Genetic Testing

INDEPENDENT CARE HEALTH PLAN

Effective Date: 10/08/2024
Revision Date: 10/08/2024
Review Date: 09/24/2024
Policy Number: WI.PA-1097
Line of Business: Medicare

Medicare Advantage Medical Coverage Policy

Table of Contents

Related Medicare Advantage Medical/Pharmacy Coverage Policies

Comprehensive Genomic Profiling and Genetic Testing for Solid Tumors
Drug Testing
Early Prostate Cancer Detection
Gene Expression Profiling for Cancer Indications
Gene Expression Profiling for Noncancer Indications
Genetic and Biomarker Testing for Alzheimer Disease
Genetic and Coagulation Testing for Noncancer Blood Disorders
Genetic Testing for Cardiac Conditions
Genetic Testing for Hematologic Malignancies and Suspected Blood Disorders
Genetic Testing for Hereditary Ataxias
Genetic Testing for Hereditary Breast, Ovarian, Pancreatic and Prostate Cancer
Genetic Testing for Hereditary Cancer
Genetic Testing for Hereditary Colorectal and Uterine Cancer
Genetic Testing for Diagnosis of Inherited Conditions
Liquid Biopsy
Measurable (Minimal) Residual Disease
Molecular Biomarkers for Prostate Cancer Risk Stratification

Molecular Diagnostic Assays and Breath Testing for Transplant Rejection
Molecular Markers in Fine Needle Aspirates of Thyroid Nodules
Molecular Testing for HLA B27 for Ankylosing Spondylitis
Multianalyte Assays with Algorithmic Analyses for Cancer Indications
Multiplex Pathogen Identification Panels for Infectious Disease
Pharmacogenomics and Companion Diagnostics
Pharmacogenomics Testing
Rheumatoid Arthritis: Biologic Markers and Pharmacologic Assessment
Serological and Fecal Testing for Inflammatory Bowel Disease
Special Stains

Related Documents

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

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories
NCD	Next Generation Sequencing	90.2		
LCD LCA	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer	L39040 A58756	J5, J8 - Wisconsin Physicians Service Insurance Corporation	IA, IN, KS, MI, MO, NE
	MolDX: Molecular Diagnostic Tests (MDT)	L36807 A57772		
	Billing and Coding: MolDX: Short Tandem Repeat (STR) Markers and Chimerism (CPT codes 81265-81268)	A55621		
	MolDX: Repeat Germline Testing	L38429 A57100		
	Billing and Coding: MolDX: Testing of Multiple Genes	A57880		
	MolDX: Defining panel services in MolDX	A59700		

LCD LCA	Molecular Pathology Procedures	L35000 A56199	J6, JK - National Government Services, Inc.	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
LCD LCA	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: MolDX: IKBKAP Genetic Testing Billing and Coding: Short Tandem Repeat (STR) Markers and Chimerism (CPT codes 81265-81268) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX	L39017 A58734 L36021 A56973 A54270 A54830 L38288 A57141 A57910 A59698	J15 - CGS Administrators, LLC	KY, OH
LCD LCA	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: Short Tandem Repeat (STR) Markers and Chimerism (CPT codes 81265-81268) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Testing of Multiple Genes	L38972 A58679 L35160 A57526 A57842 L38351 A57331 A58120	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands

	MolDX: Defining panel services in MolDX	A59685		
LCD LCA	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: Short Tandem Repeat (STR) Markers and Chimerism (CPT codes 81265-81268) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX	L38974 A58681 L36256 A57527 A57843 L38353 A57332 A58121 A59687	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
LCD LCA	Biomarkers for Oncology Biomarkers Overview Billing and Coding: Molecular Pathology and Genetic Testing	L35396 A52986 L35062 A56541 A58917	JH, JL - Novitas Solutions, Inc.	AR, CO, DC, DE, LA, MD, MS, NJ, NM, OK, PA, TX
LCD LCA	MolDX: Lab-Developed Tests for Inherited Cancer Syndromes in Patients with Cancer MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: Short Tandem Repeat (STR) Markers and Chimerism (CPT codes 81265-81268) MolDX: Repeat Germline Testing	L38966 A58652 L35025 A56853 A54832 L38274 A58017	JJ, JM - Palmetto GBA	AL, GA, NC, SC, TN, VA, WV

	Billing and Coding: MolDX: Testing of Multiple Genes MolDX: Defining panel services in MolDX	A57503 A59678		
LCD LCA	Molecular Pathology Procedures Billing and Coding: Molecular Pathology and Genetic Testing	L34519 A57451 A58918	JN - First Coast Service Options, Inc.	FL, PR, US VI

Description

Deoxyribonucleic acid (DNA) is a molecule that carries instructions for the characteristics and functions of living organisms, including humans, and are transmitted from one generation to the next. An individual's complete set of genetic instructions is referred to as the genome.

