Non-Covered Genetic Panel Tests

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INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as “Company” and collectively as “Companies”).

PLAN PRODUCT AND BENEFIT APPLICATION

☒ **Commercial** ☐ **Medicaid/OHP*** ☐ **Medicare****

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

PHP follows Guideline Notes 172 and 173 of the OHP Prioritized List of Health Services. In the absence of OHP guidance, PHP will follow this policy.

**Medicare Members

This *Company* policy may be applied to Medicare Plan members only when directed by a separate *Medicare* policy. Note that investigational services are considered **"not medically necessary"** for Medicare members.

COVERAGE CRITERIA

Notes:

- This policy does not address the following:
  - Whole exome or genome sequencing.
  - Genetic tests related to reproductive planning or prenatal testing.
- The list of non-covered panels addressed in this policy is not all-inclusive.
- Due to the rapidly changing field of genetic testing, panel names, genes included within the panel, and coding may change subsequent to the last update of this policy.
- Other Medical Policies may apply:
  - Please see Cross References section below for medical policies which may apply to specific hereditary or oncologic conditions.
  - If available, condition- or test-specific policies should be used to review singe gene or genetic panel tests. For example, genetic panel testing for hereditary colorectal cancer is addressed in the *Genetic Testing: Inherited Susceptibility to Colorectal Cancer* medical policies.
  - Please refer to the PHP *Genetic and Molecular Testing* company medical policy for genetic panel testing medical necessity criteria not addressed in more specific medical policies.

Non-Coverage Criteria

I. Genetic panel testing is considered **not medically necessary** when there is insufficient evidence that the panel has proven clinical utility. (Please see Policy Guidelines below for definition of panel testing.) To establish clinical utility, **both** of the following criteria (A. and B) must be met for each gene and/or component of the panel test:

   A. Testing allows for a definitive diagnosis or risk classification and **either** of the following are met:
      1. Other clinical and/or laboratory tests were inconclusive; **or**

2. Testing avoids a more invasive diagnostic testing (i.e., muscle biopsy); **and**

B. Test results will guide decisions in clinical management (predictive, diagnostic, prognostic, or therapeutic).

Genetic panel tests for which clinical utility has not been established are considered **not medically necessary**, including but not limited to the following tests:

Proprietary Test Name	Laboratory	Proprietary Code
AlloSure Kidney	CareDx	None
Bridge Urinary Tract Infection Detection and Resistance Test	Bridge Diagnostics	0321U
Bladder CARE™	Pangea Laboratory, LLC.	0549U
CancerTYPE ID®	Biotheranostics	None
Colvera	Clinical Genomics	None
Copper Metabolism Disorders Panel	Invitae	None
CxBladder Detect	Pacific Edge, Ltd.	0012M
CxBladder Monitor	Pacific Edge, Ltd.	0013M
CxBladder Triage	Pacific Edge, Ltd.	0363U
DecisionDx-SCC	Castel Biosciences	0315U
DetermaRx	Oncocyte Corporation	0288U
Developmental Eye Disease Panel	Molecular Vision Laboratory	None
EarlyDx MethylScan HCC	Early Diagnostics Laboratory	0565U
EpiSwitch CiRT (Checkpoint-inhibitor Response Test)	Next Bio-Research Services, LLC, Oxford BioDynamics, PLC	0332U
GeneticsNow Comprehensive Germline Panel	GoPath Diagnostics	0474U
GenoMind Professional PGx Express (includes CORE Anxiety & Depression Report [15 Genes] and/or FULL Mental Health Report [24 Genes])	Genomind	0175U
HeartCare *(i.e. combination of AlloMap Heart and AlloSure Heart dd-cfDNA)*	CareDx	0055U
Hemiplegic Migraine Panels	GeneDx	None
Invitae Comprehensive Neuromuscular Disorders Panel	Invitae	None
Invitae Comprehensive Neuropathies Panel	Invitae	None
Invitae Dystonia Comprehensive Panel	Invitae	None
Invitae Monogenic Inflammatory Bowel Disease Panel	Invitae	None

