Medical Necessity Guideline Title: Genetic and Molecular Testing		
MNG #: 002	**☒SCO ☒One Care** **☒ MA Medicare Premier** **☒ MA Medicare Value** **☒ RI Medicare Preferred** **☒ RI Medicare Value** **☒ RI Medicare Maximum**	**Prior Authorization Needed?** **☒ Yes** **☐ Yes (only if specific threshold exceeded. See this MNG for specific limits)** **☐ No**
Clinical: ☒	**Operational: ☐**	**Informational: ☐**
Medicare Benefit: **☒ Medicare** **☒ Medicaid**	**Approval Date:** 1/10/2019; 11/9/23	**Effective Date:** 4/01/2019; 11/9/23
Last Revised Date: 1/25/2019; 02/04/2021; 6/2/2022; 11/3/2022; 11/9/23	**Next Annual Review Date:** 1/10/2020; 02/04/2022; 6/2/2023; 11/3/2024	**Retire Date:**

OVERVIEW:

Genetic testing refers to any type of testing that helps to determine the *genotype* of an individual in *germline* or selected *somatic* cells. These tests analyze human chromosomes, deoxyribonucleic acid, ribonucleic acid, *genes*, and other gene products to detect inheritable and/or acquired alterations that cause or are likely to cause a particular disorder or condition. Molecular diagnostic testing is a type of genetic test that examines the changes in one or more genes to determine the order of nucleotides in an individual's genetic code. Molecular tests use DNA sequencing to detect abnormalities in the gene sequence, to test for histocompatibility antigens, to determine prognosis and/or to predict response totreatment. One particular molecular test, *next generation sequencing (NGS)*, uses parallel sequencing assays to analyze the bulk of an individual's DNA to detect *variants* in a broad range of rare and complex disorders. It is often used when single gene or panel testing has not provided a diagnosis or when the suspected condition or genetic cause is unclear.

Genetic testing has demonstrated efficacy in predicting outcomes and to be a helpful clinical decision-making tool. It may be used for predictive and pre-symptomatic testing for adult-onset and complex disorders, diagnostic and carrier screening for inherited disorders, and pharmacogenetic testing to guide drug dosage, selection, and response. The likelihood of development of disease depends on the presence of specific genetic variants, *inheritance pattern*, *penetrance*, *expressivity*, the individual's age, and other contributory genetic and environmental factors. The different methods to identify specific variants include *Sanger sequencing*, *Microarray technologies*, and NGS. Choosing the appropriate test to perform depends on the indication or presenting features, tests available for the suspected condition(s), and the available information regarding the genetic causes of the condition or presenting condition(s).

Commonwealth Care Alliance (CCA) follows applicable Medicare and Medicaid regulations for genetic testing requests, and InterQual Smart Sheets may be used when available. In addition, CCA may use an internally developed Medical Necessity Guideline (MNG) for specific genetic tests where multiple Medicare and/or Medicaid regulations apply.

DEFINITIONS:

Expressivity: The clinical differences in the way a disease is expressed.

Gene: Refers to a gene, region of a gene, and/or variants) of a gene that can be assayed serially or in parallel.

Genetic test: Test that involves an analysis of human chromosomes, deoxynucleic acid, ribonucleic acid, genes, and gene products (e.g., enzymes, proteins, metabolites) used to detect heritable or somatic variants that are related to disease.

Genotype: Refers to the DNA blueprint and is associated with the clinical manifestations of a trait or disease.

Germline: Refers to the sex cells (eggs and sperm) that reproducing organisms use to pass on their genomes from one generation to the next.

High-risk group: Refers to an individual with a personal or family history of autosomal dominant, autosomal recessive, x-linked recessive, x-linked dominant or a family history of chromosomal abnormality (e.g., chromosomal translocation or inversion).

Inheritance pattern: Describe how genetic variants are distributed in families. Certain cancer syndromes or metabolic disorders may be autosomal or sex-linked, and recessive or dominant.

Microarray technologies: Genetic testing method that uses an allele-specific oligonucleotide hybridization approach to code for target reference sequence or alternate, disease-associated variant. The purpose of the test is to identify DNA changes at the level of a single nucleotide, larger portions of one or more genes, or larger regions of one or more chromosomes.

Molecular test: A type of genetic test that looks for changes in one or more genes. These tests determine the order of nucleotides (DNA building blocks) in an individual's genetic code by DNA sequencing to detect variants in genes and to test for histocompatibility antigens.

Next generation sequencing (NGS): Genetic testing method that uses rapid, high-throughput parallel sequencing of multiple small fragments of DNA to determine sequence.

Penetrance: Refers to the likelihood that an individual with a disease genotype will actually manifest one or me of the clinical features associated with the disease.

Sanger sequencing: Genetic testing method that is used to determine the nucleotides present in a fragment of DNA. It is considered the gold standard in clinical genetic testing for the detection of point mutations and small variants.

Somatic cells: Somatic cells are diploid and contain two sets of chromosomes, one set inherited from each parent. Somatic mutations can impact the individual carrying the mutation but cannot be passed on and have no effect on the offspring.

Variant: A variation from a reference sequence for clinical testing. Variants are classified into one of five categories: pathogenic, likely pathogenic, variant of uncertain significance, likely benign, or benign.

DECISION GUIDELINES:

Clinical Coverage Criteria:

Commonwealth Care Alliance (CCA) follows applicable Medicare and Medicaid regulations and uses InterQual Smart Sheets, when available, to review prior authorization requests for medical necessity. This Medical Necessity Guideline (MNG) applies to all CCA Products unless a more expansive and applicable CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), or state-specific medical necessity guideline exists.

Clinical Eligibility:

1. CCA may cover the specific Genetic Test if the member and the testing method meets **ALL** of the following criteria:
   a. The member belongs to a *high-risk* group for a particular disease(s) based on either:
      i. Personal history, family history, documentation of a genetic variant, and/or ethnic background; *or*
      ii. The member displays clinical features of the specific variant in question; *and*
   b. Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or do not result in a definitive diagnosis of the suspected disorder; *and*
   c. The test is considered a scientifically proven method for the identification of the specific genetically linked inheritable disease or is a clinically valid test based on published peer reviewed medical literature; *and*
   d. Testing assay(s) are Food and Drug Administration (FDA) approved or cleared for the use in the member's condition; *and*
   e. The test is ordered and furnished by a qualified clinician with expertise in the treatment of the targeted disease OR from a provider with genetic counseling expertise; *and*
   f. The results of the genetic test will directly alter the treatment and/or medical management of the member's diagnosed condition and/or the member's current pregnancy.
2. CCA may cover Next Generation Sequencing (NGS) for somatic (acquired) or germline (inherited) cancer, if the member and the test meets the criteria outlined in *CMS Medicare National Coverage Determinations, Publication 100-03, Chapter 1, Part 2, Section 90.2*.