Sometimes variants (mutations) take place and can disrupt an individual's usual processes. This happens during DNA replication. The interference leads to a permanent alteration in the DNA sequence. Chromosomes, a single gene or multiple genes can mutate in a number of ways including substitutions, insertions (additions), deletions, duplications (copied at least one time) and repeat expansions (repetition of short DNA sequences). Variants can be insignificant or even beneficial; others are pathogenic (disease-causing).

Variants can be detected with genetic testing by analyzing DNA with sequencing (sometimes referred to as next-generation sequencing [NGS]) or by analyzing deletions/duplications analysis and large genomic rearrangements. Some laboratories combine these methods, which is known as comprehensive testing.

Genetic testing may be used for a variety of purposes:

- Carrier screening is performed on prospective parents to identify genetic risks that can be passed to offspring. Carriers are themselves unaffected but at risk for producing affected children.

- Diagnostic testing is utilized to identify or rule out a suspected genetic condition in an individual who exhibits signs and symptoms of the disorder.

- Pharmacogenomics testing analyzes an individual's unique genetic makeup to help determine response to a specific medication.

- Predictive testing may be used for an individual who does not exhibit signs or symptoms of a disorder but may be at increased risk for developing the disorder due to family history. There are two types of predictive testing: presymptomatic (development of symptoms is certain in the presence of a gene mutation [eg, hereditary hemochromatosis, Huntington disease]) or predispositional (development of symptoms is likely, but not certain, in the presence of a gene mutation [eg, breast cancer]).

- Preimplantation genetic testing is used as an adjunct to assist in reproductive technology (ART). Testing is performed on embryos following in vitro fertilization (IVF) to detect genetic disorders prior to implantation into the uterus.

- Prenatal genetic testing is performed during pregnancy to identify genetic disorders in fetuses.

Germline (inherited) genetic testing refers to the identification of variants associated with inherited risk of disease which can be detected by evaluating an individual's entire genome at a single time (referred to as whole genome sequencing [WGS]) or by targeting chromosomes, genes, gene regions or gene products within an individual's genome that may play a role in the development or progression of an associated disease. An individual's germline DNA is present at birth, is constant and is identical in all body tissue types. Almost any sample (eg, blood, saliva, buccal [cheek] smear, fresh or frozen tissues, formalin-fixed paraffin-embedded [FFPE] tissues, hair follicles and prenatal specimens) is suitable for germline testing. In general, germline testing for a particular disorder is performed once per lifetime; however, there are rare instances when repeat testing is appropriate.

Multigene panel is a genetic test that analyzes multiple genes at one time as opposed to single gene testing that searches for variants in one specific gene.

Whole genome sequencing (WGS) is a genetic test that analyzes an individual's complete genome at a single time.

Whole exome sequencing (WES) is an alternative to WGS. It is a genetic test that analyzes the exome, the coding region of genes that contains instructions for building proteins.

Whole mitochondrial sequencing is a genetic test that analyzes the entirety of an individual's mitochondrial DNA (mtDNA). MtDNA resides within the mitochondria and is distinct from nuclear DNA (nDNA) which is inherited. It is used to diagnose mitochondrial diseases.

Multianalyte assays with algorithmic analyses (MAAAs) are laboratory measurements that use a mathematic formula to analyze multiple markers that may be associated with a particular disease state and are designed to evaluate disease activity or an individual's risk for disease. The laboratory performs an algorithmic analysis using the results of the assays and sometimes other individual information, such as gender and age and converts the information into a numeric score, which is conveyed on a laboratory report. Generally, MAAAs are exclusive (and/or proprietary) to a single laboratory which owns the algorithm. Proposed indications for the use of MAAA testing are to assess risk and to diagnose or monitor noncancerous disease activity. Examples include, but may not be limited to:

- **Clarifi ASD** is a test that measures specific microRNAs (miRNAs) in saliva to purportedly diagnose autism spectrum disorder (ASD) in children 18 months through 6 years of age.

- **INFINITI Neural Response Panel** is a qualitative diagnostic test that uses a buccal swab specimen for the identification of an individual who may be at risk for opioid dependency. The panel is designed to identify genetic mutations involved in the brain reward pathways that are associated with increased risk of opioid use disorder and is intended for use by physicians to aid in prescribing safe and effective pain management.

- **KawasakiDx** is a serum assay that includes interferon alpha-inducible protein 27 (IFI27) and mast cell-expressed membrane protein 1 (MCEMP1) along with RNA and reverse transcription polymerase chain reaction (RT-qPCR) to report a risk score for Kawasaki disease.

- **ScoliScore** is a prognostic test that analyzes genetic markers purportedly associated with spinal curve progression and assigns a numerical value regarding the likelihood of curve progression based on the test results and other clinical information.

- **SMASH Genomic Assay** is a DNA copy number variation (CNV) test that utilizes next-generation sequencing (NGS) technology and proprietary software to purportedly assist with a diagnosis of ASD.

