Genetic and Coagulation Testing for Noncancer Blood Disorders

INDEPENDENT CARE HEALTH PLAN

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Medicare Advantage Medical Coverage Policy

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Related Documents

Please refer to CMS website for the most current applicable National Coverage Determination (NCD)/ Local Coverage Determination (LCD)/Local Coverage Article (LCA)/CMS Online Manual System/Transmittals.

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories
LCD	Molecular Pathology Procedures	L35000	J6, JK - National Government Services, Inc.	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
LCD	Biomarkers Overview	L35062	JH, JL - Novitas Solutions, Inc.	AR, CO, DE, LA, MD, MS, NJ, NM, OK, PA, TX, D.C.
LCA	Billing and Coding: Biomarkers Overview	A56541		
LCA	Billing and Coding: Molecular Pathology and Genetic Testing	A58917		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36139	J15 - CGS Administrators, LLC	KY, OH
LCD	MolDX: Blood Product Molecular Antigen Typing	L38249		
LCA	Billing and Coding: MolDX: Blood Product Molecular Antigen Typing	A57155		
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L35984		
LCD	MolDX: Molecular Diagnostic Tests (MDT)	L36021		
LCA	Billing and Coding: MolDX: FANCC Genetic Testing	A54263		
LCA	Billing and Coding: MolDX: HBB Gene Tests	A54267		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36129		

LCD	MolDX: Blood Product Molecular Antigen Typing	L38240		
LCA	Billing and Coding: MolDX: Blood Product Molecular Antigen Typing	A58308	JJ, JM - Palmetto GBA	CT, NC, NY, ME, MA, NH, RI, SC, VA, VT, WV
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36089		
LCA	Billing and Coding: MolDX: FANCC Genetic Testing	A53628		
LCA	Billing and Coding: MolDX: HBB Gene Tests	A53493		
LCD	Molecular Pathology Procedures	L34519	JN - First Coast Service Options, Inc. (Part A/B MAC)	FL, PR, U.S. VI
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36358		
LCD	MolDX: Blood Product Molecular Antigen Typing	L38331		
LCA	Billing and Coding: MolDX: Blood Product Molecular Antigen Typing	A57124		
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36155	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCA	Billing and Coding: MolDX: FANCC Genetic Testing	A55183		
LCA	Billing and Coding: MolDX: HBB Gene Tests	A55253		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36362	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY

LCD	MolDX: Blood Product Molecular Antigen Typing	L38333		
LCA	Billing and Coding: MolDX: Blood Product Molecular Antigen Typing	A57376		
LCD	MolDX: Genetic Testing for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36159		
LCA	Billing and Coding: MolDX: FANCC Genetic Testing	A55184		
LCA	Billing and Coding: MolDX: HBB Gene Tests	A55254		
LCD	MolDX: Biomarkers in Cardiovascular Risk Assessment	L36523	J5, J8 - Wisconsin Physicians Service Insurance Corporation	IA, MI, IN,KS, MO, NE
LCD	MolDX: Blood Product Molecular Antigen Typing	L38441		
LCA	Billing and Coding: MolDX: Blood Product Molecular Antigen Typing	A57110		
LCD	MolDX: Genetic Testing for Hypercoagulability/Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR)	L36400		
LCD	MolDX: Molecular Diagnostic Tests (MDT)	L36807		
LCA	Billing and Coding: MolDX: FANCC Genetic Testing	A55160		
LCA	Billing and Coding: MolDX: HBB Gene Tests	A55166		

Description

Blood disorders can affect any of the three main components of blood including erythrocytes (red blood cells [RBCs]), leukocytes (white blood cells [WBCs]), thrombocytes (platelets) or tissues where these are formed (bone marrow, lymph nodes and spleen).