LIMITATIONS/EXCLUSIONS:

1. CCA will limit diagnostic genetic testing for a disease to one test per lifetime. Repeat testing will require review from a CCA Medical Director to assess for medically necessity. A duplicate genetic test for an inherited condition may be covered if there is uncertainty about the validity of the existing test result or if repeat testing of somatically acquired variants may be required to inform appropriate therapeutic decision-making.
2. For Testing panels, including but not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, testing would be covered ONLY for the number of genes or test that are reasonable and necessary to obtain necessary information for therapeutic decision-making.
3. Medically necessary interpretation and report of the genetic and molecular diagnostic test must be written by a qualified clinician or pathologist eligible to report this service. The report is above and beyond the report of standard laboratory results and may not be reported by non-medical practitioners (e.g., PhD, scientists, etc.).
4. CCA will not cover and does not consider genetic tests that meet **ANY** of the following criteria as medically necessary:
   a. Testing for the purpose of confirming a suspected diagnosis that can be diagnosed by an alternative laboratory or clinical test.

b. Testing for the purpose of informing care of a member's family member.
c. Testing that is performed by an out-of-network laboratory when it can be performed by an in-network laboratory.
d. Tests that are scientifically unproven and where clinical validity and utility has not been definitively determined due to the paucity of data.
e. Tests that have not been approved or cleared by the FDA.
f. Tests that are unlikely to impact the treatment, outcome, and/or clinical management in the care of the member.
g. Home testing, self-referral testing, and/or direct-to-consumer genetic tests.

AUTHORIZATION:

The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not signify that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. This Medical Necessity Guideline is subject to all applicable Plan Policies and Guidelines, including requirements for prior authorization and other requirements in Provider's agreement with the Plan (including complying with Plan's Provider Manual specifications).

Table 1 – Covered Codes

Coverage of genetic tests will require documentation that supports medical necessity. Certain CPT codes may only be covered for specific ICD-10-CM diagnosis or specific genes. Not all procedure codes have related diagnosis codes or genes listed. Not all procedure codes are covered for both SCO/One Care and Medicare Advantage members.

CPT Code	Description	Applicable ICD-10-CM Codes that support Medical Necessity	Coverage	
			SCO/One Care	Medicare Advantage
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (e.g., glioma), common variants (e.g., R132H, R132C)	C71.0-C71.9, C88.8, C92.00, C92.02, C92.20, C92.22, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.00, C93.02, C93.10, C93.12, C93.Z0, C93.Z2, C93.90, C93.92, C94.00, C94.02, C94.40, C94.41, C94.42, C94.80, C94.82, C95.00, C95.02, C95.10, C95.12, C95.90, C96.Z, D45, D47.1, D47.3, D47.4, D47.Z9, D47.9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.81, D75.89, D75.9, D77, R16.1, R16.2	Yes	Yes
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], soluble) (e.g., glioma), common variants (e.g., R140W, R172M)			
81168	CCND1/IGH (t(11;14)) (e.g., mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed	C85.10-C85.99	Yes	Yes
81170	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (e.g., acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain	C91.00-C91.02, C92.10-C92.12, C92.20-C92.22	Yes	Yes

	Genetic and Molecular Testing			
81175	ASXL 1 (additional sex combs like 1, transcriptional regulator) (e.g., myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence	C88.8, C92.00, C92.02, C92.20, C92.22, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.00, C93.02, C93.10, C93.12, C93.Z0, C93.Z2, C93.90, C93.92, C94.00, C94.02, C94.40, C94.41, C94.42, C94.6, C94.80, C94.82, C95.00, C95.02, C95.10, C95.12, C95.90, C95.92, C96.Z, C96.9, D45, D46.0, D46.1, D46.20, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9, D47.1, D47.3, D47.4, D47.Z9, D61.818, D69.49, D69.6, D69.8, D69.9, D70.8, D70.9, D72.810, D72.818, D72.819, D72.821, D72.828, D72.829, D72.89, D72.9, D75.81, D75.89, D75.9, D77, R16.1, D16.2	Yes	Yes
81176	ASXL 1 (additional sex combs like 1, transcriptional regulator) (e.g., myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (e.g., exon 12)			
81206	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; major breakpoint,	C91.00-C91.02, C92.10-C92.12,	Yes	Yes

	qualitative or quantitative	C91.20-C92.22, C92.90-92.92, D47.3, D72.829		
81207	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative			
81208	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; major breakpoint, other breakpoint, qualitative or quantitative			
81209	BLM (Bloom syndrome, RecQ helicase-like) (e.g., Bloom syndrome) gene analysis, 2281del6ins7 variant	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81210	BRAF (V-RAF Murine Sarcoma Viral Oncogene Homolog B1) (e.g., colon cancer, gene analysis, V600E variant)	C17.0-C17.9, C18.0-C19.0, C20, C21.1, C21.2, C21.8, C33-C34.92, C43.0-C43.9, C78.4, C78.5, C91.40-C91.42, D03.0-D03.9, Z85.038, Z85.048, Z85.820	Yes	Yes
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (e.g., acute myeloid leukemia), gene analysis, full gene sequence	C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.00, C93.02, C94.00, C94.02, C94.80, C94.82, C95.0, C95.02, C95.90, C95.92, R16.1, R16.2	Yes	Yes
81219	CALR (calreticulin) (e.g., myeloproliferative disorders), gene analysis, common variants in exon 9	C88.8, C92.20, C92.22, C93.10, C93.12, C93.Z0,	Yes	Yes

		String, C93.92, C94.40, C94.41, C94.42, C94.6, C95.10, C95.12, C96.Z, D45, D47.1, D47.3, D47.4, D47.Z9, D47.9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.1, D75.81, D75.89, D75.9, D77, R16.1, R16.2		
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; common variants (e.g., ACMG/ACOG guidelines)	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; known familial variants			
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; duplication/deletion variants			
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; full gene sequence			
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; intron 8 poly-T analysis (e.g., male infertility)			
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)	I20.0, I20.1, I20.8, I20.9, I21.11, I21.19, I21.29, I21.3, I21.4, I24.0, I24.1, I24.8, I24.9, I25.110, I25.118, I25.119, I25.700, I25.701, I25.708, I25.710, I25.711, I25.718, I25.719-I25.721, I25.728-I25.731, I25.738, I25.739, I25.750,	Yes	Yes