Short tandem repeat (STR) analysis is a method to examine specific regions in DNA where short sequences of base pairs (the building blocks of DNA) are repeated. Key clinical indications of STR analysis include paternity testing, bone marrow transplantation monitoring, diagnosis of certain genetic disorders such as Huntington disease and preimplantation genetic diagnosis.

Coverage Determination

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

CMS outlines coverage for items and services including molecular diagnostic tests (MDTs) and laboratory developed tests (LDTs) through National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs) and Local Coverage Articles (LCAs). Humana provides coverage for MDTs and LDTs identified as covered in an NCD, LCD or LCA when medical necessity criteria are met; however, ***for jurisdictions with no Medicare guidance about a specific MDT or LDT, Humana utilizes the DEX Diagnostics Exchange Registry (DEX) established by the Molecular Diagnostic Services Program (MolDX) as the standard to evaluate analytical and clinical validity and clinical utility.*** *MDTs and LDTs must meet analytical and clinical validity standards and demonstrate clinical utility to fulfill the CMS "reasonable and necessary" requirement. In the absence of clear CMS guidance, Humana may also develop and publish Medical Coverage Policies to determine medical necessity 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 to determine medical necessity. An MDT or LDT must be ordered by a physician who is treating the beneficiary and the results must be used in the management of a beneficiary's specific medical problem.*[50,64,65]

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

General Criteria for Genetic Testing
Apply General Criteria for Genetic Testing when test specific criteria are not available on any medical coverage policy.

Genetic testing will be considered medically reasonable and necessary when the following requirements are met:

- Analytic validity, clinical validity and clinical utility of the MDT or LDT is supported by the MolDX Program[50,64,65]; **OR**
    - FDA approval/clearance performed within FDA labeling indications **AND** approved by the MolDX Program[50,64,65]; **AND**
- Individual displays signs and symptoms of a hereditary disease; **AND**
- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; **AND**
- Results of the genetic testing must directly impact treatment or management of the individual; **AND**
- The test analyzes genes or genetic variants with definitive or well-established guidelines required for clinical decision making for its intended use that can be reasonably detected by the test

Multigene Panel Testing

Multigene panel testing will be considered medically reasonable and necessary when the following requirements are met:

- Individual meets General Criteria for Genetic Testing above; **AND**
- More than one gene on the panel impacts the clinical management of the individual being tested; **AND**
- The panel evaluates genes and/or alleles in accordance with the panel's indicated use

Exome Sequencing

For all jurisdictions, genetic testing for exome sequencing will be considered medically reasonable and necessary (and thus impacting therapeutic decision-making in clinical management) when the individual to be tested meets General Criteria for Genetic Testing.

Known Familial Pathogenic or Likely Pathogenic Variant

Known familial variant (KFV) genetic testing will be considered medically reasonable and necessary when the individual to be tested is affected and has a first- second-or third-degree relative with a pathogenic or likely pathogenic variant. Genetic testing should be limited to the KFV.[34-37]

Repeat Germline Genetic Testing

Repeat germline genetic testing will be considered medically reasonable and necessary when technological advancements for genetic testing may detect previously missed pathogenic variants (eg, evaluation of

deletions and large genomic rearrangement has become available and initial testing included sequencing only or new methods for capturing and sequencing DNA).[66]

Short Tandem Repeat Analysis

For jurisdictions without an LCD/LCA, Humana determines medical necessity for **short tandem repeat (STR) analysis** (codes 81265-81268) for the management of **bone marrow transplantation** based on the criteria contained in LCA – Billing and Coding: MolDX: Short Tandem Repeat (STR) Markers and Chimerism (CPT codes 81265-81268) (A57842).[23]

The use of the criteria above provides clinical benefits highly likely to outweigh any clinical harms including, but not limited to, adverse effects resulting from false-positive results and the subsequent need for further testing and biopsies, providing false reassurance to individuals who may have increased risks for developing cancer or emotional, social or financial consequences of test results.[59] 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 tests may not be considered a benefit (statutory exclusion):

- ~~Recipient/donor testing and twin zygosity (comparative analysis using~~ Short tandem repeat (STR) analysis ~~markers~~ (codes 81265-81268) ~~81265/81266])~~ ~~including, but may not be limited to:~~ for twin zygosity including, but may not be limited to, Twin Zygosity PLA (code 0060U)[20-24]

  - ~~Twin Zygosity PLA (0060U)~~

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law[64]; **OR**
- Tests performed to determine carrier screening[30]; **OR**
- Prenatal diagnostic testing[30]; **OR**
- Tests that confirm a diagnosis or known information[64]; **OR**
- Tests to determine risk for developing a disease or condition[64]; **OR**
- Tests performed to measure the quality of a process[64]; **OR**

- Tests without diagnosis specific indications[64]; **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[64]

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).

