other behavioral disturbance
F02.A2	Dementia in other diseases classified elsewhere, mild, with psychotic disturbance
F02.A3	Dementia in other diseases classified elsewhere, mild, with mood disturbance
F02.A4	Dementia in other diseases classified elsewhere, mild, with anxiety
F02.B0	Dementia in other diseases classified elsewhere, moderate, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F02.B11	Dementia in other diseases classified elsewhere, moderate, with agitation
F02.B18	Dementia in other diseases classified elsewhere, moderate, with other behavioral disturbance
F02.B2	Dementia in other diseases classified elsewhere, moderate, with psychotic disturbance
F02.B3	Dementia in other diseases classified elsewhere, moderate, with mood disturbance
F02.B4	Dementia in other diseases classified elsewhere, moderate, with anxiety
F02.C0	Dementia in other diseases classified elsewhere, severe, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F02.C11	Dementia in other diseases classified elsewhere, severe, with agitation
F02.C18	Dementia in other diseases classified elsewhere, severe, with other behavioral disturbance
F02.C2	Dementia in other diseases classified elsewhere, severe, with psychotic disturbance
F02.C3	Dementia in other diseases classified elsewhere, severe, with mood disturbance
F02.C4	Dementia in other diseases classified elsewhere, severe, with anxiety
F03.90	Unspecified dementia, unspecified severity, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F03.911	Unspecified dementia, unspecified severity, with agitation
F03.918	Unspecified dementia, unspecified severity, with other behavioral disturbance
F03.92	Unspecified dementia, unspecified severity, with psychotic disturbance
F03.93	Unspecified dementia, unspecified severity, with mood disturbance
F03.94	Unspecified dementia, unspecified severity, with anxiety
F03.A0	Unspecified dementia, mild, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F03.A11	Unspecified dementia, mild, with agitation
F03.A18	Unspecified dementia, mild, with other behavioral disturbance
F03.A2	Unspecified dementia, mild, with psychotic disturbance
F03.A3	Unspecified dementia, mild, with mood disturbance
F03.A4	Unspecified dementia, mild, with anxiety
F03.B0	Unspecified dementia, moderate, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F03.B11	Unspecified dementia, moderate, with agitation

ICD-10-CM Diagnosis Codes	Description
F03.B18	Unspecified dementia, moderate, with other behavioral disturbance
F03.B2	Unspecified dementia, moderate, with psychotic disturbance
F03.B3	Unspecified dementia, moderate, with mood disturbance
F03.B4	Unspecified dementia, moderate, with anxiety
F03.C0	Unspecified dementia, severe, without behavioral disturbance, psychotic disturbance, mood disturbance, and anxiety
F03.C11	Unspecified dementia, severe, with agitation
F03.C18	Unspecified dementia, severe, with other behavioral disturbance
F03.C2	Unspecified dementia, severe, with psychotic disturbance
F03.C3	Unspecified dementia, severe, with mood disturbance
F03.C4	Unspecified dementia, severe, with anxiety
F10.10	Alcohol abuse, uncomplicated
F10.11	Alcohol abuse, in remission
F10.120	Alcohol abuse with intoxication, uncomplicated
F10.121	Alcohol abuse with intoxication delirium
F10.129	Alcohol abuse with intoxication, unspecified
F10.130	Alcohol abuse with withdrawal, uncomplicated
F10.131	Alcohol abuse with withdrawal delirium
F10.132	Alcohol abuse with withdrawal with perceptual disturbance
F10.139	Alcohol abuse with withdrawal, unspecified
F10.14	Alcohol abuse with alcohol-induced mood disorder
F10.150	Alcohol abuse with alcohol-induced psychotic disorder with delusions
F10.151	Alcohol abuse with alcohol-induced psychotic disorder with hallucinations
F10.159	Alcohol abuse with alcohol-induced psychotic disorder, unspecified
F10.180	Alcohol abuse with alcohol-induced anxiety disorder
F10.181	Alcohol abuse with alcohol-induced sexual dysfunction
F10.182	Alcohol abuse with alcohol-induced sleep disorder
F10.188	Alcohol abuse with other alcohol-induced disorder
F10.19	Alcohol abuse with unspecified alcohol-induced disorder
F10.20	Alcohol dependence, uncomplicated
F10.21	Alcohol dependence, in remission
F10.220	Alcohol dependence with intoxication, uncomplicated
F10.221	Alcohol dependence with intoxication delirium
F10.229	Alcohol dependence with intoxication, unspecified
F10.230	Alcohol dependence with withdrawal, uncomplicated
F10.231	Alcohol dependence with withdrawal delirium
F10.232	Alcohol dependence with withdrawal with perceptual disturbance
F10.239	Alcohol dependence with withdrawal, unspecified
F10.24	Alcohol dependence with alcohol-induced mood disorder
F10.250	Alcohol dependence with alcohol-induced psychotic disorder with delusions
F10.251	Alcohol dependence with alcohol-induced psychotic disorder with hallucinations
F10.259	Alcohol dependence with alcohol-induced psychotic disorder, unspecified
F10.26	Alcohol dependence with alcohol-induced persisting amnesic disorder
F10.27	Alcohol dependence with alcohol-induced persisting dementia
F10.280	Alcohol dependence with alcohol-induced anxiety disorder
F10.281	Alcohol dependence with alcohol-induced sexual dysfunction
F10.282	Alcohol dependence with alcohol-induced sleep disorder
F10.288	Alcohol dependence with other alcohol-induced disorder