		I25.751, I25.758-I25.761, I25.769, I25.790, I25.791, I25.798, I25.799		
81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)	E75.22, G10	Yes	Yes
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *5, *6)	G35	Yes	Yes
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants [e.g., bacterial artificial chromosome (BAC) or oligo-based comparative genomic hybridization (CGH) microarray analysis]	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	No
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities			
81235	EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis, common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)	C33.0-C34.92	Yes	No
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (e.g., myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (e.g., diffuse large Bcell lymphoma) gene analysis, common variant(s) (e.g., codon 646)			
81245	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (i.e., exons 14, 15)	C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.0, C93.02, C94.0, C94.02, C94.80, C94.82, C95.0,	Yes	Yes
81246	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (e.g., D835, I836)			

		C91.10, C95.90, C95.92, R16.1, R16.2		
81256	HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g., C282Y, H63D)	E83.10, E83.110, E83.118, E83.119, E83.19	Yes	Yes
81261	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (e.g., polymerase chain reaction)	C82.00-C83.99, C85.10-C85.99, C91.00-C91.02, D72.828, D72.89	Yes	Yes
81262	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (e.g., Southern blot)			
81263	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemia and lymphoma, B-cell), variable region somatic mutation analysis			
81264	IGK@ (Immunoglobulin kappa light chain locus) (e.g., leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)			
81265	Comparative analysis using short tandem repeat (STR) markers; Patient and comparative specimen (e.g., pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline (e.g., buccal swab or other germline tissue sample) and donor testing, twin zygosity testing, or maternal cell contamination of fetal cells)	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81266	Comparative analysis using short tandem repeat (STR) markers; each additional specimen (e.g., 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)			
81267	Chimerism (engraftment) analysis, post transplantation specimen (e.g., hematopoietic stem cell), includes comparison to previously performed baseline analyses; without cell selection			
81268	Chimerism (engraftment) analysis, post transplantation specimen (e.g., hematopoietic stem cell), includes comparison to previously performed baseline analyses; with cell selection (e.g., CD3, CD33), each cell type			

81270	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder), gene analysis, p.Val617Phe (V617F) variant	C81.20, C81.22, C93.10, C93.12, C93.Z0, C93.90, C93.92, C94.40, C94.41, C94.42, C94.6, C95.10, C95.12, C96.Z, D45, D47.1, D47.3, D47.4, D47.Z9, D47.9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.1, D75.81, D75.89, D75.9, D77, R16.1, R16.2	Yes	Yes
81272	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (e.g., exons 8, 11, 13, 17, 18)	C43.0-C43.9, C49.A0-C49.A9, C92.00, C92.02, C92.30, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.0, C93.02, C94.0, C94.02, C94.80, C94.82, C95.0, C95.02, C95.90, C95.92, C96.20, C96.21, C96.22, C96.29, D03.0-D03.9, D47.01, D47.02, D48.1, R16.1, R16.2, Z85.820	Yes	Yes
81273	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., mastocytosis), gene analysis, D816 variant(s)	D47.01, D47.02	Yes	Yes
81275	KRAS(V-KI-RAS2 Kirsten Rat Sarcoma viral oncogene)	C17.0-C17.9,	Yes	Yes

	gene analysis, variants in codons 12 and 13	C18.0-C19.0, C20.0, C21.1, C21.2, C21.8, C33.0-C34.92, Z85.038, Z85.048		
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)			
81279	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)	C88.8, C92.20, C92.22, C93.10, C93.12, C93.Z0, C93.90, C93.92, C94.40, C94.41, C94.42, C94.6, C95.10, C95.12, C96.Z, D45, D47.1, D47.3, D47.4, D47.Z9, D47.9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.1, D75.81, D75.89, D75.9, D77, R16.1, R16.2	Yes	Yes
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (e.g., glioblastoma multiforme), promoter methylation analysis	C71.0-C71.9	Yes	Yes
81301	Microsatellite instability analysis of markers for mismatch repair deficiency, includes comparison of neoplastic and normal tissue	C17.0-C17.9, C18.0-C19.0, C20.0, C21.1, C21.2, C21.8, C33.0-C34.92, Z85.038, Z85.048	Yes	Yes
81305	MYD88 (myeloid differentiation primary response 88) (e.g., Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant	C83.00-C83.09, C85.80-C85.89, C88.0	Yes	Yes
81307	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene analysis; full gene sequence	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81308	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene analysis; known familial variant			

81309	PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (e.g., colorectal and breast cancer) gene analysis, targeted sequence analysis (e.g., exons 7, 9, 20)	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81310	NPM1 (nucleophosmin) (e.g., acute myeloid leukemia) gene analysis, exon 12 variants	C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.00, C93.02, C94.00, C94.02, C94.80, C94.82, C95.00, C95.02, C95.90, C95.92, R16.1, R16.2	Yes	Yes
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)	C17.0-C17.9, C18.0-C19.0, C20, C21.1, C21.2, C21.8, Z85.038, Z85.048	Yes	Yes
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (e.g., prostate cancer)	R97.20	Yes	Yes
81314	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (e.g., gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (e.g., exons 12, 18)	C49.A0-C49.A9, C92.10-C92.12, C93.10-C93.12, D48.1	Yes	Yes
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; common breakpoints (e.g., intron 3 and intron 6), qualitative or quantitative	C92.40-C92.42	Yes	Yes
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; single			

	breakpoint (e.g., intron 3, intron 6), qualitative or quantitative			
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, Member 1) (e.g., alpha-1-antitrypsin deficiency), gene analysis, common variants (e.g., *S and *Z)	E88.01	Yes	Yes
81334	RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (e.g., exons 3-8)	C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C92.90, C92.92, C93.00, C93.02, C93.10, C93.12, C93.Z0, C93.Z2, C93.90, C93.92, C94.00, C94.02, C94.6, C94.80, C94.82, C95.00, C95.02, C95.10, C95.12, C95.90, C95.92, C96.Z, C96.9, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.Z, D46.9, D61.818, D69.49, D69.6, D69.8, D69.9, D70.8, D70.9, D72.810, D72.818, D72.819, D75.89, D75.9, D77, R16.1, R16.2	Yes	Yes
81335	TPMT (thiopurine S-methyltransferase) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3)	C91.00-C91.02, C91.12, C91.30, C91.40, C91.50, C91.60, C91.A0,	Yes	Yes