For jurisdictions with no specific Medicare guidance about a specific MDT or LDT, the test is not covered **UNLESS** analytical validity, clinical validity and clinical utility have been established by one of the following[50,64,65]:

- MolDX Program approved technical assessment

- FDA approval/clearance performed within FDA labeling indications **AND** approved by the MolDX Program

The following items for genetic testing will not be considered medically reasonable and necessary:

- Any laboratory test that investigates the same germline genetic content, for the same genetic information, that has already been tested in the same individual

- Cytogenic (genome-wide) analysis for constitutional chromosomal abnormalities (code 81349)[48]

- Genome sequence analysis (codes 81425-81427)[48]

- Nuclear encoded mitochondrial genes, genomic sequence panel (code 81440)[48]

- Whole mitochondrial genome, genomic sequence (code 81460) and large deletion analysis panel (code 81465)[48]

A review of the current medical literature shows that the evidence is insufficient to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature (as defined by CMS) examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Summary of Evidence

Molecular Diagnostic Tests (MDTs) and Lab Developed Tests (LDTs) without Molecular Diagnostic Services Program (MolDX) Approval or FDA Approval/Clearance

Medicare ensures a specific set of health benefits to eligible beneficiaries, meaning that Medicare is a defined benefit program. The Medicare Benefit Policy Manual (IOM 100-2, Ch. 15, Sec 10) identifies laboratory tests as a benefit category while the Social Security Act (Sec. 1862[a][1][A]) further defines what is covered by Medicare by stating that items and services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.[50,65,70]

An MDT is a type of medical test that involves the detection or identification of nucleic acids (deoxyribonucleic acid [DNA]/ribonucleic acid [RNA]), proteins, chromosomes, enzymes, cancer chemotherapy sensitivity and/or other metabolites. These tests look for specific changes in these molecules that may indicate the presence of a disease, an inherited condition or an individual's response to a particular medication. There are different types of MDTs, some of which may only involve analyzing a single gene for a specific variant (mutation). Others may involve more complex procedures and analyze multiple genes or molecules. In some cases, these tests may use algorithms or other forms of data evaluation to interpret results and assist with clinical decision making. An LDT is a medical test developed and performed by a specific laboratory. LDTs typically are not US Food and Drug Administration (FDA) approved/cleared.[43-47]

Under Medicare Benefit requirements, some types of tests may be denied as statutory exclusions and deemed as ineligible for coverage. This includes, but is not limited to, "tests identified as investigational by available literature and/or the literature supplied by the developer, and are not part of a clinical trial.[65]"

MDTs and LDTs must meet analytical and clinical validity standards and demonstrate clinical utility, which fulfills the CMS reasonable and necessary requirement for coverage. Analytical validity focuses on the technical performance of a test, referring to its accuracy and reliability in measuring what it is designed to measure. Clinical validity is the ability of a test to accurately identify or predict the presence or absence of a specific condition. Clinical utility refers to the usefulness of a test in improving clinical outcomes or guiding clinical decision-making. Even if a test is deemed safe and effective in terms of analytical and clinical validity, CMS mandates that the test must also be "reasonable and necessary" which is demonstrated by the test's clinical utility.[43-47,60]

The MolDX Program was created to provide a process for determining if an MDT or LDT meets analytical and clinical validity criteria and demonstrates clinical utility at a level that meets the Medicare reasonable and necessary requirement. To this end, MolDX completes a Technical Assessment evaluation by reviewing best practices, societal guidelines, available evidence, technical reviews and expert opinion. Laboratories that perform FDA approved/cleared tests with proven utility and only perform the test within labeling indications may be exempt from the MolDX Technical Assessment. Following the Technical Assessment outcomes, the MolDX Program sets coverage determinations as follows: covered without restrictions beyond inherent design and purpose limitations, limited coverage (eg, for a specific diagnosis or clinical indication) or noncovered if the test was not deemed medically reasonable and necessary for the individual's diagnosis and/or treatment. The DEX Diagnostics Exchange Registry (DEX) is a centralized database of evaluated MDTs and LDTs and is publicly available.[64,65]

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
81171	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81172	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)	
81200	ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)	
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X)	
81209	BLM (Bloom syndrome, RecQ helicase-like) (eg, Bloom syndrome) gene analysis, 2281del6ins7 variant	
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)	
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants	
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants	
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence	
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)	
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)	
81242	FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T)	
81243	FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	

81244	FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and promoter methylation status)	
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)	
81251	GBA (glucosidase, beta, acid) (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A)	
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence	
81253	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants	
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])	
81255	HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)	
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	
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (eg, familial dysautonomia) gene analysis, common variants (eg, 2507+6T>C, R696P)	
81265	Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample] and donor testing, twin zygosity testing, or maternal cell contamination of fetal cells)	