Coagulation (blood clotting) disorders are defects in the liver's ability to make sufficient amounts of proteins (eg, fibrinogen, prothrombin) needed to assist in the formation of blood clots and can result in hemorrhage (too little clotting) or thrombosis (too much clotting). Blood and coagulation disorders may be acquired (caused by disease or side effects of medication) or inherited (caused by genes). Most bleeding and clotting disorders are caused by abnormalities in hemostasis (eg, dysfunction of platelets and/or clotting proteins). Less commonly, excessive bleeding or clotting can be caused by abnormalities in the fibrinolytic system (fibrinolysis).[102]

Atypical hemolytic uremic syndrome (aHUS) is a disorder that causes abnormal blood clots to form in small blood vessels in the kidneys or other parts of the body (thrombotic microangiopathy [TMA]). These clots can restrict or block blood flow causing hemolytic anemia, thrombocytopenia and kidney failure. aHUS can occur at any age and often results from a combination of acquired and inherited factors. *G6PD* gene testing has been proposed to detect pathogenic variants for the diagnoses of hemolytic anemia and jaundice which is associated with G6PD enzyme deficiency.

Blood group antigens play a role in recognizing foreign cells in the bloodstream. If a blood type mismatch occurs during a blood transfusion it could lead to an immune response and possible illness. RBC antigen genotyping assays have been proposed as an alternative approach to determining compatibility of donated blood. Blood group genotyping purportedly overcomes blood grouping limitations by looking directly into the DNA sequence and thereby avoiding any donor cell or antibody interference.

Bone marrow failure syndromes (BMFS) are rare diseases that occur in an individual who produces an insufficient amount of red blood cells, white blood cells or platelets and may be acquired or inherited. Inherited BMFS occurs from germline mutations that are passed down from parents. The majority are inherited in an autosomal recessive manner (eg, Fanconi anemia, Shwachman-Diamond syndrome, congenital amegakaryocytic thrombocytopenia, reticular dysgenesis) while a small subset is inherited in X-linked recessive (eg, dyskeratosis congenita) or autosomal dominant patterns (eg, Blackfan-Diamond anemia, reticular dysgenesis). Large multigene panels have been proposed to diagnose these disorders.

Hemoglobinopathies are a group of inherited blood disorders that primarily affect RBCs causing abnormal production or structure of the hemoglobin molecule. They are inherited single-gene disorders and include sickle cell anemia, alpha- and beta-thalassemias.

Methylene tetrahydrofolate reductase (MTHFR) enzyme is encoded by the *MTHFR* gene. This enzyme plays a role in processing amino acids (the building blocks of proteins) which is important for a chemical reaction involving forms of the vitamin folate and is required for the multistep process that converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds. Variations in the *MTHFR* gene have been studied as risk factors for numerous conditions, including behavioral disorders, cardiovascular disease, thrombophilia, stroke, hypertension,

pharmacological management or risk testing and pregnancy-related complications; however, its role remains unclear.

Neutropenia is a condition characterized by abnormally low levels of neutrophils, a type of white blood cell that is mainly produced in the bone marrow. Most causes of neutropenia are acquired (eg, autoimmune disorders, infection, side effects of medication/chemotherapy) with congenital neutropenia being less common.

Plasminogen activator inhibitor-1 (PAI-1) is an inhibitor of fibrinolysis, the clot dissolving portion of the coagulation process. PAI-1 is under investigation as a risk factor for conditions such as cardiovascular disease, thrombophilia and pregnancy-related complications. The PAI-1 test is an antibody-based enzyme assay.

Sickle cell disease (SCD) is an autosomal recessive genetic condition that alters the shape and function of the hemoglobin molecule in RBCs. SCD is characterized by frequent and unpredictable vaso-occlusive complications (VOCs) that result from reduced blood flow in the microvasculature, including red cell stickiness and erythrocyte sickling. These processes lead to pain, chronic organ damage and decreased life expectancy. Flow-based adhesion and mechanical fragility assays are proposed to measure possible biomarkers associated with anemia/hemolysis, cellular adhesion, cellular aggregates, inflammation, coagulation, microparticles and nitric oxide metabolism during a VOC state to help assess an individual's response to disease modifying therapy.