ICD-10-CM Diagnosis Codes	Description
F10.29	Alcohol dependence with unspecified alcohol-induced disorder
F10.90	Alcohol use, unspecified, uncomplicated
F10.91	Alcohol use, unspecified, in remission
F10.920	Alcohol use, unspecified with intoxication, uncomplicated
F10.921	Alcohol use, unspecified with intoxication delirium
F10.929	Alcohol use, unspecified with intoxication, unspecified
F10.931	Alcohol use, unspecified with withdrawal delirium
F10.932	Alcohol use, unspecified with withdrawal with perceptual disturbance
F10.939	Alcohol use, unspecified with withdrawal, unspecified
F10.94	Alcohol use, unspecified with alcohol-induced mood disorder
F10.950	Alcohol use, unspecified with alcohol-induced psychotic disorder with delusions
F10.951	Alcohol use, unspecified with alcohol-induced psychotic disorder with hallucinations
F10.959	Alcohol use, unspecified with alcohol-induced psychotic disorder, unspecified
F10.96	Alcohol use, unspecified with alcohol-induced persisting amnesic disorder
F10.97	Alcohol use, unspecified with alcohol-induced persisting dementia
F10.980	Alcohol use, unspecified with alcohol-induced anxiety disorder
F10.981	Alcohol use, unspecified with alcohol-induced sexual dysfunction
F10.982	Alcohol use, unspecified with alcohol-induced sleep disorder
F10.988	Alcohol use, unspecified with other alcohol-induced disorder
F10.99	Alcohol use, unspecified with unspecified alcohol-induced disorder
F50.00	Anorexia nervosa, unspecified
F50.010	Anorexia nervosa, restricting type, mild
F50.011	Anorexia nervosa, restricting type, moderate
F50.012	Anorexia nervosa, restricting type, severe
F50.013	Anorexia nervosa, restricting type, extreme
F50.014	Anorexia nervosa, restricting type, in remission
F50.019	Anorexia nervosa, restricting type, unspecified
F50.020	Anorexia nervosa, binge eating/purging type, mild
F50.021	Anorexia nervosa, binge eating/purging type, moderate
F50.022	Anorexia nervosa, binge eating/purging type, severe
F50.023	Anorexia nervosa, binge eating/purging type, extreme
F50.024	Anorexia nervosa, binge eating/purging type, in remission
F50.029	Anorexia nervosa, binge eating/purging type, unspecified
F50.20	Bulimia nervosa, unspecified
F50.21	Bulimia nervosa, mild
F50.22	Bulimia nervosa, moderate
F50.23	Bulimia nervosa, severe
F50.24	Bulimia nervosa, extreme
F50.25	Bulimia nervosa, in remission
F50.810	Binge eating disorder, mild
F50.811	Binge eating disorder, moderate
F50.812	Binge eating disorder, severe
F50.813	Binge eating disorder, extreme
F50.814	Binge eating disorder, in remission
F50.819	Binge eating disorder, unspecified
F50.82	Avoidant/restrictive food intake disorder
F50.83	Pica in adults