81266	Comparative analysis using Short Tandem Repeat (STR) markers; each additional specimen (eg, additional cord blood donor, additional fetal samples from different cultures, or additional zygosity in multiple birth pregnancies) (List separately in addition to code for primary procedure)	
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	
81290	MCOLN1 (mucolipin 1) (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)	
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed	
81330	SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)	
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence	
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)	
81349	Cytogenic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis	
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	
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	
81402	MOLECULAR PATHOLOGY PROCEDURE LEVEL 3	
81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4	
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5	
81405	MOLECULAR PATHOLOGY PROCEDURE LEVEL 6	
81406	MOLECULAR PATHOLOGY PROCEDURE LEVEL 7	

81412	Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1	
81415	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis	
81416	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)	
81417	Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)	
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood	
81425	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis	
81426	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)	
81427	Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)	
81430	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1	
81431	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes	

81440	Nuclear encoded mitochondrial genes (eg, neurologic or myopathic phenotypes), genomic sequence panel, must include analysis of at least 100 genes, including BCS1L, C10orf2, COQ2, COX10, DGUOK, MPV17, OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, and TYMP	
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)	
81460	Whole mitochondrial genome (eg, Leigh syndrome, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes [MELAS], myoclonic epilepsy with ragged-red fibers [MERFF], neuropathy, ataxia, and retinitis pigmentosa [NARP], Leber hereditary optic neuropathy [LHON]), genomic sequence, must include sequence analysis of entire mitochondrial genome with heteroplasmy detection	
81465	Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed	
81479	Unlisted molecular pathology procedure	
83080	b-Hexosaminidase, each assay	
0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score	
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood	
0078U	Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positiv	

0079U	Comparative DNA analysis using multiple selected single-nucleotide polymorphisms (SNPs), urine and buccal DNA, for specimen identity verification	
0094U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis	
0156U	Copy number (eg, intellectual disability, dysmorphology), sequence analysis	
0170U	Neurology (autism spectrum disorder [ASD]), RNA, next-generation sequencing, saliva, algorithmic analysis, and results reported as predictive probability of ASD diagnosis	
0205U	Ophthalmology (age-related macular degeneration), analysis of 3 gene variants (2 CFH gene, 1 ARMS2 gene), using PCR and MALDI-TOF, buccal swab, reported as positive or negative for neovascular age-related macular-degeneration risk associated with zinc supplements	
0209U	Cytogenomic constitutional (genome-wide) analysis, interrogation of genomic regions for copy number, structural changes and areas of homozygosity for chromosomal abnormalities	
0212U	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, proband	
0213U	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, each comparator genome (eg, parent, sibling)	
0214U	Rare diseases (constitutional/heritable disorders), whole exome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, proband	

0215U	Rare diseases (constitutional/heritable disorders), whole exome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, each comparator exome (eg, parent, sibling)	
0236U	SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (eg, spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications, deletions, and mobile element insertions	
0252U	Fetal aneuploidy short tandem-repeat comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy	
0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy, per embryo tested	
0260U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping	
0264U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping	
0265U	Rare constitutional and other heritable disorders, whole genome and mitochondrial DNA sequence analysis, blood, frozen and formalin-fixed paraffin-embedded (FFPE) tissue, saliva, buccal swabs or cell lines, identification of single nucleotide and copy number variants	
0266U	Unexplained constitutional or other heritable disorders or syndromes, tissue-specific gene expression by whole-transcriptome and next-generation sequencing, blood, formalin-fixed paraffin-embedded (FFPE) tissue or fresh frozen tissue, reported as presence or absence of splicing or expression changes	

0267U	Rare constitutional and other heritable disorders, identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping and whole genome sequencing	
0327U	Fetal aneuploidy (trisomy 13, 18, and 21), DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy, includes sex reporting, if performed	
0335U	Rare diseases (constitutional/heritable disorders), whole genome sequence analysis, including small sequence changes, copy number variants, deletions, duplications, mobile element insertions, uniparental disomy (UPD), inversions, aneuploidy, mitochondrial genome sequence analysis with heteroplasmy and large deletions, short tandem repeat (STR) gene expansions, fetal sample, identification and categorization of genetic variants	
0336U	Rare diseases (constitutional/heritable disorders), whole genome sequence analysis, including small sequence changes, copy number variants, deletions, duplications, mobile element insertions, uniparental disomy (UPD), inversions, aneuploidy, mitochondrial genome sequence analysis with heteroplasmy and large deletions, short tandem repeat (STR) gene expansions, blood or saliva, identification and categorization of genetic variants, each comparator genome (eg, parent)	
0341U	Fetal aneuploidy DNA sequencing comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploid	
0355U	APOL1 (apolipoprotein L1) (eg, chronic kidney disease), risk variants (G1, G2)	
0389U	Pediatric febrille illness (Kawasaki disease [KD]), interferon alpha-inducible protein 27 (IF127) and mast cell-expressed membrane protein 1 (MCEMP1), RNA, using quantitative reverse transcription polymerase chain reaction (RT-qPCR), blood, reported as a risk score for KD	
0396U	Obstetrics (pre-implantation genetic testing), evaluation of 300000 DNA single-nucleotide polymorphisms (SNPs) by microarray, embryonic tissue, algorithm reported as a probability for single-gene germline conditions	