Johns Hopkins Metagenomic Next Generation Sequencing Assay for Infectious Disease	Johns Hopkins Medical Microbiology Laboratory	0323U
Maternal Fetal Screen T1	Eurofins	None
MindX Blood Test- Longevity	MindX Sciences	0294U
MindX Blood Test- Memory/Alzheimer's	MindX Sciences	0289U
MindX Blood Test- Mood	MindX Sciences	0291U
MindX Blood Test- Pain	MindX Sciences	0290U
MindX Blood Test- Stress	MindX Sciences	0292U
MindX Blood Test- Suicidality	MindX Sciences	0293U
Mind.Px	Mindera	0258U
Molecular Microscope MMDx Heart Test	Kashi Clinical Labs	0087U
Molecular Microscope MMDx Kidney Test	Kashi Clinical Labs	0088U
mRNA Cancer Detect	Viome Life Sciences	0296U
Oncotype DX Colon Cancer	Genomic Health	None
Oncuria Detect, Monitor, and Predict	DiaCarta Clinical Lab	0365U, 0366U, 0367U
Optic Atrophy Panel	Blueprint Genetics	None
PancraGen test	Interpace Diagnostics	None
Percepta Genomic Sequencing Classifier	Veracyte Inc	None
Peripheral Neuropathy Genetics Panel	Mayo Clinic Laboratories	None
Praxis Somatic Transcriptome	Praxis Genomics	0298U
Praxis Transcriptome	Praxis Genomics	0266U
PreTransplant Risk Assessment (PTRA)	Verici Dx	0319U
PrismaRA	Scipher Medicine	0456U
Prospera Assay	Natera Inc.,	0493U
+RNAinsight for CancerNext	Ambry Genetics	0134U
+RNAingight for ATM	Ambry Genetics	0136U
Tissue of Origin (TOO)	Cancer Genetics Inc.	None
TruDiagnostic tests	TrueDiagnostic Inc.	0616U, 0617U, 0618U, 0619U, 0620U, 0621U, 0622U, 0623U, 0624U, 0625U, 0626U, 0627U
Tuteva	Verici Dx	0320U
UriFind Blood Cancer Assay	DiaCarta	0465U
Versiti congenital Neutropenia Panel	Versiti Diagnostic Laboratories	0271U
Vita Risk	Arctic Medical Laboratories	0205U

Link to Evidence Summary

POLICY CROSS REFERENCES

- Genetic and Molecular Testing, MP215
- Genetic Counseling, MP316
- Genetic Testing for CADASIL Disease, MP238
- Genetic Testing for Cytochrome *P450* and *VKORC1* Polymorphisms, MP313
- Gene Expression Profile Testing for Breast Cancer, MP47
- Genetic Testing for Hereditary Breast Ovarian, and Pancreatic Cancer, MP143
- Genetic Testing for Inherited Susceptibility to Colorectal, Endometrial and Gastric Cancer, MP115
- Genetic Testing for Inherited Thrombophilia, MP266
- Genetic Testing for *MTHFR*, MP311
- Genetic Testing for Myeloproliferative Diseases, MP72
- Genetic Testing for Reproductive Planning and Prenatal Testing, MP78
- Whole Exome, Whole Genome and Proteogenomic Sequencing and Genetic Testing for Mitochondrial Disorders, MP219

The full Company portfolio of current Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

DOCUMENTATION REQUIREMENTS

In order to determine the clinical utility of a genetic test, the following documentation must be provided at the time of the request:

- Name of the panel test or the name of the gene(s) and/or components of the test
- Name of laboratory that performed or is performing the test
- Clinical notes should include the following:
  - Reason for performing test, including the suspected condition
  - Signs/symptoms/test results related to rationale for genetic testing
  - Family history, if applicable
  - How test results will impact clinical decision making
- CPT codes billed

BACKGROUND

Genetic panel tests are genetic tests that may be comprised of as few as three genes to as many as thousands of genes. The advantage of genetic panel tests is that they allow for simultaneous testing of test of multiple genes and/or mutations, potentially improving the scope and efficiency of a patient's genetic evaluation. One major disadvantage of genetic panel tests is that the results may provide information on genetic mutations that are of unclear clinical significance, or which would not lead to changes in patient management. These results may potentially cause harm by leading to additional unnecessary interventions and anxiety that would not otherwise be considered based on the patient's clinical presentation and/or family history.

