Genetic Testing

INDEPENDENT CARE HEALTH PLAN

Effective Date: 01/01/2024
Revision Date: Click or tap to enter a date.
Review Date: Click or tap to enter a date.
Policy Number: WI.PA-1097-000
Line of Business: Medicare

Medicare Advantage Medical Coverage Policy

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Related Documents

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

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories
NCD	Next Generation Sequencing	90.2		
LCD LCA	MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Repeat Germline Testing	L36807 A57772 L38429 A57100	J5 - Wisconsin Physicians Service Insurance Corporation J8 - Wisconsin Physicians Service Insurance Corporation	IA, KS, MO, NE IN, MI
LCD LCA	Molecular Pathology Procedures Billing and Coding: Molecular Pathology Procedures	L35000 A56199	J6 - National Government Services, Inc. (Part A/B MAC) JK - National Government	IL, MN, WI CT, NY, ME, MA, NH, RI, VT

			Services, Inc. (Part A/B MAC	
LCD LCA	MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Repeat Germline Testing	L38288 A56973 L36021 A57141	J15 - CGS Administrators, LLC (Part A/B MAC)	KY, OH
LCD LCA	MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Repeat Germline Testing	L35160 A57526 L38351 A57331	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCD LCA	MolDX: Molecular Diagnostic Tests (MDT) Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Repeat Germline Testing	L36256 A57527 L38353 A57332	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 L35062 A58917	JH - Novitas Solutions, Inc. (Part A/B MAC) JL - Novitas Solutions, Inc. (Part A/B MAC)	AR, CO, NM, OK, TX, LA, MS DE, D.C., MD, NJ, PA
LCD	MolDX: Molecular Diagnostic Tests (MDT)	L35025	JJ - Palmetto GBA (Part A/B MAC)	AL, GA, TN

LCA	Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) MolDX: Repeat Germline Testing Billing and Coding: MolDX: Repeat Germline Testing	A56853 L38274 A58017	JM - Palmetto GBA (Part A/B MAC)	NC, SC, VA, WV
LCD LCA	Molecular Pathology Procedures Billing and Coding: Molecular Pathology and Genetic Testing	L34519 A58918	JN - First Coast Service Options, Inc. (Part A/B MAC)	FL, PR, U.S. 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.

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.

Somatic (tumor) testing differs from germline genetic testing. Genetic alterations in tumor tissue occur after birth and throughout the lifetime. As mentioned above, germline testing may be performed on essentially any sample; somatic analysis requires the applicable tumor tissue. Repeat somatic testing may be necessary when certain clinical situations arise.

Sometimes when tumor tissue is analyzed, a germline variant may be discovered. When this occurs the results should be validated with germline analysis, known as confirmatory testing. Laboratories may offer paired testing (somatic and germline analysis performed concurrently).

Genetic testing may be used for a variety of purposes including, diagnostic to identify or rule out a suspected genetic condition in an individual who exhibits signs and symptoms of the disorder and pharmacogenomics testing which analyzes an individual's unique genetic makeup to help determine response to a specific medication.

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.

Exome sequencing, also referred to as whole exome sequencing (WES), is an alternative to whole genome sequencing (WGS). It is a laboratory test used to determine the sequence of the protein coding regions of the genome. The exome is the part of the genome that encodes protein, where roughly 85% of variants are known to contribute to diseases in humans. Exome sequencing has been proposed as a diagnostic method to identify these genetic variants in an individual not diagnosed by traditional diagnostic and genetic testing approaches.

Coverage Determination

iCare follows the CMS requirements that only allows 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.

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, iCare will utilize the 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 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 (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 the MolDX Program or 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; **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 Medicare beneficiary; **AND**

- A multigene panel is defined as a test that analyzes more than one gene simultaneously. A panel will be considered medically reasonable and necessary if more than one gene impacts the clinical management of the individual being tested. The panel must evaluate genes and/or alleles in accordance with the panel's indicated use.

Exome Sequencing

Exome sequencing will be considered medically reasonable and necessary when the following requirements are met:[54]

- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; **AND**

- 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 the MolDX Program or 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; **AND**

- Results of the genetic testing must directly impact treatment or management of the Medicare beneficiary

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.