0400U	Obstetrics (expanded carrier screening), 145 genes by next-generation sequencing, fragment analysis and multiplex ligation- dependent probe amplification, DNA, reported as carrier positive or negative	
0417U	Rare diseases (constitutional/heritable disorders), whole mitochondrial genome sequence with heteroplasmy detection and deletion analysis, nuclear-encoded mitochondrial gene analysis of 335 nuclear genes, including sequence changes, deletions, insertions, and copy number variants analysis, blood or saliva, identification and categorization of mitochondrial disorder–associated genetic variants	
0425U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis, each comparator genome (eg, parents, siblings)	
0426U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), ultra-rapid sequence analysis	
0449U	Carrier screening for severe inherited conditions (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia), regardless of race or self-identified ancestry, genomic sequence analysis panel, must include analysis of 5 genes (CFTR, SMN1, HBB,HBA1, HBA2)	
0454U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping	
0469U	Rare diseases (constitutional/heritable disorders), whole genome sequence analysis for chromosomal abnormalities, copy number variants, duplications/deletions, inversions, unbalanced translocations, regions of homozygosity (ROH), inheritance pattern that indicate uniparental disomy (UPD), and aneuploidy, fetal sample (amniotic fluid, chorionic villus sample, or products of conception), identification and categorization of genetic variants, diagnostic report of fetal results based on phenotype with maternal sample and paternal sample, if performed, as comparators and/or maternal cell contamination	
0482U	Obstetrics (preeclampsia), biochemical assay of soluble fms-like tyrosine kinase 1 (sFlt-1) and placental growth factor (PlGF), serum, ratio reported for sFlt-1/PlGF, with risk of progression for preeclampsia with severe features within 2 weeks	**New Code Effective Date 10/01/2024**
0488U	Obstetrics (fetal antigen noninvasive prenatal test), cell-free DNA sequence analysis for detection of fetal presence or absence of 1 or more of the Rh, C, c, D, E, Duffy (Fya), or Kell (K)	**New Code Effective Date 10/01/2024**

	antigen in alloimmunized pregnancies, reported as selected antigen(s) detected or not detected	
0489U	Obstetrics (single-gene noninvasive prenatal test), cell-free DNA sequence analysis of 1 or more targets (eg, CFTR, SMN1, HBB, HBA1, HBA2) to identify paternally inherited pathogenic variants, and relative mutation-dosage analysis based on molecular counts to determine fetal inheritance of maternal mutation, algorithm reported as a fetal risk score for the condition (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia)	**New Code Effective Date 10/01/2024**
0494U	Red blood cell antigen (fetal RhD gene analysis), next-generation sequencing of circulating cell-free DNA (cfDNA) of blood in pregnant individuals known to be RhD negative, reported as positive or negative	**New Code Effective Date 10/01/2024**
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
S3845	Genetic testing for alpha-thalassemia	**Not Covered**
S3846	Genetic testing for hemoglobin E beta-thalassemia	**Not Covered**
S3850	Genetic testing for sickle cell anemia	**Not Covered**
S3870	Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or intellectual disability	**Not Covered**

References

1. American College of Medical Genetics and Genomics (ACMG). ACMG Policy Statement. Clinical utility of genetic and genomic services: a position statement of the American College of Medical Genetics and Genomics. https://www.acmg.net. Published March 12, 2015.

2. American College of Medical Genetics and Genomics (ACMG). ACMG Policy Statement. Points to consider in the clinical application of genomic sequencing. https://www.acmg.net. Published 2012.

3. American College of Medical Genetics and Genomics (ACMG). ACMG Practice Guidelines. Incidental findings in clinical genomics: a clarification. https://www.acmg.net. Published August 2013.

4. American College of Medical Genetics and Genomics (ACMG). ACMG Practice Statement. Incidental detection of acquired variants in germline genetic and genomic testing: a points to consider statement of the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published August 2021.

5. American College of Medical Genetics and Genomics (ACMG). ACMG Statement. DNA-based screening and personal health: a points to consider statement for individuals and health-care providers from the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published 2021.

6. American College of Medical Genetics and Genomics (ACMG). ACMG Statement. Points to consider in the reevaluation and reanalysis of genomic test results: a statement of the American College of Medical Genetics and Genomics. https://www.acmg.net. Published June 2019.

7. American College of Medical Genetics and Genomics (ACMG). ACMG Statement. The use of ACMG secondary findings recommendations for general population screening: a policy statement of the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published April 2019.

8. American College of Medical Genetics and Genomics (ACMG). ACMG Technical Standard. Next-generation sequencing for constitutional variants in the clinical laboratory, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published March 2021.

9. American College of Medical Genetics and Genomics (ACMG). ACMG Technical Standards. Diagnostic gene sequencing panels: from design to report – a technical standard of the American College of Medical Genetics and Genomics. https://www.acmg.net. Published March 2020.