ICD-10-CM Diagnosis Codes	Description
F50.84	Rumination disorder in adults
F50.89	Other specified eating disorder
F50.9	Eating disorder, unspecified
G31.01	Pick's disease
G31.09	Other frontotemporal neurocognitive disorder
G31.1	Senile degeneration of brain, not elsewhere classified
G31.2	Degeneration of nervous system due to alcohol
G31.81	Alpers disease
G31.82	Leigh's disease
G31.83	Neurocognitive disorder with Lewy bodies
G31.84	Mild cognitive impairment of uncertain or unknown etiology
G31.85	Corticobasal degeneration
G31.87	Primary progressive apraxia of speech
G31.89	Other specified degenerative diseases of nervous system
G31.9	Degenerative disease of nervous system, unspecified
G60.3	Idiopathic progressive neuropathy
G62.0	Drug-induced polyneuropathy
G62.1	Alcoholic polyneuropathy
G62.2	Polyneuropathy due to other toxic agents
G62.81	Critical illness polyneuropathy
G62.82	Radiation-induced polyneuropathy
G62.89	Other specified polyneuropathies
G62.9	Polyneuropathy, unspecified
G64	Other disorders of peripheral nervous system
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction

ICD-10-CM Diagnosis Codes	Description
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K70.0	Alcoholic fatty liver
K70.10	Alcoholic hepatitis without ascites
K70.11	Alcoholic hepatitis with ascites
K70.2	Alcoholic fibrosis and sclerosis of liver
K70.30	Alcoholic cirrhosis of liver without ascites
K70.31	Alcoholic cirrhosis of liver with ascites
K70.40	Alcoholic hepatic failure without coma
K70.41	Alcoholic hepatic failure with coma
K70.9	Alcoholic liver disease, unspecified
K86.81	Exocrine pancreatic insufficiency
K90.0	Celiac disease
K90.1	Tropical sprue
K90.81	Whipple's disease
K90.821	Short bowel syndrome with colon in continuity
K90.822	Short bowel syndrome without colon in continuity
K90.89	Other intestinal malabsorption
K90.9	Intestinal malabsorption, unspecified
K91.2	Postsurgical malabsorption, not elsewhere classified
Q00.0	Anencephaly
Q00.1	Craniorachischisis
Q00.2	Iniencephaly
Q01.0	Frontal encephalocele
Q01.1	Nasofrontal encephalocele
Q01.2	Occipital encephalocele
Q01.8	Encephalocele of other sites
Q01.9	Encephalocele, unspecified
Q02	Microcephaly
Q03.0	Malformations of aqueduct of Sylvius
Q03.1	Atresia of foramina of Magendie and Luschka
Q03.8	Other congenital hydrocephalus
Q03.9	Congenital hydrocephalus, unspecified
Q04.0	Congenital malformations of corpus callosum
Q04.1	Arhinencephaly
Q04.2	Holoprosencephaly
Q04.3	Other reduction deformities of brain
Q04.4	Septo-optic dysplasia of brain
Q04.5	Megalencephaly
Q04.6	Congenital cerebral cysts
Q04.8	Other specified congenital malformations of brain
Q04.9	Congenital malformation of brain, unspecified
Q05.0	Cervical spina bifida with hydrocephalus
Q05.1	Thoracic spina bifida with hydrocephalus
Q05.2	Lumbar spina bifida with hydrocephalus
Q05.3	Sacral spina bifida with hydrocephalus