Numerous commercially available genetic panel tests are available for diagnostic, prognostic and management purposes for individuals harboring symptoms of hereditary conditions or oncologic indications. In addition, panel tests have also been marketed for risk assessment and screening purposes in asymptomatic individuals. However, high-quality studies published in peer-reviewed literature have only shown that certain genetic panel tests are valuable when diagnosing conditions, conferring risk or guiding treatment. To date, the majority of genetic panel tests have not been well studied.
This policy lists a number of genetic panel tests where there is insufficient evidence in published peer-reviewed literature to indicate that they consistently lead to improved diagnostic rates and/or health outcomes. These tests are considered not medically necessary.

REGULATORY STATUS

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

General Principles of Genetic Testing

Due to the high complexity of genetic panel tests and their interpretation, tests must be Food and Drug Administration (FDA)-approved and/or performed in a Clinical Laboratory Improvement Amendments (CLIA)-accredited laboratory. Furthermore, the laboratory offering a panel test must have scientifically validated the panel test for the indication for which the panel has been developed and is being requested.

CLINICAL EVIDENCE AND LITERATURE REVIEW

EVIDENCE REVIEW

The panels addressed in this policy underwent a focused review using the GeneReviews, ECRI, Hayes, and NIH Genetic and Rare Diseases (GARD) databases as well as information extracted from the testing laboratory's website.

The main criterion for inclusion in this policy was the limited evidence of clinical utility for every gene or test component of a specific genetic panel test. (Please see Policy Guidelines section above for definition of clinical utility.)

CLINICAL PRACTICE GUIDELINES

American Society of Clinical Oncology (ASCO)

The 2015 update of a policy statement on genetic and genomic testing for cancer susceptibility from the American Society of Clinical Oncology (ASCO) addressed multigene panel testing and stated the following:[1]

> "ASCO recognizes that concurrent multigene testing (ie, panel testing) *may be efficient* in circumstances that require evaluation of multiple high-penetrance genes of established clinical utility as possible explanations for a patient's personal or family history of cancer. Depending on the specific genes included on the panel employed, panel testing may also identify mutations in genes associated with moderate or low cancer risks and mutations in high-penetrance genes that would not have been evaluated on the basis of the presenting personal or family history. Multigene panel testing will also identify variants of uncertain significance (VUSs) in a substantial proportion of patient cases, simply as a result of the multiplicity of genes tested. ASCO affirms that it is sufficient for cancer risk assessment to evaluate genes of established clinical utility that are suggested by the patient's personal and/or family history. Because of the current uncertainties and knowledge gaps, providers with particular expertise in cancer risk assessment should be involved in the ordering and interpretation of multigene panels that include genes of uncertain clinical utility and genes not suggested by the patient's personal and/or family history…"

In addition, ASCO stated:

> "So far, there is little consensus as to which genes should be included on panels offered for cancer susceptibility testing- this heterogeneity presents a number of challenges. All panels include high-penetrance genes that are known to cause autosomal-dominant predisposition syndromes, but often include genes that are not necessarily linked to the disease for which the testing is being offered. There is uncertainty regarding the appropriate risk estimates and management strategies for families with unexpected mutations in high-penetrance genes when there is no evidence of the associated syndrome. Clinical utility remains the fundamental issue with respect to testing for mutations in moderate penetrance genes. It is not yet clear whether clinical management should change based on the presence or absence of a mutation. There is insufficient evidence at the present time to conclusively demonstrate the clinical utility of testing for moderate-penetrance mutations, and no guidelines exist to assist oncology providers.
>
> … [A] substantial proportion of tests identify [variants of uncertain significance] VUS in one or more genes. VUSs are alterations in the genetic code that may or may not affect the function of the protein. VUSs are more common in broad-panel testing both because of the number of genes tested and because of the limited understanding of the range of normal variation in some of these genes. It is usually inappropriate to change the clinical management of a patient based on the finding of a VUS. Unfortunately, there is some evidence that clinicians may overinterpret VUSs and make recommendations that should be reserved for individuals with clearly deleterious mutations."

EVIDENCE SUMMARY

There is insufficient evidence that the genetic panels listed in this policy have proven clinical utility. Specifically, there is insufficient evidence that all genes and/or components in a given genetic panel test have proven to provide actionable risk, diagnostic or prognostic information, or information impacting medical management, that has led to improved health outcomes.

HEALTH EQUITY CONSIDERATIONS

The Centers for Disease Control and Prevention (CDC) defines health equity as the state in which everyone has a fair and just opportunity to attain their highest level of health. Achieving health equity

requires addressing health disparities and social determinants of health. A health disparity is the occurrence of diseases at greater levels among certain population groups more than among others. Health disparities are linked to social determinants of health which are non-medical factors that influence health outcomes such as the conditions in which people are born, grow, work, live, age, and the wider set of forces and systems shaping the conditions of daily life. Social determinants of health include unequal access to health care, lack of education, poverty, stigma, and racism.

The U.S. Department of Health and Human Services Office of Minority Health calls out unique areas where health disparities are noted based on race and ethnicity. Providence Health Plan (PHP) regularly reviews these areas of opportunity to see if any changes can be made to our medical or pharmacy policies to support our members obtaining their highest level of health. Upon review, PHP creates a Coverage Recommendation (CORE) form detailing which groups are impacted by the disparity, the research surrounding the disparity, and recommendations from professional organizations. PHP Health Equity COREs are updated regularly and can be found online here.

BILLING GUIDELINES AND CODING

CODES*		
CPT	0012M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and XCR2), utilizing urine, algorithm reported as a risk score for having urothelial carcinoma
	0013M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm reported as a risk score for having recurrent urothelial carcinoma
	0087U	Cardiology (heart transplant), mRNA gene expression profiling by microarray of 1283 genes, transplant biopsy tissue, allograft rejection and injury algorithm reported as a probability score
	0088U	Transplantation medicine (kidney allograft rejection), microarray gene expression profiling of 1494 genes, utilizing transplant biopsy tissue, algorithm reported as a probability score for rejection
	0134U	Hereditary pan cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes) (List separately in addition to code for primary procedure)
	0136U	ATM (ataxia telangiectasia mutated) (eg, ataxia telangiectasia) mRNA sequence analysis (List separately in addition to code for primary procedure)
	0175U	Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes
	0205U	Ophthalmology (age-related macular degeneration), analysis of 3 gene variants (2 CFH gene, 1 ARMS2 gene), using PCR and MALDI-TOF, buccal swab, reported as positive or negative for neovascular age-related macular-degeneration risk associated with zinc supplements
	0258U	Autoimmune (psoriasis), mRNA, next-generation sequencing, gene expression profiling of 50-100 genes, skin-surface collection using adhesive patch, algorithm reported as likelihood of response to psoriasis biologics