Thrombocytopenia is a condition characterized by abnormally low levels of thrombocytes in the blood that can lead to hypocoagulation. Fetal and neonatal alloimmune thrombocytopenia (FNAIT) (fetomaternal alloimmune thrombocytopenia [FMAIT]) is the most common cause of severe thrombocytopenia in a fetus or newborn.[86] This occurs when inherited platelet antigens from the mother and father are incompatible, resulting in fetal platelet destruction. Maternal and paternal human platelet antigen (HPA) genotyping is commonly used to confirm a diagnosis. Heparin-induced thrombocytopenia (HIT) is a rare immune response to the drug heparin (a blood thinning medication) and is associated with arterial and venous thrombosis.

Thrombophilia (**also known as hypercoagulability)** is a disorder of blood coagulation that increases the risk for blood clots (thrombosis) in veins or arteries. Thrombophilia can be acquired or inherited. The most common acquired thrombophilias occur as a result of injury, surgery or a medical condition. The most common hereditary thrombophilias are factor V Leiden (FVL), due to a variant in the *F5* gene and prothrombin G20210A, as a result of a variant in the *F2* gene.

Von Willebrand disease (VWD) is the most common inherited blood clotting disorder and affects approximately 1 in 100 individuals. VWD is caused by deficient or defective plasma von Willebrand factor (VWF), a large multimeric glycoprotein that assists with primary hemostasis to prevent and stop bleeding. VWD is most commonly characterized by mucocutaneous (eg, epistaxis, genitourinary, gastrointestinal, gingival or petechiae) bleeding. The types of inherited VWD include type 1, type 2 (contains various subtypes), type 3 and platelet type. Acquired Von Willebrand syndrome (aVWS) is less common and may be associated with the use of extracorporeal membrane oxygenation (ECMO) or left ventricular assist devices (LVAD). Conditions such as aortic stenosis, autoimmune disorders (eg, antiphospholipid antibody syndrome, scleroderma and systemic lupus erythrematosus), congenital cardiac anomalies or myeloproliferative neoplasms may also contribute to aVWS.

Multigene (or expanded) panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene) and have been proposed to evaluate the DNA of an individual with a personal and/or family history of more than one hereditary condition or syndrome or hereditary conditions/syndromes associated with more than one gene. Panels often include medically actionable genes but may also include those with unclear medical management. **Targeted (or focused) multigene panels** analyze a limited number of genes targeted to a specific condition.

Coverage Determination

iCare follows the CMS requirement that only allows coverage and payment for services that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS "reasonable and necessary" criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary's specific medical problem.

For jurisdictions with no Medicare guidance for a particular test, iCare will utilize the MolDX program MolDX Program and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare's reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the following criteria:

General Criteria for Genetic and Coagulation Testing for Noncancer Blood Disorders
Apply General Criteria for Genetic and Coagulation Testing for Noncancer Blood Disorders when disease- or gene-specific criteria are not available on this medical coverage policy.

Genetic and coagulation testing for noncancer blood disorders will be considered medically reasonable and necessary if:

- Individual to be tested is under active management or being evaluated for a noncancer blood disorder; **AND**
- Individual is within the population and has the indication for the test's intended use; **AND**
- Results of testing must directly impact treatment or management of the Medicare beneficiary; **AND**

- Analytic validity, clinical validity and clinical utility of the genetic test is supported by the MolDX program; **AND**

- Test is ordered by a physician who is treating the individual

Criteria for Specific Noncancer Blood Disorders

GERMLINE (HEREDITARY) TESTING:

Alpha Thalassemia (*HBA1* and *HBA2* Genes)
***HBA1/HBA2* gene testing** will be considered medically reasonable and necessary for alpha thalassemia when the following requirements are met:

- HBA1/HBA2 deletion/duplication testing for individuals with a protein-based hemoglobin analysis suggestive of alpha thalassemia; **OR**