ICD-10-CM Diagnosis Codes	Description
Q05.4	Unspecified spina bifida with hydrocephalus
Q05.5	Cervical spina bifida without hydrocephalus
Q05.6	Thoracic spina bifida without hydrocephalus
Q05.7	Lumbar spina bifida without hydrocephalus
Q05.8	Sacral spina bifida without hydrocephalus
Q05.9	Spina bifida, unspecified
Q06.0	Amyelia
Q06.1	Hypoplasia and dysplasia of spinal cord
Q06.2	Diastematomyelia
Q06.3	Other congenital cauda equina malformations
Q06.4	Hydromyelia
Q06.8	Other specified congenital malformations of spinal cord
Q06.9	Congenital malformation of spinal cord, unspecified
Q07.00	Arnold-Chiari syndrome without spina bifida or hydrocephalus
Q07.01	Arnold-Chiari syndrome with spina bifida
Q07.02	Arnold-Chiari syndrome with hydrocephalus
Q07.03	Arnold-Chiari syndrome with spina bifida and hydrocephalus
Q07.8	Other specified congenital malformations of nervous system
Q07.9	Congenital malformation of nervous system, unspecified
Z98.84	Bariatric surgery status

Not Covered or Reimbursable:

ICD-10-CM Diagnosis Codes	Description
	All other diagnosis codes

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
82747	Folic Acid; RBC

ICD-10-CM Diagnosis Codes	Description
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.22	Refractory anemia with excess of blasts 2
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.C	Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality

ICD-10-CM Diagnosis Codes	Description
D46.Z	Other myelodysplastic syndromes

Not Covered or Reimbursable:

ICD-10-CM Diagnosis Codes	Description
	All other diagnosis codes

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Chicago, IL.**

General Background

Folate, also called vitamin B9 is a water-soluble B vitamin. Folate has many chemical forms, including naturally in foods such as leafy greens, fruits, nuts, beans, peas, seafood, eggs, dairy products, meat, and poultry. Folic acid is the synthetic form of folate that is found in supplements and added to fortified foods.

The recommended daily intake of folate ranges from 65 mcg of dietary folate equivalents in infants to 400 mcg of dietary folate equivalents in adults, with higher requirements during pregnancy and lactation (600 and 500 mcg, respectively). Total body folate stores are estimated to be approximately 500 to 20,000 mcg (0.5 to 20 mg). If folate intake ceases, deficiency may develop within weeks to months, or more rapidly if demands for folate are increased. Folic acid overdose is not a major consideration since excess is excreted in the urine.

Folate deficiency has become less common in the United States and many other resource-rich countries following the implementation of routine folic acid supplementation of foods. The Food Fortification Initiative (FFI) has been instituted in many countries, which focuses on the fortification of industrially milled wheat flour, maize flour and rice. This is primarily aimed at reducing the risk of neural tube defects during embryogenesis. However, populations with poor access to nutritious foods or reduced dietary intake are still at risk.

Folate Deficiency

Folate measurements should only be ordered to confirm a deficiency in a symptomatic individual. They should not be used to assess the risk of neural tube defects (NTD) or be used as a population screening tool. Most commonly, folate testing is used in the workup of megaloblastic anemia and the workup of neurologic disease.

Conditions that may be associated with folate deficiency include but are not limited to the following:

- Increased requirements:
 - Pregnancy
 - Hemolytic anemia
 - Exfoliative skin diseases
- Intestinal malabsorption
- Certain medications
- Loss during hemodialysis

- Decreased dietary intake
- Rare genetic disorders

There are conditions that are associated with increased cell proliferation, which increased the need for folates for DNA synthesis. Individuals that are pregnant have chronic hemolytic anemias or exfoliative skin diseases, such as severe eczema, are often given daily folic acid to prevent deficiency. Folate deficiency in pregnancy can result in birth defects (anencephaly and spina bifida), which underlies the strong recommendation for folic acid supplementation in women of reproductive age. Inadequate maternal folate intake has also been associated with low infant birth weight, preterm delivery, and fetal growth retardation.

Malabsorption of folates/folic acid supplements can occur if the intestinal absorptive surface has been removed or is dysfunctional. This can result from surgery (e.g., gastric bypass) or inflammatory disorders such as celiac disease and tropical sprue. Medications can interfere with folate metabolism and may cause folate deficiency and/or megaloblastic anemia due to effects on DNA synthesis. These medications include methotrexate and sulfasalazine. When patients are unable to consume a varied, nutrient-rich diet may develop folate deficiency. Examples include those with restrictive diets, chronic alcohol use with a limited diet, severe anorexia, or reduced oral intake in the setting of a systemic illness.