	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
	0271U	Hematology (congenital neutropenia), genomic sequence analysis of 24 genes, blood, buccal swab, or amniotic fluid
	0288U	Oncology (lung), mRNA, quantitative PCR analysis of 11 genes (BAG1, BRCA1, CDC6, CDK2AP1, ERBB3, FUT3, IL11, LCK, RND3, SH3BGR, WNT3A) and 3 reference genes (ESD, TBP, YAP1), formalin-fixed paraffin-embedded (FFPE) tumor tissue, algorithmic interpretation reported as a recurrence risk score
	0289U	Neurology (Alzheimer disease), mRNA, gene expression profiling by RNA sequencing of 24 genes, whole blood, algorithm reported as predictive risk score
	0290U	Pain management, mRNA, gene expression profiling by RNA sequencing of 36 genes, whole blood, algorithm reported as predictive risk score
	0291U	Psychiatry (mood disorders), mRNA, gene expression profiling by RNA sequencing of 144 genes, whole blood, algorithm reported as predictive risk score
	0292U	Psychiatry (stress disorders), mRNA, gene expression profiling by RNA sequencing of 72 genes, whole blood, algorithm reported as predictive risk score
	0293U	Psychiatry (suicidal ideation), mRNA, gene expression profiling by RNA sequencing of 54 genes, whole blood, algorithm reported as predictive risk score
	0294U	Longevity and mortality risk, mRNA, gene expression profiling by RNA sequencing of 18 genes, whole blood, algorithm reported as predictive risk score
	0296U	Oncology (oral and/or oropharyngeal cancer), gene expression profiling by RNA sequencing at least 20 molecular features (eg, human and/or microbial mRNA), saliva, algorithm reported as positive or negative for signature associated with malignancy
	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
	0315U	Oncology (cutaneous squamous cell carcinoma), mRNA gene expression profiling by RT-PCR of 40 genes (34 content and 6 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical risk result (ie, Class 1, Class 2A, Class 2B)
	0319U	Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using pretransplant peripheral blood, algorithm reported as a risk score for early acute rejection
	0320U	Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using posttransplant peripheral blood, algorithm reported as a risk score for acute cellular rejection
	0321U	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogens, identification of 20 bacterial and fungal organisms and identification of 16 associated antibiotic-resistance genes, multiplex amplified probe technique
	0323U	Infectious agent detection by nucleic acid (DNA and RNA), central nervous system pathogen, metagenomic next-generation sequencing, cerebrospinal fluid (CSF), identification of pathogenic bacteria, viruses, parasites, or fungi

	0332U	Oncology (pan-tumor), genetic profiling of 8 DNA-regulatory (epigenetic) markers by quantitative polymerase chain reaction (qPCR), whole blood, reported as a high or low probability of responding to immune checkpoint–inhibitor therapy
	0363U	Oncology (urothelial), mRNA, geneexpression profiling by real-time quantitative PCR of 5 genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm incorporates age, sex, smoking history, and macrohematuria frequency, reported as a risk score for having urothelial carcinoma
	0365U	Oncology (bladder), 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA), by immunoassays, urine, diagnostic algorithm, including patient's age, race and gender, reported as a probability of harboring urothelial bladder cancer
	0366U	Oncology (bladder), analysis of 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA) by immunoassays, urine, algorithm reported as a probability of recurrent bladder cancer
	0367U	Oncology (bladder), analysis of 10 protein biomarkers (A1AT, ANG, APOE, CA9, IL8, MMP9, MMP10, PAI1, SDC1 and VEGFA) by immunoassays, urine, diagnostic algorithm reported as a risk score for probability of rapid recurrence of recurrent or persistent cancer following transurethral resection
	0420U	Oncology (urothelial), mRNA expression profiling by real-time quantitative PCR of MDK, HOXA13, CDC2, IGFBP5, and CXCR2 in combination with droplet digital PCR (ddPCR) analysis of 6 single-nucleotide polymorphisms (SNPs) genes TERT and FGFR3, urine, algorithm reported as a risk score for urothelial carcinoma
	~~0423U~~	**TERMED 7/1/2026** ~~Psychiatry (eg, depression, anxiety), genomic analysis panel, including variant analysis of 26 genes, buccal swab, report including metabolizer status and risk of drug toxicity by condition~~
	0437U	Psychiatry (anxiety disorders), mRNA, gene expression profiling by RNA sequencing of 15 biomarkers, whole blood, algorithm reported as predictive risk score
	0465U	Oncology (urothelial carcinoma), DNA, quantitative methylationspecific PCR of 2 genes (ONECUT2, VIM), algorithmic analysis reported as positive or negative
	0474U	Hereditary pan-cancer (eg, hereditary sarcomas, hereditary endocrine tumors, hereditary neuroendocrine tumors, hereditary cutaneous melanoma), genomic sequence analysis panel of 88 genes with 20 duplications/deletions using nextgeneration sequencing (NGS), Sanger sequencing, blood or saliva, reported as positive or negative for germline variants, each gene
	0549U	Oncology (urothelial), DNA, quantitative methylated real-time PCR of TRNA-Cys, SIM2, and NKX1-1, using urine, diagnostic algorithm reported as a probability index for bladder cancer
	0565U	Oncology (hepatocellular carcinoma), next-generation sequencing methylation pattern assay to detect 6626 epigenetic alterations, cell-free DNA, plasma, algorithm reported as cancer signal detected or not detected
	0586U	Oncology, mRNA, gene expression profiling of 216 genes (204 targeted and 12 housekeeping genes), RNA expression analysis, formalin-fixed paraffin-embedded (FFPE) tissue, quantitative, reported as log2 ratio per gene
	0588U	Infectious disease (bacterial or viral), 32 genes (29 informative and 3 housekeeping), immune response mRNA, gene expression profiling by splitwell multiplex reverse transcription loop-mediated isothermal amplification (RTLAMP),