		C91.70, K50.00, Z94.84		
81338	MPL (MPL proto-oncogene, thrombopoietin receptor) (e.g., myeloproliferative disorder) gene analysis; common variants (e.g., W515A, W515K, W515L, W515R)	C88.8, C92.20, C92.22, C93.10, C93.12, C93.Z0, C93.90, C93.92, C94.40, C94.41, C94.42, C94.6, C95.10, C95.12, C96.Z, D45, D47.1, D47.3, D47.4, D47.Z9, D47.9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.1, D75.81, D75.89, D75.9, D77, R16.1, R16.2	Yes	Yes
81339	MPL (MPL proto-oncogene, thrombopoietin receptor) (e.g., myeloproliferative disorder) gene analysis; sequence analysis, exon 10			
81340	TRB@ (T cell antigen receptor, beta) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (e.g., polymerase chain reaction)	C91.00-C91.02, C95.90-C95.92, C96.20, C96.21, C96.22, C96.29, D47.01, D47.02, D47.09, D60.0, D60.1, D60.8, D61.01, D61.09, D61.1, D61.2, D61.3, D61.89, D61.9	Yes	Yes
81341	TRB@ (T cell antigen receptor, beta) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using direct probe methodology (e.g., Southern blot)			
81342	TRG@ (T cell antigen receptor, gamma) (e.g., leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)			
81345	TERT (telomerase reverse transcriptase) (e.g., thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (e.g., promoter region)	C71.0-C71.9	Yes	Yes
81347	SF3B1 (splicing factor [3b] subunit B1) (e.g., myelodysplastic syndrome/acute myeloid leukemia) gene analysis, common variants (e.g., A672T, E622D, L833F, R625C, R625L)	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81348	SRSF2 (serine and arginine-rich splicing factor 2) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (e.g., P95H, P95L)			
81351	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; full gene sequence	C88.8, C92.0, C92.02, C92.20, C92.22, C92.30,	Yes	Yes
81352	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome)			

	gene analysis; targeted sequence analysis (e.g., oncology)	C91.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z2, C92.90, C92.92, C93.00, C93.02, C93.10, C93.12, C93.Z0, C93.Z2, C93.90, C93.92, C94.00, C94.41, C94.42, C94.6, C94.80, C94.82, C95.00, C95.02, C95.10, C95.12, C95.90, C95.92, C96.Z, C96.9, D45, D46.0, D46.1, D46.2, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9, D47.1, D47.3, D47.4, D47.Z9, D47.9, D61.818, D69.49, D69.6, D69.8, D69.9, D70.8, D70.9, D72.810, D72.818, D72.819, D72.821, D72.828, D72.829, D72.89, D72.9, D75.81, D75.89, D75.9, D77, R16.1, R16.2		
81370	HLA Class I and II typing, low resolution (e.g., antigen equivalents): HLA-A, -B, -C, -DRB 1/3/4/5, and –DQB1	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81371	HLA Class I and II typing, low resolution (e.g., antigen equivalents): HLA-A, -B, and – DRB1 (e.g., verification typing)			
81372	HLA Class I typing, low resolution (e.g., antigen equivalents); complete (i.e., HLA-A, -B, and-C)			
81373	HLA Class I typing, low resolution (e.g., antigen			

	equivalents); one locus (e.g., HLA-A, -B, or -C, each)			
81374	HLA Class I typing, low resolution (e.g., antigen equivalents); one antigen equivalent (e.g., B*27), each			
81375	HLA Class II typing, low resolution (e.g., antigen equivalents); HLA-DRB1/3/4/5 and – DQB1			
81376	HLA Class II typing, low resolution (e.g., antigen equivalents); one locus (e.g., HLADRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or –DPA1), each			
81377	HLA Class II typing, low resolution (e.g., antigen equivalents); one antigen equivalent, each			
81378	HLA Class I and II typing, high resolution (i.e., alleles or allele groups), HLA-A, -B, -C, and -DRB1			
81379	HLA Class I typing, high resolution (i.e., alleles or allele groups); complete (i.e., HLA-A, - B, and -C)			
81380	HLA Class I typing, high resolution (i.e., alleles or allele groups); 1 locus (e.g., HLA-A, - B, or -C), each			
81381	HLA Class I typing, high resolution (i.e., alleles or allele groups); 1 allele or allele group (e.g., B*57:01P), each			
81382	HLA Class II typing, high resolution (i.e., alleles or allele groups); one locus (e.g., HLADRB1, - DRB3, 4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each			
81383	HLA Class II typing, high resolution (i.e., alleles or allele groups); 1 allele or allele group (e.g., HLA-DQB1*06:02P), each			
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53		Yes	Yes
81518	Oncology (breast), mRNA, gene expression profiling by real-time RTPCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy	C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412,	Yes	Yes
81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score (Oncotype DX®, Genomic Health)			

		C50.419, , C50.421, , C50.422, , C50.429, C50.511, C50.512, , C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, D05.01, D05.02, D05.10, D05.11, D05.12, D05.80, D05.81, D05.82, D05.90, D05.91, D05.92, Z17.0		
81520	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score (Prosigna® Breast Cancer Assay, NanoString Technologies, Inc.)	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81522	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score (Prosigna® Breast Cancer Assay, NanoString Technologies, Inc.)	C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321,	Yes	Yes
81523	Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis			

		C50.322, C50329, C50.411, C50.412, , C50.419, , C50.421, , C50.422, , C50.429, C50.511, C50.512, , C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, D05.01, D05.02, D05.10, D05.11, D05.12, D05.80, D05.81, D05.82, D05.90, D05.91, D05.92, Z17.0		
81552	Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis	Please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	Yes
81595	Cardiology (heart transplant), mRNA, gene expression profiling by real-time quantitative PCR of 20 genes (11 content and 9 housekeeping), utilizing subfraction of peripheral blood, algorithm reported as a rejection risk score	Z48.21, Z94.1	Yes	Yes
0027U	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15 (JAK2 Exons 12 to 15 Sequencing, Mayo Clinic)	C88.8, C92.20, C92.22, C93.10, C93.12, C93.Z0, C93.90, C93.92, C94.40, C94.41,	Yes	Yes