Presentation of folate deficiency is frequently associated with a history of excessive alcohol intake with concurrent poor diet intake. Other patients may be pregnant or lactating; may take certain drugs, such as phenytoin, sulfonamides, or methotrexate; may have chronic hemolytic anemia; or may have underlying malabsorption. Patients with folate deficiency can present with anemia and/or have vague or nonspecific symptoms (fatigue, irritability, cognitive decline), which are partly due to anemia. Additionally, some patients complain of a sore tongue or pain upon swallowing and irritated, cracked sores on one or both corners of your mouth may be observed. These oral lesions typically occur at the time when folate depletion is severe enough to cause megaloblastic anemia, although, occasionally, lesions may occur before the anemia. Patients may also present with gastrointestinal (GI) signs and symptoms, such as nausea, vomiting, abdominal pain, and diarrhea, especially after meals. Anorexia in combination with the above symptoms, may lead to marked weight loss. Neuropsychiatric presentations of folate deficiency may occur and include cognitive impairment, dementia, and depression.

There are certain malabsorptive conditions which may be associated with a combined deficiency of vitamin B12 and folate or combined deficiency of one of these vitamins and iron. Examples include:

- Bariatric surgery
- Malabsorptive states
- Severely limited diets

Anemia is defined as a reduction in one or more of the major red blood cell (RBC) measurements obtained in the complete blood count (CBC): hemoglobin concentration, hematocrit, or RBC count. A low hemoglobin concentration and/or low hematocrit are the parameters most widely used to diagnose anemia. The red blood cell (RBC) indices describe RBC size, hemoglobin content, and uniformity of the RBC population. These values can be very helpful in determining the cause of anemia. The mean corpuscular volume (MCV) and red cell distribution width (RDW) are generally the most useful. Deficiencies of vitamin B12 and/or folate can cause megaloblastic anemia (macrocytic anemia with other features due to impaired cell division).

Megaloblastic anemia (or megaloblastic changes) describes a subset of macrocytic anemias in which the increased size of RBCs is caused by abnormal cell division in RBC precursors in the bone

marrow. Megaloblastic anemia is a form of macrocytic anemia from ineffective red blood cell production and intramedullary hemolysis (Barcellini, 2022). Megaloblastic anemia is most commonly caused by folate deficiency from dietary deficiency, alcoholism, or malabsorption syndromes or by vitamin B12 deficiency, usually due to pernicious anemia

When assessing unexplained macrocytosis (high MCV) or macrocytic anemia, the CBC and/or blood smear would guide diagnosis. For a folate or B12 deficiency, the findings can include the following:

- Anemia
- Macrocytic red blood cells (RBCs; e.g., mean corpuscular volume [MCV] > 100 fL) or macro-ovalocytosis
- Mild leukopenia and/or thrombocytopenia
- Low reticulocyte count
- Hypersegmented neutrophils on the peripheral blood smear

Oral folic acid (1 to 5 mg daily) is the most common treatment of a folate deficiency, even if malabsorption is present. This dose is usually sufficient because it is above the 200 mcg (0.2 mg) recommended dietary allowance. For women at low risk of NTD, the standard folic acid supplement (multivitamin, prenatal vitamin) is 0.4 mg daily, beginning at least one month prior to attempting conception and continuing throughout pregnancy and for four to six weeks postpartum or until completion of breastfeeding. This is in addition to the amount of food folate contained in a healthy eating pattern. Females who are at higher risk of having a child with an NTD are candidates for higher dose folic acid supplementation.

The reversible causes of deficiency are generally treated for one to four months or until there is laboratory evidence of hematologic recovery. For those with a chronic cause of folate deficiency, such as chronic hemolytic anemia, therapy may be given indefinitely. Periconceptional folic acid supplementation, food fortification with folic acid, and prenatal screening for NTDs combined with access to pregnancy termination have led to a decrease in the prevalence of NTDs at birth where these interventions are applied. Intravenous folic acid may be appropriate in certain settings, such as individuals who are unable to take an oral medication (e.g., due to vomiting or obtundation) or those who have severe or symptomatic anemia due to folate deficiency and hence have a more urgent need for rapid correction.