10. American College of Medical Genetics and Genomics (ACMG). ACMG Technical Standard. Next-generation sequencing for constitutional variants in the clinical laboratory, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published 2021.

11. American College of Medical Genetics and Genomics (ACMG). Clarifications to ACMG's recent statement on the use of ACMG secondary findings recommendations for general population screening: a policy statement of the American College of Medical Genetics and Genomics (ACMG). https://www.acmg.net. Published 2019.

12. American College of Obstetricians and Gynecologists (ACOG). Committee Opinion. Cascade testing: testing women with known hereditary genetic mutations associated with cancer. https://www.acog.org. Published January 2018. Updated 2022.

13. American College of Obstetricians and Gynecologists (ACOG). Committee Opinion. Ethical issues in genetic testing. https://www.acog.org. Published June 2008. Updated 2020.

14. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: defining panel services in MolDX (A59678). https://www.cms.gov. Published February 29, 2024.

15. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: defining panel services in MolDX (A59685). https://www.cms.gov. Published February 29, 2024.

16. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: defining panel services in MolDX (A59687). https://www.cms.gov. Published February 29, 2024.

17. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: defining panel services in MolDX (A59698). https://www.cms.gov. Published February 29, 2024.

18. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: defining panel services in MolDX (A59700). https://www.cms.gov. Published February 29, 2024.

19. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: IKBKAP genetic testing (A54270). https://www.cms.gov. Published October 1, 2015. Updated November 22, 2023.

20. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: short tandem repeat (STR) markers and chimerism (CPT codes 81265-81268) (A54830). https://www.cms.gov. Published January 7, 2016. Updated November 16, 2023.

21. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: short tandem repeat (STR) markers and chimerism (CPT codes 81265-81268) (A54832). https://www.cms.gov. Published January 17, 2016. Updated March 17, 2022.

22. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: short tandem repeat (STR) markers and chimerism (CPT codes 81265-81268) (A55621). https://www.cms.gov. Published August 15, 2017. Updated March 31, 2022.

23. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: short tandem repeat (STR) markers and chimerism (CPT codes 81265-81268) (A57842). https://www.cms.gov. Published March 3, 2022. Updated March 17, 2022.

24. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: short tandem repeat (STR) markers and chimerism (CPT codes 81265-81268) (A57843). https://www.cms.gov. Published March 3, 2022. Updated March 17, 2022.

25. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: testing of multiple genes (A57503). https://www.cms.gov. Published October 21, 2019. Updated February 10, 2022.

26. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: testing of multiple genes (A57880). https://www.cms.gov. Published December 26, 2019. Updated December 28, 2023.

27. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: testing of multiple genes (A57910). https://www.cms.gov. Published January 1, 2020. Updated November 22, 2023.

28. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: testing of multiple genes (A58120). https://www.cms.gov. Published June 7, 2020. Updated February 10, 2022.

29. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: MolDX: testing of multiple genes (A58121). https://www.cms.gov. Published June 7, 2020. Updated February 10, 2022.

30. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: molecular pathology and genetic testing (A58917). https://www.cms.gov. Published November 8, 2021. Updated July 1, 2024.

31. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and coding: molecular pathology and genetic testing (A58918). https://www.cms.gov. Published November 8, 2021. Updated July 1, 2024.

32. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Biomarkers for oncology (L35396). https://www.cms.gov. Published October 1, 2015. Updated December 13, 2020.

33. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Biomarkers overview (L35062). https://www.cms.gov. Published October 1, 2015. Updated December 12, 2021.

34. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: lab-developed tests for inherited cancer syndromes in patients with cancer (L38966). https://www.cms.gov. Published July 3, 2022. Updated March 30, 2023.

35. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: lab-developed tests for inherited cancer syndromes in patients with cancer (L38972). https://www.cms.gov. Published August 8, 2022.

36. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: lab-developed tests for inherited cancer syndromes in patients with cancer (L38974). https://www.cms.gov. Published August 8, 2022.

37. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: lab-developed tests for inherited cancer syndromes in patients with cancer (L39017). https://www.cms.gov. Published August 21, 2022. Updated March 30, 2023.

38. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: lab-developed tests for inherited cancer syndromes in patients with cancer (L39040). https://www.cms.gov. Published July 3, 2022.

39. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: repeat germline testing (L38274). https://www.cms.gov. Published May 31, 2020. Updated December 30, 2021.

40. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: repeat germline testing (L38288). https://www.cms.gov. Published June 07, 2020. Updated December 7, 2023.

41. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: repeat germline testing (L38351). https://www.cms.gov. Published August 03, 2020. Updated December 30, 2021.

42. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: repeat germline testing (L38429). https://www.cms.gov. Published June 14, 2020. Updated February 1, 2024.

43. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L35160). https://www.cms.gov. Published October 1, 2015. Revised May 4, 2023.

44. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L36021). https://www.cms.gov. Published October 1, 2015. Revised May 4, 2023.

45. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L36256). https://www.cms.gov. Published October 1, 2015. Revised May 4, 2023.

46. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L35025). https://www.cms.gov. Published October 1, 2015. Revised May 4, 2023.

47. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: molecular diagnostic tests (MDT) (L36807). https://www.cms.gov. Published February 16, 2017. Revised April 27, 2023.

48. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Molecular pathology procedures (L35000). https://www.cms.gov. Published October 1, 2015. Revised August 6, 2023.

49. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Molecular pathology procedures (L34519). https://www.cms.gov. Published October 1, 2015. Revised December 12, 2021.

50. Centers for Medicare & Medicaid Services (CMS). Medicare benefit policy manual: chapter 15 - covered medical and other health services. https://www.cms.gov. Updated March 7, 2024.

51. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD). Next-generation sequencing (90.2). https://www.cms.gov. Published November 13, 2020.

52. Hayes, Inc. Clinical Utility Evaluation. Clinical utility of whole genome sequencing (WGS) and whole exome sequencing (WES) in patients with intellectual disability (ID). https://evidence.hayesinc.com. Published January 21, 2021. Updated March 15, 2024.

53. Hayes, Inc. Clinical Utility Evaluation. Prenatal whole genome sequencing and prenatal whole exome sequencing. https://evidence.hayesinc.com. Published June 15, 2020. Updated May 12, 2023.

54. Hayes, Inc. Clinical Utility Evaluation. Whole genome sequencing (WGS) In neonatal and pediatric patients. https://evidence.hayesinc.com. Published September 22, 2016. Updated August 12, 2019.

55. Hayes, Inc. Clinical Utility Evaluation. Whole exome/genome sequencing for neuromuscular disease and movement disorders in adults. https://evidence.hayesinc.com. Published March 9, 2022. Updated March 15, 2024.

56. Hayes, Inc. Clinical Utility Evaluation. Whole exome/genome sequencing for previously undiagnosed pediatric neurodevelopmental disorders. https://evidence.hayesinc.com. Published November 12, 2021. Updated December 1, 2023.

57. Hayes, Inc. Precision Medicine Insights. Whole mitochondrial genome sequencing. https://evidence.hayesinc.com. Published March 13, 2024.

58. Hayes, Inc. Precision Medicine Research Brief. Rapid whole exome and rapid whole genome sequencing for critically ill infants. https://evidence.hayesinc.com. Published July 28, 2023.

59. MedlinePlus. What are the risks and limitations of genetic testing? https://medlineplus.gov. Updated July 28, 2021.

60. National Academies of Sciences, Engineering and Medicine. An evidence framework for genetic testing. https://www.ncbi.nlm.nih.gov. Published 2017.

61. National Society of Genetic Counselors (NSGC). Position Statement. Family health history. https://www.nsgc.org. Published March 3, 2020. Updated 2023.

62. National Society of Genetic Counselors (NSGC). Position Statement. Secondary and incidental findings in genetic testing. https://www.nsgc.org. Published March 23, 2020. Updated June 15, 2023.

63. National Society of Genetic Counselors (NSGC). Position Statement. Use of multi-gene panel tests. https://www.nsgc.org. Published 2017. Updated June 15, 2023.

64. Palmetto GBA. Molecular diagnostic program (MolDX): coverage, coding, and pricing standards and requirements (M00106). https://www.palmettogba.com/MolDx. Published December 2019.

65. Palmetto GBA. Molecular diagnostic tests and Medicare. https://www.palmettogba.com. Published June 23, 2023.

66. UpToDate, Inc. Genetic testing. https://www.uptodate.com. Updated February 2024.

67. UpToDate, Inc. Next-generation DNA sequencing (NGS): principles and clinical applications. https://www.uptodate.com. Updated February 7, 2024.

68. UpToDate, Inc. Personalized medicine. https://www.uptodate.com. Updated February 2024.

69. UpToDate, Inc. Secondary findings from genetic testing. https://www.uptodate.com. Updated February 2024.

70. US Congress. United States Code: Social Security Act, 42 U.S.C. §§ 301- 1940. Sec. 1862(a)(1)(A): exclusions from coverage and Medicare as a secondary payer. https://www.ssa.gov. Published 1940.

Appendix

Appendix A
Family Relationships

Degree of Relationship	Relative of the Individual to be Tested
First-degree	Child, full-sibling, parent
Second-degree	Aunt, uncle, grandchild, grandparent, nephew, niece, half-sibling
Third-degree	First cousin, great aunt, great-uncle, great-grandchild, great-grandparent, half-aunt, half-uncle

Change Summary

01/01/2024 New Policy.
03/26/2024 Provider Claims Codes Update, No Coverage Change.
04/23/2024 Annual Review, Coverage Change.
08/06/2024 Update, Coverage Change. Provider Claims Codes Update.
09/10/2024 Provider Claims Codes Update, No Coverage Change.
09/24/2024 Update, Coverage Change.