		C94.42, C94.6, C95.10, C95.12, C96.Z, D45, D47.1, D47.3, D47.4, D47.Z9, D47.9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.1, D75.81, D75.89, D75.9, D77, R16.1, R16.2		
0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, common and select rare variants (ie, *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN) (CYP2D6 Common Variants and Copy Number, Mayo Clinic, Laboratory Developed Test)	E75.22, G10	Yes	Yes
81107	Human platelet antigen 3 genotyping (HPA-2), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (I843S)	For individual consideration, please refer to the appropriate Federal, State, InterQual, or CCA guidance for the indications that support medical necessity.	Yes	No
81108	Human platelet antigen 4 genotyping (HPA-1), ITGB3 (Integrin, Beta 3 [Platelet glycoprotein IIA], Antigen CD61 [GPIIIA]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], Post-transfusion purpura), Gene analysis, common variant, HPA-4A/B (R143Q)		Yes	No
81109	Human platelet antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (e.g., HPA-5a/b (K505E))		Yes	No
81110	Human platelet antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa] (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6a/b (R489Q)		Yes	No
81111	Human platelet antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa] (e.g., neonatal alloimmune		Yes	No

	thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (T144M)			
81112	Human platelet antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb] (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (S682Y)		Yes	No
81161	DMD (dystrophin) (e.g., duchenne/becker muscular dystrophy) deletion analysis, and duplication analysis, if performed		Yes	No
81177	ATN1 (atrophin 1) (e.g., dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81178	ATXN1 (ataxin 1) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81179	ATXN2 (ataxin 2) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81180	ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles		Yes	Yes
81181	ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81182	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81183	ATXN10 (ataxin 10) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81184	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (e.g., spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81185	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (e.g., spinocerebellar ataxia) gene analysis; full gene sequence		Yes	Yes
81186	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (e.g., spinocerebellar ataxia) gene analysis; known familial variant		Yes	Yes
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (e.g., myotonic dystrophy type 2) gene analysis,		Yes	Yes

	evaluation to detect abnormal (e.g., expanded) alleles			
81188	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81189	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence		Yes	Yes
81190	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)		Yes	Yes
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (e.g., solid tumors) translocation analysis		Yes	Yes
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (e.g., solid tumors) translocation analysis		Yes	Yes
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (e.g., solid tumors) translocation analysis		Yes	Yes
81194	NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (e.g., solid tumors) translocation analysis		Yes	Yes
81200	ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)		Yes	No
81201	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated [FAP] gene analysis; full gene sequence		Yes	No
81202	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated [FAP] gene analysis; known familial variants		Yes	No
81203	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated [FAP] gene analysis; duplication/deletion variants		Yes	No
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (e.g., Maple syrup urine disease) gene analysis, common variants (e.g., R183P, G278S, E422X)		Yes	No
81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis		Yes	No
81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization [CGH] microarray analysis		Yes	No
81233	BTK (Bruton's tyrosine kinase) (e.g., chronic lymphocytic leukemia) gene analysis, common variants (e.g., C481S, C481R, C481F)		Yes	Yes

81238	F9 (coagulation factor IX) (e.g., hemophilia B), full gene sequence		Yes	No
81240	F2 (prothrombin, coagulation factor II) (e.g., hereditary hypercoagulability) gene analysis, 20210G>A variant		Yes	No
81241	F5 (coagulation factor V) (e.g., hereditary hypercoagulability) gene analysis; Leiden variant		Yes	No
81242	FANCC (Fanconi anemia, complementation group C) (egg, Fanconi anemia, type C) gene analysis, common variant (e.g., IVS4+4A>T)		Yes	No
81243	FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles		Yes	No
81244	FMR1 (fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; characterization of alleles (e.g., expanded size and methylation status)		Yes	No
81248	G6PD (glucose-6-phosphate dehydrogenase) (e.g., hemolytic anemia, jaundice), gene analysis; known familial variant(s)		Yes	No
81249	G6PD (glucose-6-phosphate dehydrogenase) (e.g., hemolytic anemia, jaundice), gene analysis; full gene sequence		Yes	No
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (e.g., Glycogen storage disease, Type 1a, von Gierke disease) gene analysis, common variants (e.g., R83C, Q347X)		Yes	No
81251	GBA (glucosidase, beta, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2+1G>A)		Yes	No
81252	GJB2 (gap junction protein, beta 2, 26kDa; connexin 26) (e.g., nonsyndromic hearing loss) gene analysis; full gene sequence		Yes	No
81253	GJB2 (gap junction protein, beta 2, 26kDa; connexin 26) (e.g., nonsyndromic hearing loss) gene analysis; known familial variants		Yes	No
81254	GJB6 (gap junction protein, beta 6, 30 kda, connexin 30) (e.g., nonsyndromic hearing loss) gene analysis, common variants (e.g., 309kb [DEL(GJB6-D13S1830)] and 232KB [DEL(GJB6-D13S1854)])		Yes	No
81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278insTATC, 1421+1G>C, G269S)		Yes	No
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2 (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or		Yes	No

	variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring)	**d Molecular Te sting Medical Necessity Guide line**		
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant		Yes	No
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (e.g., familial dysautonomia) gene analysis, common variants (e.g., 2507+6T>C, R696P)		Yes	No
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants		Yes	No
81277	Cytogenomic neoplasia (genome-wide) microarray analysis, interrogation of genomic regions for copy number and loss-of-heterozygosity variants for chromosomal abnormalities		Yes	Yes
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis		Yes	Yes
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis		Yes	Yes
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants		Yes	Yes
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants		Yes	Yes
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis		Yes	Yes
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants		Yes	Yes
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary nonpolyposis colorectal cancer,		Yes	Yes

	Lynch syndrome) gene analysis; duplication/deletion variants			
81298	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis		Yes	Yes
81299	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants		Yes	Yes
81300	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants		Yes	Yes
81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis		Yes	No
81303	MECP2 (methyl CPG binding protein 2) (e.g., rett syndrome) gene analysis; known familial variant		Yes	No
81304	MECP2 (methyl CPG binding protein 2) (e.g., rett syndrome) gene analysis; duplication/deletion variants		Yes	No
81306	NUDT15 (nudix hydrolase 15) (e.g., drug metabolism) gene analysis, common variant(s) (e.g., *2, *3, *4, *5, *6)		Yes	Yes
81312	PABPN1 (poly[A] binding protein nuclear 1) (e.g., oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis		Yes	Yes
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants		Yes	Yes
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants		Yes	Yes
81320	PLCG2 (phospholipase C gamma 2) (e.g., chronic lymphocytic leukemia) gene analysis, common variants (e.g., R665W, S707F, L845F)		Yes	Yes
81321	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis		Yes	Yes
81322	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene		Yes	Yes

	analysis; known familial variant			
81323	PTEN (phosphatase and tensin homolog) (PTEN Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant		Yes	Yes
81324	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis		Yes	No
81325	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis		Yes	No
81326	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant		Yes	No
81329	SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy) gene analysis; dosage/deletion analysis (e.g., carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed		Yes	No
81330	SMPD1 (sphingomyelin phosphodiesterase 1, acid lysosomal) (e.g., Niemann-Pick disease, Type A) gene analysis, common variants (e.g., R496L, L302P, fsP330)		Yes	No
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis		Yes	No
81333	TGFBI (transforming growth factor beta-induced) (e.g., corneal dystrophy) gene analysis, common variants (e.g., R124H, R124C, R124L, R555W, R555Q)		Yes	Yes
81343	PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81344	TBP (TATA box binding protein) (e.g., spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (e.g., expanded) alleles		Yes	Yes
81352	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (e.g., 4 oncology)		Yes	Yes
81353	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; known familial variant		Yes	Yes
81357	U2AF1 (U2 small nuclear RNA auxiliary factor 1) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (e.g., S34F, S34Y, Q157R, Q157P)		Yes	Yes