Literature Review - Folate Deficiency

There is a paucity of evidence evaluating the benefit and harm of testing for folate deficiency in the general population. Peer-reviewed scientific literature primarily investigates the effects of folic acid supplementation, not testing.

Literature Review - Methods of Folate Testing

Except in the initial evaluation of cytopenia(s) when myelodysplasia is suspected, there is insufficient evidence to support the accuracy and clinical utility RBC folate testing for the diagnosis of a folate deficiency.

Laboratory tests in folic acid deficiency would reveal anemia, manifesting as a decrease in hemoglobin and hematocrit levels. Plasma/serum folate may also be measured and is a short-term measurement of folate status based recent folic acid intake. Red blood cell (RBC) folate concentration is a measurement of folate in tissue and is a long-term measurement of folate status over the lifetime of RBCs (Means and Fairfield, 2024b).

There is very poor standardization between folate assays. In one report, a comparison of five automated serum and RBC folate assays showed differences of up to 40% for serum folate and up

to 250% for RBC folate. Studies comparing serum folate with RBC folate have found that addition of RBC folate to serum folate testing does not provide substantially more clinical information (Owen and Roberts, 2003). Red blood cell folate is proposed to provide long term folate status, however, the methodology of measuring folate in the presence of the red cell protein matrix has led to poor reproducibility, and the assay cannot be recommended for routine clinical use outside of research investigations (Stabler, 2024).

Cummings et al. (2017) conducted a cross-sectional study of dietary and genetic predictors of blood folate levels in healthy young adults. The study investigated blood folate level determinants in healthy young adults (n=265), including intake of naturally occurring food folate, synthetic FA, and the interaction of naturally occurring food folate with a common missense variant in the FOLH1 gene thought to affect absorption. The study reported that in healthy young individuals exposed to folic acid fortification, blood folate level is dependent on relative intake from naturally occurring food folate and synthetic sources of folic acid, and on genetic variation in FOLH1 484 genotype. The study also compared serum folate to RBC folate and explained that compared to serum folate, RBC folate is thought to provide a better estimate of folate levels within body tissues. However, RBC folate measurement may be considerably more vulnerable to small variations in sample storage and analysis, which may make it a less reliable measure of folate status. The study also mentioned that RBC folate assays are not standardized and results in the study obtained using ECLIA could not be compared to epidemiological cutoffs for RBC folate insufficiency.

Gilfix (2014) reviewed the utility of serum folate testing compared to red blood cell (RBC) folate testing in the era of folate fortification of flour, which has increased folate concentrations in the general population. Data from three hospitals in Canada on both serum and RBC folate levels were analyzed. While theoretically RBC folate is less susceptible to rapid changes in dietary intake, analytically, the assays have large imprecisions, which limit their usefulness. The authors concluded that there is no evidence to support routine ordering of RBC or serum folate. Even pre-selection of patients seems not to increase the prevalence of measured folate deficiency. Additionally, based on the performance statistics, and as serum folate provides equivalent results to RBC folate in almost all clinical scenarios, routine ordering of RBC folate is no longer warranted.

Farrell et al. (2013) conducted a comprehensive published review of the two folate methods and concluded that assessing a patient's folate status can be clinically important evaluation and laboratories are readily able to provide the measurement of serum or red cell folate using automated competitive protein binding (CPB) assays. However, "after assessing many different aspects of the performance of serum and red cell folate assays, this review did not find evidence to justify the higher cost of routinely measuring red cell folate".

Professional Societies/Organizations – Cancer

National Comprehensive Cancer Network® (NCCN): The NCCN GUIDELINES™ Clinical Guidelines in Oncology™ on Myelodysplastic Syndromes (Version 3.2024 — July 25, 2024) states that Initial evaluation of cytopenia(s), suspect myelodysplasia should include:

- RBC folate and vitamin B12 evaluation*

*RBC folate is a more representative measure of folate stores and is the preferred test to serum folate. Serum methylmalonic acid testing is an accurate way to assess B12 status and is mandatory to the vitamin B12 evaluation, particularly for patients with possible pernicious anemia (MDS-1).