- Individual to be tested has equivocal or indeterminate diagnosis based on results of prior testing such as complete blood count (CBC) and hemoglobin analysis by qualitative/quantitative electrophoresis, high performance liquid chromatography (HPLC) or isoelectric focusing; **OR**

- To establish disease-causing variant in an individual with a confirmed diagnosis

  Testing strategy:[73]
  1. Targeted analysis for common deletions of *HBA1* and *HBA2*

  2. Perform sequence analysis of *HBA1* and *HBA2* if a common deletion of *HBA1/2* is not identified

  3. Deletion/duplication analysis of *HBA1, HBA2* and MCS-R2 for uncommon deletions may be performed next, if no pathogenic variant is identified with sequence analysis

Prothrombin G20210A Thrombophilia (*F2* Gene) and Factor V Leiden (FVL) Thrombophilia (*F5* Gene)
***F2* and *F5* gene testing** for prothrombin G20210A thrombophilia factor II and factor V Leiden (FVL) thrombophilia will be considered medically reasonable and necessary for pregnant individuals when all the following requirements are met: [29,39-42]

- Individual has a personal history of venous thromboembolism (VTE) associated with a nonrecurrent risk factor (eg, surgery, trauma); **AND**

- Individual is not currently receiving anticoagulant prophylaxis; **AND**

- Results of genetic testing will inform risk stratification for VTE recurrence and subsequent need for antenatal prophylaxis

RBC Genotyping Assays

RBC Genotyping Assays will be considered medically reasonable and necessary when the following requirements are met: [8-12, 30-34]

- Test is FDA approved and tests for multiple antigens (eg, 0001U and 0084U); **AND**
- Testing is being performed as part of a pre-transfusion evaluation for an individual who may require or is expected to require a blood product transfusion (leukocytes, platelets or RBCs) when conventional serologic testing methods are inadequate or at a high risk of producing unreliable or misleading results

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following test types are examples of testing services that may not be considered a benefit (statutory excluded) and denied as Medicare Excluded tests:

- *FANCC* gene testing (eg, 81242, 81412 and 81413);[13-17] **OR**
- *G6PD* gene testing (eg, 81247, 81248 and 81249);[38] **OR**
- *HBB* gene testing (eg, 81361, 81362, 81363, 81364, 81443);[18-22] **OR**
- Human platelet antigen HPA-1a/b – 6a/b, 9a/b, 15a/b genotyping (eg, 81105 to 81112);[8-12] **OR**
- Individual RBC antigen tests that are not part of a comprehensive antigen evaluation (eg, 0180U-0201U, 0221U, 0222U) or comprehensive panels that are not FDA approved (eg, 0246U, 0282U);[8-12, 30-34] **OR**
- *MTHFR* gene testing (eg, 81291), individually or as part of a panel;[39-43] **OR**
- Plasminogen activator inhibitor-1 (PAI-1) testing (85415)[25-29]
- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law;[79] **OR**
- Tests that confirm a diagnosis or known information;[79] **OR**

- Tests that investigate the same germline genetic content, for the same genetic information, that has already been tested in the same individual; [8-12, 30-34] **OR**
- Tests to determine risk for developing a disease or condition;[79] **OR**
- Tests performed to measure the quality of a process;[79] **OR**
- Tests without diagnosis specific indications;[79] **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial[79]

These treatments and services fall within the Medicare program's statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act). Other services/items fall within the Medicare program's statutory exclusion at 1862(a)(12), which prohibits payment.

Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program will not be considered medically reasonable and necessary. A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

The following genetic and coagulations tests for noncancer blood disorders are considered not medically reasonable and necessary for any indication:

- Flow-based adhesion or mechanical fragility assays (0121U, 0122U, 0123U, 0303U, 0304U and 0305U)
- Versiti Heparin-Induced Thrombocytopenia Evaluation – PEA (0275U)
- Versiti VWF Collagen III Binding (0279U)
- Versiti VWF Collagen IV Binding (0280U)
- Versiti VWF Propeptide Antigen (0281U)
- Versiti VWD Type 2B Evaluation (0283U)
- Versiti VWD Type 2N Binding (0284U)

A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Genetic Testing for Inherited Thrombophilias (*F2* and *F5* Genes)
The Medicare guidelines state that genetic testing for the *F2* and *F5* genes for cardiovascular risk assessment is not medically necessary as it is unlikely to impact clinical management except in pregnant individuals. There is no Medicare benefit for assessment of thrombosis risk in asymptomatic individuals (eg,

screening for inherited thrombophilia) or in asymptomatic individuals that have a documented family history of inherited thrombophilia.[24,39-42]

Multigene (or expanded) panels are considered not medically reasonable and necessary for any indication unless **ALL** genes in the panel meet disease- or gene-specific criteria (Refer to Coverage Determination section or Limitations section for single genes in a panel). Examples include, but may not be limited to:

- Multigene (or expanded) panel testing for the diagnosis of inherited BMFS (81441)
- Versiti aHUS Genetic Evaluation (0268U)
- Versiti Autosomal Dominant Thrombocytopenia Panel (0269U)
- Versiti Coagulation Disorder Panel (0270U)
- Versiti Comprehensive Bleeding Disorder Panel (0272U)
- Versiti Comprehensive Platelet Disorder Panel (0274U)
- Versiti Congenital Neutropenia Panel (0271U)
- Versiti Fibrinolytic Disorder Panel (0273U)
- Versiti Inherited Thrombocytopenia Panel (0276U)
- Versiti Platelet Function Disorder Panel (0277U)
- Versiti Thrombosis Panel (0278U)

A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Summary of Evidence

Multigene Panels Versus Multigene (or Expanded) Panels including but not limited to, multiple genes or multiple conditions and in cases where a tiered approach/method is clinically available, testing would be covered only for the number of genes or test that are reasonable and necessary to establish a diagnosis.[32]

Flow-based Adhesion or Mechanical Fragility Assays
The gold standard for assessment of the pain associated with Sickle cell disease is the individual's (or family's) report of the pain severity and similarity to or difference from previous vaso-occlusive pain episodes. There are no specific laboratory findings associated with vaso-occlusive pain.[86]

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81105	Human Platelet Antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-1a/b (L33P)	
81106	Human Platelet Antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2a/b (T145M)	
81107	Human Platelet Antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (I843S)	
81108	Human Platelet Antigen 4 genotyping (HPA-4), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-4a/b (R143Q)	
81109	Human Platelet Antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (eg, HPA-5a/b (K505E))	
81110	Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6a/b (R489Q)	
81111	Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (V837M)	
81112	Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15a/b (S682Y)	

81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant	
81241	F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant	
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)	
81248	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)	
81249	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; full gene sequence	
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, Constant Spring)	
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant	
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence	
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants	
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative	
81361	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)	
81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)	
81363	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)	
81364	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence	

81441	Inherited bone marrow failure syndromes (IBMFS) (eg, Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, GATA2 deficiency syndrome, congenital amegakaryocytic thrombocytopenia) sequence analysis panel, must include sequencing of at least 30 genes, including BRCA2, BRIP1, DKC1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, GATA1, GATA2, MPL, NHP2, NOP10, PALB2, RAD51C, RPL11, RPL35A, RPL5, RPS10, RPS19, RPS24, RPS26, RPS7, SBDS, TERT, and TINF2	
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)	
85415	Fibrinolytic factors and inhibitors; plasminogen activator	
86022	Antibody identification; platelet antibodies	
0001U	Red blood cell antigen typing, DNA, human erythrocyte antigen gene analysis of 35 antigens from 11 blood groups, utilizing whole blood, common RBC alleles reported	
0084U	Red blood cell antigen typing, DNA, genotyping of 10 blood groups with phenotype prediction of 37 red blood cell antigens	
0121U	Sickle cell disease, microfluidic flow adhesion (VCAM-1), whole blood	
0122U	Sickle cell disease, microfluidic flow adhesion (P-Selectin), whole blood	
0123U	Mechanical fragility, RBC, shear stress and spectral analysis profiling	
0180U	Red cell antigen (ABO blood group) genotyping (ABO), gene analysis Sanger/chain termination/conventional sequencing, ABO (ABO, alpha 1-3-N-acetylgalactosaminyltransferase and alpha 1-3-galactosyltransferase) gene, including subtyping, 7 exons	