81360	ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/arginine-rich 2) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (e.g., E65fs, E122fs, R448fs)		Yes	Yes
81361	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (e.g., HbS, HbC, HbE)		Yes	No
81362	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)		Yes	No
81363	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)		Yes	No
81364	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence		Yes	No
81419	Epilepsy genomic sequence analysis panel, must include analyses for ALDH7A1, CACNA1A, CDKL5, CHD2, GABRG2, GRIN2A, KCNQ2, MECP2, PCDH19, POLG, PRRT2, SCN1A, SCN1B, SCN2A, SCN8A, SLC2A1, SLC9A6, STXBP1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2		Yes	Yes
81420	Fetal chromosomal aneuploidy (e.g., trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21		Yes	No
81507	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy		Yes	No
81529	Oncology (cutaneous melanoma), mRNA, gene expression profiling by real-time RT-PCR of 31 genes (28 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk, including likelihood of sentinel lymph node metastasis		Yes	Yes
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as metastasis risk score		Yes	Yes
81554	Pulmonary disease (idiopathic pulmonary fibrosis [IPF]), mRNA, gene expression analysis of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as categorical result (e.g., positive, or negative for high probability of usual interstitial pneumonia [UIP])		Yes	Yes

81599	Unlisted multianalyte assay with algorithmic analysis		Yes	Yes
CPT Code	**Description**	**Genes that may be covered if medical necessity is determined**	**Coverage**	
			SCO/One Care	**Medicare Advantage**
81400	Molecular pathology procedure, Level 1 (e.g., identification of single germline variant [e.g., SNP] by techniques such as restriction enzyme digestion or melt curve analysis)	ACE, F13B, F5, F7, FGB	Yes	Yes
		ABCC8, ACADM, AGTR1, CCR5, CLRN1, DYT1 (TOR1A), FGFR3, IL28B, IVD, TOR1A	No	No
81401	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)	CBFB-MYH11, E2A/PBX1, EML4-ALK, ETV6-RUNX1, EWSR1/ERG, EWSR1/FLI1, EWSR1/WT1, F11coagulation factor X1, FIP1L1-PDGFR, FOXO1/PAX3, FOXO1/PAX7, MUTYH (mutY homolog [E. coli]), NPM/ALK, PAX8/PPARG, RUNX1/RUNX1T1	Yes	Yes

		ADRB2, APOE, ATN1, CFH/ARMS2, DEK/NUP214, FGFR3, GALT (galactose-1-phosphate uridylyl transferase), H19, KCNQ10T1 (KCNQ1 overlapping transcript 1), MEG3/DLK1, MLL/AFF, MT-ATP6, MT-ND4, MT-ND6, MT-ND5 mitochondrially encoded tRNA leucine 1 [UUA/G] mitochondrially encoded NADH dehydrogenase 5), MT-RNR1 (mitochondrially encoded 12S RNA), MT-TK (mitochondrially encoded tRNA lysine), MT-TL1, MT-TS1, PRSS1 (protease, serine, 1 [trypsin 1])	No	No
81402	Molecular pathology procedure, Level 3 (e.g., > 10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [Typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])	CYP21A2, Chromosome 18q-, MEFV (Mediterranean fever) (e.g., familial Mediterranean fever), TRD 81402 Uniparental disomy (UPD)	No	No

81403	Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)	F8 (coagulation factor VIII), VHL (von Hippel-Lindau tumor suppressor)	Yes	Yes
		ANG (angiogenin, ribonuclease, RNase A family, 5), FGFR3 (fibroblast growth factor receptor 3) one exon, GJB1 (gap junction protein, beta 1) (e.g., Charcot-Marie-Tooth X-linked), full gene sequence, HRAS (v-Ha-ras Harvey rat sarcoma viral oncogene homolog Costello syndrome), MT-RNR1 (mitochondrially encoded 12S RNA), MT-TS1 (mitochondrially encoded tRNA serine 1)	No	No

81404	Molecular pathology procedure, Level 15 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)	CDKN2A (cyclin-dependent kinase inhibitor 2A), PRSS1 (protease, serine, 1 [trypsin 1]), MEN1 (multiple endocrine neoplasia 1) (e.g., multiple endocrine neoplasia type 1, Wemer syndrome), duplication/deletion, TP53 (tumor protein 53) (e.g., tumor samples), targeted sequence analysis of 2-5 exons, VHL (von Hippel-Lindau tumor suppressor)	Yes	Yes
		ACADS (acyl-CoA dehydrogenase), AQP2 (aquaporin 2 [collecting duct]), ARX (aristaless related homeobox), BTD (biotinidase), CAV3 (caveolin 3) (e.g., CAV3-related distal myopathy, limb-girdle muscular dystrophy type 1C), full gene sequence, CLRN1 (clarin 1), CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1), EGR2 (early	No	No

	Genetic and Molecular Te Medical Necessity Guide	growth response 2) (e.g., Charcot-Marie-Tooth), FGFR2 (fibroblast growth factor receptor 2) (2 EXONS), FGFR3 (fibroblast growth factor receptor 3) (4 EXONS), FKRP (Fukutin related protein), FOXG1 (forkhead box G1), FSHMD1A (facioscapulohumeral muscular dystrophy 1A), FSHMD1A (facioscapulohumeral muscular dystrophy 1A), HNF1B (HNF1 homeobox B), HRAS (v-Ha-ras Harvey rat sarcoma viral oncogene homolog), KCNJ10 (potassium inwardly-rectifying channel, subfamily J, member 10), SLC25A4 (solute carrier family 25 [mitochondrial carrier; adenine nucleotide translocation], VWF (von Willebrand factor)		

81405	Molecular pathology procedure, Level 4 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of > 5 exons.	Yes	Yes
		CASR (CAR, EIG8, extracellular calcium-sensing receptor, FHH, FIH, GPRC2A, HHC, HHC1, NSHPT, PCAR1), CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide2), MPZ (myelin protein zero)	No	No
81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)	ATP7B (ATPase, Cu++ transporting, beta polypeptide)	Yes	Yes
		ACADVL (acyl-CoA dehydrogenase, very long chain), CBS (cystathionine-beta-synthase), CDKL5 (cyclin-dependent kinase-like 5) DLAT (dihydrolipoamide S-acetyltransferase), DLD (dihydrolipoamide dehydrogenase), F8 (coagulation factor VIII), GALT	No	No