Other useful recommended laboratory screening tests include serum erythropoietin (sEPO), vitamin B12, RBC folate levels, serum ferritin, iron, and total iron-binding capacity (TIBC). RBC

folate and serum folate levels should not be considered equivalent, and RBC folate is preferred. RBC folate levels are more indicative of folate stores, whereas serum folate levels are reflective of recent nutrition. However, if RBC folate cannot be evaluated, serum folate should be considered as an alternative, although clinicians should be advised of the limitations (MS-10)(NCCN, 2024).

NCCN: The NCCN GUIDELINES™ Clinical Guidelines in Oncology™ on Acute Myeloid Leukemia (AML) (Version 3.2024 — May 17, 2024) states for age ≥18 years, evaluation for AML should include B12 and folic acid evaluation (EVAL-1) (NCCN, 2024).

Professional Societies/Organizations – Neural Tube Defects

US Preventive Services Task Force (USPSTF): In 2023, the USPSTF reaffirmed that “for persons who are planning to or could become pregnant, there is high certainty that folic acid supplementation has a substantial net benefit to prevent neural tube defects in their offspring”. The task force recommended that all persons planning to or who could become pregnant take a daily supplement containing 0.4 to 0.8mg (400 to 800 µg) of folic acid (USPSTF, 2023).

American College of Obstetricians and Gynecologists (ACOG): ACOG’s 2021 update on anemia in pregnancy stated that all pregnant women should be screened for anemia using a complete blood count in the first trimester and again at 24 0/7–28 6/7 weeks of gestation. Patients with hematocrit levels less than 33% in the first and third trimesters and less than 32% in the second trimester should be evaluated further to determine the cause. If iron deficiency is ruled out, other etiologies should be investigated. This recommendation is based primarily on consensus and expert opinion (ACOG, 2021).

ACOG’s joint committee opinion with American Society for Reproductive Medicine (2019) on prepregnancy counseling stated that female prepregnancy folic acid supplementation should be encouraged to reduce the risk of neural tube defects. There was no mention of measuring serum folate.

ACOG’s 2017 practice bulletin on neural tube defects (NTDs) stated that the association between folic acid supplementation and decreased risk of NTDs is well established. Folate supplementation is an important prepregnancy and prenatal recommendation. ACOG recommended the following (ACOG, 2017):

- All women who are planning a pregnancy or able to become pregnant should take folic acid supplementation of 400 micrograms daily.
- Supplementation should start at least 1 month prior to pregnancy and continue through the first 12 weeks of pregnancy.
- Those who are at high risk of NTDs should take 4,000 micrograms of folic acid daily. This should start 3 months before pregnancy and continue until 12 weeks of gestational age.

Professional Societies/Organizations – Bariatric Procedures

American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE), The Obesity Society (TOH), American Society for Metabolic & Bariatric Surgery (ASMBS), Obesity Medicine Association (OMA), American Society of Anesthesiologists (ASA): In 2019, the AACE, ACE, TOH, ASMBS, OMA and ASA published an update to the 2013 clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures. In regard to folate testing the guideline recommended (Mechanick, et al., 2020):

- malabsorptive bariatric procedures can cause nutritional anemias that may involve deficiencies in vitamin B12, folate, protein, copper, selenium, and zinc and may be evaluated when routine aggressive case finding for iron-deficiency anemia is negative.

American Society for Metabolic and Bariatric Surgery (ASMBS): The 2016 integrated health nutritional guidelines for the surgical weight loss patient on micronutrients recommended that pre-weight loss surgery (WLS) nutrient screening should be recommended for all patients. A folate deficiency would be suspected when the RBC folate is decreased, the serum homocysteine is increased and a normal MMA level.

Additionally, the ASMBS recommended for the prevention of micronutrient deficiency post-weight loss surgery (WLS) patients should take 400–800 mg oral folate daily from their multivitamin and women of childbearing age should take 800–1000 mg oral folate daily (Parrott, et al., 2017).