0181U	Red cell antigen (Colton blood group) genotyping (CO), gene analysis, AQP1 (aquaporin 1 [Colton blood group]) exon 1	
0182U	Red cell antigen (Cromer blood group) genotyping (CROM), gene analysis, CD55 (CD55 molecule [Cromer blood group]) exons 1-10	
0183U	Red cell antigen (Diego blood group) genotyping (DI), gene analysis, SLC4A1 (solute carrier family 4 member 1 [Diego blood group]) exon 19	
0184U	Red cell antigen (Dombrock blood group) genotyping (DO), gene analysis, ART4 (ADP-ribosyltransferase 4 [Dombrock blood group]) exon 2	
0185U	Red cell antigen (H blood group) genotyping (FUT1), gene analysis, FUT1 (fucosyltransferase 1 [H blood group]) exon 4	
0186U	Red cell antigen (H blood group) genotyping (FUT2), gene analysis, FUT2 (fucosyltransferase 2) exon 2	
0187U	Red cell antigen (Duffy blood group) genotyping (FY), gene analysis, ACKR1 (atypical chemokine receptor 1 [Duffy blood group]) exons 1-2	
0188U	Red cell antigen (Gerbich blood group) genotyping (GE), gene analysis, GYPC (glycophorin C [Gerbich blood group]) exons 1-4	
0189U	Red cell antigen (MNS blood group) genotyping (GYPA), gene analysis, GYPA (glycophorin A [MNS blood group]) introns 1, 5, exon 2	
0190U	Red cell antigen (MNS blood group) genotyping (GYPB), gene analysis, GYPB (glycophorin B [MNS blood group]) introns 1, 5, pseudoexon 3	
0191U	Red cell antigen (Indian blood group) genotyping (IN), gene analysis, CD44 (CD44 molecule [Indian blood group]) exons 2, 3, 6	
0192U	Red cell antigen (Kidd blood group) genotyping (JK), gene analysis, SLC14A1 (solute carrier family 14 member 1 [Kidd blood group]) gene promoter, exon 9	
0193U	Red cell antigen (JR blood group) genotyping (JR), gene analysis, ABCG2 (ATP binding cassette subfamily G member 2 [Junior blood group]) exons 2-26	
0194U	Red cell antigen (Kell blood group) genotyping (KEL), gene analysis, KEL (Kell metallo-endopeptidase [Kell blood group]) exon 8	