Repeat Germline Genetic Testing

Repeat germline genetic testing will be considered medically reasonable and necessary when the following requirements are met:[18]

- Individual to be tested is affected with a condition known to be relevant to germline testing and a pathogenic or likely pathogenic KFV identified has been identified in a separate first- second-or third-degree relative not involved in the initial analysis and has not received prior genetic testing for the condition that would have found the KFV; **OR**

- 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)

Repeat Somatic Genetic Testing

Repeat somatic genetic testing will be considered medically reasonable and necessary when the following requirements are met:

- Examination of a new sample of the primary tumor; **AND**

- Individual diagnosed with recurrence, relapse, is nonresponsive to treatment or experiences progression of disease while off treatment

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 tests may not be considered a benefit (statutory exclusion):

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law;[106] **OR**
- Tests performed to determine carrier screening;[41] **OR**
- Prenatal diagnostic testing;[41] **OR**
- Tests that confirm a diagnosis or known information;[106] **OR**
- Tests to determine risk for developing a disease or condition;[106] **OR**
- Tests performed to measure the quality of a process;[106] **OR**
- Tests without diagnosis specific indications;[106] **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[106]

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.

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
- Deletion/duplication information is obtained as part of the sequencing procedure but submitted as an independent analysis
- Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program
- Individual to be tested has an affected first-, second- or third-degree relative with an uninformative (negative or variant of unknown significance [VUS]) genetic test result for the associated condition
- KFV detection analysis if the individual to be tested previously received KFV testing, single gene analysis or multigene panel testing that would have detected the KFV
- Repeat somatic genetic testing of the same tissue sample as the original somatic genetic test
- Role of the gene to be analyzed has no known disease relationship

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.

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)	
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)	
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)	
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)	
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	
0036U	Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses	
0094U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis	
0211U	Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association	
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)	
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	
0297U	Oncology (pan tumor), whole genome sequencing of paired malignant and normal DNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and variant identification	
0298U	Oncology (pan tumor), whole transcriptome sequencing of paired malignant and normal RNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and expression level and chimeric transcript identification	
0299U	Oncology (pan tumor), whole genome optical genome mapping of paired malignant and normal DNA specimens, fresh frozen tissue, blood, or bone marrow, comparative structural variant identification	
0300U	Oncology (pan tumor), whole genome sequencing and optical genome mapping of paired malignant and normal DNA specimens, fresh tissue, blood, or bone marrow, comparative sequence analyses and variant identification	
0306U	Oncology (minimal residual disease [MRD]), next-generation targeted sequencing analysis, cell-free DNA, initial (baseline) assessment to determine a patient specific panel for future comparisons to evaluate for MRD	
0307U	Oncology (minimal residual disease [MRD]), next-generation targeted sequencing analysis of a patient-specific panel, cell-free DNA, subsequent assessment with comparison to previously analyzed patient specimens to evaluate for MRD	
0331U	Oncology (hematolymphoid neoplasia), optical genome mapping for copy number alterations and gene rearrangements utilizing DNA from blood or bone marrow, report of clinically significant alterations	
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)	
0355U	APOL1 (apolipoprotein L1) (eg, chronic kidney disease), risk variants (G1, G2)	
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	
0413U	Oncology (hematolymphoid neoplasm), optical genome mapping for copy number alterations, aneuploidy, and balanced/complex structural rearrangements, DNA from blood or bone marrow, report of clinically significant alterations	
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	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

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2. American Academy of Neurology (AAN). Special Article. Evidence-based guideline summary: diagnosis and treatment of limb-girdle and distal dystrophies. https://www.aan.com. Published October 13, 2014. Accessed February 15, 2023.

3. American Academy of Neurology (AAN). Special Article. Evidence-based guideline summary: evaluation, diagnosis and management of congenital muscular dystrophy. https://www.aan.com. Published March 30, 2015. Accessed February 15, 2023.

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5. American Academy of Ophthalmology (AAO). Recommendations for genetic testing of inherited eye diseases – 2014. https://www.aao.org. Published February 2014. Accessed February 14, 2023.

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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.