Professional Societies/Organizations – Gastrointestinal Malabsorption

American College of Gastroenterology (ACG): In 2023, the ACG updated the 2013 diagnosis and management of celiac disease guideline. Patients with symptoms, signs, or laboratory evidence suggestive of malabsorption, such as chronic diarrhea with weight loss, steatorrhea, irritable bowel syndrome, abdominal pain, and bloating, should be considered for testing for CD. Testing an EGD with biopsies and serology (tissue transglutaminase [TTG]), other tests could be used which includes complete blood count, alanine aminotransferase, aspartate aminotransferase, vitamins (A, D, E, B12), copper, zinc, folic acid, ferritin, and iron. There is no recommendation or level of evidence attached to this statement (Rubio-Tapi, et al., 2023).

The ACG clinical practice update (2022) on management of short bowel syndrome provided a best practice advice for a nutritional assessment. The initial comprehensive nutritional assessment should be performed by a dietitian experienced in SBS. All patients should be assessed and folate is one of the vitamins to be assessed with recommended supplementation of 1 mg of folate daily.

American Gastroenterological Association (AGA): The AGA clinical practice update, expert review on the epidemiology, evaluation, and management of exocrine pancreatic insufficiency (EPI) explained that clinical features of EPI include steatorrhea with or without diarrhea, weight loss, bloating, excessive flatulence, fat soluble vitamin deficiencies, and protein-calorie malnutrition. The AGA's best practice advice included that "screening for vitamin and mineral deficiencies (vitamins A, D, E, K, B12, folate, magnesium, selenium zinc, and iron studies) at the time of diagnosis and then annually based on the clinical status of the patient, remains essential" (Whitcomb, et al., 2023).

In the AGA's clinical practice update on management of refractory celiac disease: expert review a detailed nutritional assessment should be done for macronutrient and micronutrient deficiencies. The deficiencies should be corrected using oral supplementation (Green, et al., 2022).

Professional Societies/Organizations – Eating Disorders

American Psychiatric Association (APA): In 2023, the APA's practice guideline for the treatment of patients with eating disorders recommended the following:

- initial physical examination should include (Crone, et al., 2023):
 - vital signs, including temperature, resting heart rate, blood pressure, orthostatic pulse, and orthostatic blood pressure; height, weight, and BMI and physical appearance, including signs of malnutrition or purging behaviors.
 - laboratory assessment should include a complete blood count and a comprehensive metabolic panel, including electrolytes, liver enzymes, and renal function tests.

American Academy of Pediatrics (AAP): The AAP (2021) recommended a comprehensive assessment of children and adolescents with suspected eating disorders that includes a detailed and comprehensive physical examination and a full psychosocial assessment. Initial laboratory testing is done to screen for medical complications of eating disorders or to rule out alternate diagnoses. Typical initial laboratory testing includes a complete blood cell count; serum electrolytes, calcium, magnesium, phosphorus, and glucose; liver transaminases; urinalysis; and thyroid-stimulating hormone. Additionally, screening for specific vitamin and mineral deficiencies (e.g., vitamin B12, vitamin D, iron, and zinc) may be done on an individual basis depending on the nutritional history of the patient. The AAP explained that laboratory values are often normal in patients with eating disorders, however normal results do not exclude the presence of serious illness with an eating disorder or the need for hospitalization for medical stabilization (Hornberger, et al., 2021).

Professional Societies/Organizations – General

American Society for Clinical Pathology (ASCP): The (ASCP publication titled Twenty Things Physicians and Patients Should Question (September 19, 2017) states:

- #19 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.

Since 1998, when the U.S. and Canada mandated that foods with processed grains be fortified with folic acid, there has been a significant decline in the incidence of folate deficiency. For the rare patient suspected of having a folate deficiency, simply treating with folic acid is a more cost-effective approach than blood testing. 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).

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No National Coverage Determination found	
LCD	Novitas Solutions, Inc.	Assays for Vitamins and Metabolic Function (L34914)	7/1/2020

Note: Please review the current Medicare Policy for the most up-to-date information. (NCD = National Coverage Determination; LCD = Local Coverage Determination)

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Revision Details

Type of Revision	Summary of Changes	Date
Focused Review	No policy statement changes	10/15/2025
Annual revision	Revised policy statement for red blood cell (RBC) folic acid testing (82747)	12/15/2024
Annual Revision	New coverage policy.	8/17/2024

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