0195U	KLF1 (Kruppel-like factor 1), targeted sequencing (ie, exon 13)	
0196U	Red cell antigen (Lutheran blood group) genotyping (LU), gene analysis, BCAM (basal cell adhesion molecule [Lutheran blood group]) exon 3	
0197U	Red cell antigen (Landsteiner-Wiener blood group) genotyping (LW), gene analysis, ICAM4 (intercellular adhesion molecule 4 [Landsteiner-Wiener blood group]) exon 1	
0198U	Red cell antigen (RH blood group) genotyping (RHD and RHCE), gene analysis Sanger/chain termination/conventional sequencing, RHD (Rh blood group D antigen) exons 1-10 and RHCE (Rh blood group CcEe antigens) exon 5	
0199U	Red cell antigen (Scianna blood group) genotyping (SC), gene analysis, ERMAP (erythroblast membrane associated protein [Scianna blood group]) exons 4, 12	
0200U	Red cell antigen (Kx blood group) genotyping (XK), gene analysis, XK (X-linked Kx blood group) exons 1-3	
0201U	Red cell antigen (Yt blood group) genotyping (YT), gene analysis, ACHE (acetylcholinesterase [Cartwright blood group]) exon 2	
0221U	Red cell antigen (ABO blood group) genotyping (ABO), gene analysis, next-generation sequencing, ABO (ABO, alpha 1-3-N-acetylgalactosaminyltransferase and alpha 1-3-galactosyltransferase) gene	
0222U	Red cell antigen (RH blood group) genotyping (RHD and RHCE), gene analysis, next-generation sequencing, RH proximal promoter, exons 1-10, portions of introns 2-3	
0246U	Red blood cell antigen typing, DNA, genotyping of at least 16 blood groups with phenotype prediction of at least 51 red blood cell antigens	
0268U	Hematology (atypical hemolytic uremic syndrome [aHUS]), genomic sequence analysis of 15 genes, blood, buccal swab, or amniotic fluid	
0269U	Hematology (autosomal dominant congenital thrombocytopenia), genomic sequence analysis of 14 genes, blood, buccal swab, or amniotic fluid	
0270U	Hematology (congenital coagulation disorders), genomic sequence analysis of 20 genes, blood, buccal swab, or amniotic fluid	
0271U	Hematology (congenital neutropenia), genomic sequence analysis of 23 genes, blood, buccal swab, or amniotic fluid	

0272U	Hematology (genetic bleeding disorders), genomic sequence analysis of 51 genes, blood, buccal swab, or amniotic fluid, comprehensive	
0273U	Hematology (genetic hyperfibrinolysis, delayed bleeding), genomic sequence analysis of 8 genes (F13A1, F13B, FGA, FGB, FGG, SERPINA1, SERPINE1, SERPINF2, PLAU), blood, buccal swab, or amniotic fluid	
0274U	Hematology (genetic platelet disorders), genomic sequence analysis of 43 genes, blood, buccal swab, or amniotic fluid	
0275U	Hematology (heparin-induced thrombocytopenia), platelet antibody reactivity by flow cytometry, serum	
0276U	Hematology (inherited thrombocytopenia), genomic sequence analysis of 23 genes, blood, buccal swab, or amniotic fluid	
0277U	Hematology (genetic platelet function disorder), genomic sequence analysis of 31 genes, blood, buccal swab, or amniotic fluid	
0278U	Hematology (genetic thrombosis), genomic sequence analysis of 12 genes, blood, buccal swab, or amniotic fluid	
0279U	Hematology (von Willebrand disease [VWD]), von Willebrand factor (VWF) and collagen III binding by enzyme-linked immunosorbent assays (ELISA), plasma, report of collagen III binding	
0280U	Hematology (von Willebrand disease [VWD]), von Willebrand factor (VWF) and collagen IV binding by enzyme-linked immunosorbent assays (ELISA), plasma, report of collagen IV binding	
0281U	Hematology (von Willebrand disease [VWD]), von Willebrand propeptide, enzyme-linked immunosorbent assays (ELISA), plasma, diagnostic report of von Willebrand factor (VWF) propeptide antigen level	
0282U	Red blood cell antigen typing, DNA, genotyping of 12 blood group system genes to predict 44 red blood cell antigen phenotypes	
0283U	von Willebrand factor (VWF), type 2B, platelet-binding evaluation, radioimmunoassay, plasma	
0284U	von Willebrand factor (VWF), type 2N, factor VIII and VWF binding evaluation, enzyme-linked immunosorbent assays (ELISA), plasma	

0303U	Hematology, red blood cell (RBC) adhesion to endothelial/subendothelial adhesion molecules, functional assessment, whole blood, with algorithmic analysis and result reported as an RBC adhesion index; hypoxic	
0304U	Hematology, red blood cell (RBC) adhesion to endothelial/subendothelial adhesion molecules, functional assessment, whole blood, with algorithmic analysis and result reported as an RBC adhesion index; normoxic	
0305U	Hematology, red blood cell (RBC) functionality and deformity as a function of shear stress, whole blood, reported as a maximum elongation index	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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Change Summary

- 01/01/2024 New Policy.
-