	Genetic and Molecular Te **Medical Necessity Guide**	(galactose-1-phosphate uridylyl transferase), HADHA (hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase [trifunctional protein] alpha subunit), HEXA (hexosaminidase A, alpha polypeptide), LMNA (lamin A/C), MUTYH (mutY homolog [E. coli]), NF2 (neurofibromin 2 [merlin]), NSD1 (nuclear receptor binding SET domain protein 1), PAH (phenylalanine hydroxylase), PAX2 (paired box 2), PDHA1 (pyruvate dehydrogenase [lipoamide] alpha1), POLG (polymerase [DNA directed], gamma), PRKAG2 (protein kinase, AMP-activated, gamma 2 non-catalytic subunit), PTPN11 (protein tyrosine phosphatase, non-receptor type 11), RET (ret-proto-oncogene) (e.g.,		

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		Hirschsprung disease), full gene sequence, SLC9A6 (solute carrier family 9 [sodium/hydrogen exchanger] member 6), SOS1 (son of sevenless homolog 1), TAZ (tafazzin), TSC1 (tuberous sclerosis 1), TSC2 (tuberous sclerosis 2), UBE3A (ubiquitin protein ligase)		
81407	Molecular pathology procedure, Level 8 (e.g., analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of > 50 exons, sequence analysis of multiple genes on one platform) APOB (apolipoprotein B) (e.g., familial hypercholesterolemia type B) full gene sequence	Level 8 Molecular Pathology Procedures, F8 (coagulation factor VIII)	No	No
81408	Molecular pathology procedure, Level 9 (e.g., analysis of > 50 exons in a single gene by DNA sequence analysis)	Level 9 Molecular Pathology Procedures	No	No
81479	Unlisted molecular pathology procedure	PIK3C, PI3Ks, PI(3)Ks, PI-3Ks, AKT1, MEK1, VEGFR2 (CD309, FLK1, VEGFR), LPA intron 25 genotype, KIF6, SPG4, C9orf72, MLH1, AIRE (APSI), SDA2, HAX1 (HAX1_HUMAN, HCLS1- associated protein X-1, HCLSBP1, HS1- associating protein X-1, HS1 binding protein, HS1-binding protein 1,	No	No

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Non-Covered Codes:
The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not signify that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service.

Table 2 – Non-covered Codes
Genetic testing procedures submitted under the following CPT codes are unlikely to impact therapeutic decision-making in the clinical management of the patient and will be denied automatically as not medically necessary.

CPT Code	Description	Coverage	
		SCO/One Care	Medicare Advantage
81105	Human platelet antigen 1 genotyping (HPA-1), ITGB2 (Integrin, Beta 2 [Platelet glycoprotein IIIA], Antigen CD61 [GPIIIA]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], Post-transfusion purpura), Gene analysis, common variant, HPA-1A/B (L33P)	No	No
81106	Human platelet antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2a/b (T145M)	No	No
81171	AFF2 (AF4/FMR2 Family, member 2 [FMR2]) (e.g., fragile X mental retardation 2 [FRAXE]) Gene analysis; Evaluation to detect abnormal (e.g., expanded) alleles	No	No
81172	AFF2 (AF4/FMR2 Family, member 2 [FMR2]) (e.g., Fragile X mental retardation 2 [FRAXE] gene analysis; characterization of alleles (e.g., expanded size and methylation status)	No	No
81173	AR (Androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis, full gene sequence	No	No
81174	AR (Androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis, known familial variant	No	No
81204	AR (Androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X Chromosome inactivation) gene analysis; Characterization of alleles (e.g., expanded size of methylation status)	No	No

81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (e.g., drug metabolism), gene analysis, common variant(s) (e.g., *2, *22)	No	No
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (e.g., drug metabolism), gene analysis, common variant(s) (e.g., *2, *3, *4, *5, *6, *7)	No	No
81232	DPYD (dihydropyrimidine dehydrogenase) (e.g., 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (e.g., *2A, *4, *5, *6)	No	No
81234	DMPK (DM1 protein kinase) (e.g., myotonic dystrophy type I) gene analysis; evaluation to detect abnormal (expanded) alleles	No	No
81239	DMPK (DM1 protein kinase) (e.g., myotonic dystrophy type I) gene analysis; characterization of alleles (e.g., expanded size)	No	No
81247	G6PD (glucose-6-phosphate dehydrogenase) (e.g., hemolytic anemia, jaundice), gene analysis; common variant(s) (e.g., A, A-)	No	No
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence	No	No
81271	HTT (huntingtin) (e.g., Huntington disease) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles	No	No
81274	HTT (huntingtin) (e.g., Huntington disease) gene analysis; characterization of alleles (e.g., expanded size)	No	No
81283	IFNL3 (interferon, lambda 3) (e.g., drug response), gene analysis, RS12979860 variant	No	No
81284	HTT (huntingtin) (e.g., Huntington disease) gene analysis; characterization of alleles (e.g., expanded size)	No	No
81285	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis evaluation; characterization of alleles (e.g., expanded size)	No	No
81286	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis; full gene sequence	No	No
81289	FXN (frataxin) (e.g., Friedreich ataxia) gene analysis evaluation; known familial variant(s)	No	No
81290	MCOLN1 (mucolipin 1)(e.g., Mucolipidosis, type IV) gene analysis, common variants (e.g., IVS3-2A>G, del6, 4kb)	No	No
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (e.g., hereditary hypercoagulability) gene analysis, common variants (e.g., 677T, 1298C)	No	No
81327	SEPT7 (SEPTIN9) (e.g., colorectal cancer) promoter methylation analysis	No	No

81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (e.g., adverse drug reaction) gene analysis, common variant(s) (e.g., *5)	No	No
81336	SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy) gene analysis; full gene sequence	No	No
81337	SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy) gene analysis; known familial sequence variant(s)	No	No
81346	TYMS (thymidylate synthetase) (e.g., 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (e.g., tandem repeat variant)	No	No
81349	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis	No	No
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (e.g., drug metabolism, hereditary unconjugated hyperbilirubinemia [Gilbert syndrome]) gene analysis, common variants (e.g., *28, *36, *37)	No	No
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (e.g., warfarin metabolism), gene analysis, common variant(s) (e.g., -1639G>A, C.173+1000C>T)	No	No
81410	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK	No	No
81411	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1	No	No
81412	Ashkenazi Jewish associated disorders (e.g., bloom syndrome, canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group c, Gaucher disease, Tay-Sachs's disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1	No	No
81413	Cardiac ion channelopathies (e.g., brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence	No	No

	analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CPVT1, KCNJ5, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A		
81414	Cardiac ion channelopathies (e.g., brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1	No	No
81415	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis	No	No
81416	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (e.g., parents, siblings) (List separately in addition to code for primary procedure)	No	No
81417	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (e.g., updated knowledge or unrelated condition/syndrome)	No	No
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (e.g., DiGeorge syndrome, cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood	No	No
81425	Genome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis	No	No
81426	Genome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (e.g., parents, siblings) (List separately in addition to code for primary procedure)	No	No
81427	Genome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (e.g., updated knowledge or unrelated condition/syndrome)	No	No
81430	Hearing loss (e.g., 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	No	No
81431	Hearing loss (e.g., 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	No	No
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA@, MLH1, MSH2, and STK11	No	No

81434	Hereditary retinal disorders (e.g., inherited macular dystrophies, retinitis pigmentosa, congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A	No	No
81435	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11	No	No
81436	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11	No	No
81437	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL	No	No
81438	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL	No	No
81439	Inherited cardiomyopathy (e.g., hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy) genomic sequence analysis panel, must include sequencing of at least 5 genes, including DSG2, MYBPC3, MYH7, PKP2, and TTN	No	No
81440	Nuclear encoded mitochondrial genes (e.g., 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	No	No
81442	Noonan spectrum disorders (e.g., Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic	No	No

	sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1	ar T esting eline	
81443	Genetic testing for severe inherited conditions (e.g., cystic fibrosis, Ashkenazi Jewish-associated disorders [e.g., Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sach's disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (e.g., ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH	No	No
81448	Hereditary peripheral neuropathies (e.g., Charcot-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (e.g., BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)	No	No
81460	Whole mitochondrial genome (e.g., 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	No	No
81465	Whole mitochondrial genome large deletion analysis panel (e.g., Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed	No	No
81470	X-linked intellectual disability (XLID) (e.g., syndromic and non-syndromic XLID); genomic sequence analysis panel, must include sequencing of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2	No	No
81471	X-linked intellectual disability (XLID) (e.g., syndromic and non-syndromic XLID); duplication/deletion gene analysis, must include analysis of at least 60 genes, including ARX,	No	No

	ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2	**ular T esting Medical Necessity Guid eline**	
81493	Coronary artery disease, MRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score	No	No
81500	Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score	No	No
81503	Oncology (ovarian), biochemical assays of five proteins (CA-125, apolipoprotein A1, beta-2 microglobulin, transferrin, and pre-albumin), utilizing serum, algorithm reported as a risk score	No	No
81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores	No	No
81521	Oncology (breast), MRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis	No	No
81525	Oncology (colon), MRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score	No	No
81535	Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; first single drug or drug combination	No	No
81536	Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; each additional single drug or drug combination (List separately in addition to code for primary procedure)	No	No
81538	Oncology (lung); mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival	No	No
81540	Oncology (tumor of unknown origin), MRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-	No	No

	embedded tissue, algorithm reported as predicted main cancer type and likelihood		
81541	Oncology (prostate), MRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score	No	No
81551	Oncology (prostate), promoter methylation profiling by real-time PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a likelihood of prostate cancer detection on retreat biopsy	No	No

Genetic and Molecular Testing
Medical Necessity Guideline

REGULATORY NOTES:

Medical Necessity Guidelines are published to provide a better understanding of the basis upon which coverage decisions are made. CCA makes coverage decisions on a case-by-case basis by considering the individual member's health care needs. If at any time an applicable CMS LCD or NCD or state-specific MNG is more expansive than the criteria set forth herein, the NCD, LCD, or state-specific MNG criteria shall supersede these criteria. This MNG references the specific regulations, coverage, limitations, service conditions, and/or prior authorization requirements in the following:

This MNG references the specific regulations, coverage, limitations, service conditions, and/or prior authorization requirements in the following:

Medicare Benefit Policy Manual, Publication 100-02, Chapter 15, Section 80.1
Medicare National Coverage Determinations, Publication 100-03, Chapter 1, Part 2, Section 90.2
Medicare Claims Processing Manual, Publication 100-04, Chapter 16, Section 70
National Correct Coding Initiative Policy Manual for Medicare Services, Chapter X Pathology/Laboratory Services, CPT Codes 80000-89999, Section F
Medicare, Local Coverage Determination (L35000)
Medicare, Local Coverage Article (A56199)
Medicare, Local Coverage Article (A57880)
MassHealth, 130 CMR 433.000: Physician Services
MassHealth, 130 CMR 401.000, Independent Clinical Laboratory Manual, Subchapter 4

Disclaimer

This Medical Necessity Guideline is not a rigid rule. As with all of CCA's criteria, the fact that a member does not meet these criteria does not, in and of itself, indicate that no coverage can be issued for these services. Providers are advised, however, that if they request services for any member who they know does not meet our criteria, the request should be accompanied by clear and convincing documentation of medical necessity. The preferred type of documentation is the letter of medical necessity, indicating that a request should be covered either because there is supporting science indicating medical necessity (supporting literature (full text preferred) should be attached to the request), or describing the member's unique clinical circumstances, and describing why this service or supply will be more effective and/or less costly than another service which would otherwise be covered. Note that both supporting scientific evidence and a description of the member's unique clinical circumstances will generally be required.

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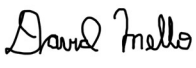
REVISION LOG:

REVISION	DESCRIPTION
12/31/23	Utilization Management Committee approval
11/9/23	CPT 81432 removed from Table 2 Noncovered codes, added to Table 1 covered codes. CPT codes removed, 81162, 81163, 81164, 81165, 81166, 81167, 81212, 81215, 81216, 81217; refer to Genetic Testing: BRCA-Related Breast and/or Ovarian Cancer Syndrome MNG.
9/26/22	Format of CPT codes changed. References to other internally developed genetic test MNGs added.
9/20/22	Noncovered CPT codes added.
6/2/2022	Template update. Background information added to the overview and definitions section. Clinical eligibility and limitations updated to reflect CMS local coverage determination (L35000) and article (A56199). CPT codes added.

APPROVALS:

David Mello
CCA Senior Clinical Lead [Print]

Senior Medical Director, Utilization Review and Medical Policy
Title [Print]


Signature

12/22/23
Date

Click here to enter text.
CCA Senior Operational Lead [Print]

Title [Print]

Signature

Date

Chief Medical Officer

Nazlim Hagmann
CCA CMO or Designee [Print]

Title [Print]

12/22/23


Signature

Date