		whole blood, reported as continuous risk scores for likelihood of bacterial and viral infection and likelihood of severe illness within the next 7 days
	0616U	Neurology (dementia), DNA methylation analysis of more than 30,000 sites, whole blood, algorithm reported as positive or negative risk
	0617U	Cardiovascular (atherosclerotic cardiovascular disease [ASCVD]), DNA methylation analysis of more than 20,000 sites, whole blood, algorithm reported as positive or negative risk
	0618U	Psychiatry (bipolar disorder), DNA methylation analysis of more than 10,000 sites, whole blood, algorithm reported as positive or negative risk
	0619U	Pulmonary (chronic obstructive pulmonary disease [COPD]), DNA methylation analysis of more than 18,000 sites, whole blood, algorithm reported as positive or negative risk
	0620U	Oncology (hepatocellular carcinoma), DNA methylation analysis of more than 5,000 sites, whole blood, algorithm reported as positive or negative risk
	0621U	Infectious disease (Lyme borreliosis), DNA methylation analysis of more than 10,000 sites, whole blood, algorithm reported as positive or negative risk
	0622U	Psychiatry (major depressive disorder), DNA methylation analysis of more than 20,000 sites, whole blood, algorithm reported as positive or negative risk
	0623U	Autoimmune (multiple sclerosis), DNA methylation analysis of more than 5,000 sites, whole blood, algorithm reported as positive or negative risk
	0624U	Hepatology (nonalcoholic steatohepatitis [NASH]), DNA methylation analysis of 5,000 sites, whole blood, algorithm reported as positive or negative risk
	0625U	Endocrinology (osteoporosis), DNA methylation analysis of more than 5,000 sites, whole blood, algorithm reported as positive or negative risk
	0626U	Neurology (Parkinson disease), DNA methylation analysis of more than 20,000 sites, whole blood, algorithm reported as positive or negative risk
	0627U	Psychiatry (schizophrenia), DNA methylation analysis of more than 15,000 sites, whole blood, algorithm reported as positive or negative risk
	0635U	Autoimmune (atopic dermatitis), mRNA, next-generation sequencing (NGS), gene expression profiling of 487 genes, noninvasive skinsurface scraping, algorithm reported as likelihood of response to therapy
	81195	Cytogenomic (genome-wide) analysis, hematologic malignancy, structural variants and copy number variants, optical genome mapping (OGM)
	81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
	81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism variants, comparative genomic hybridization [CGH] microarray analysis
	81301	Microsatellite instability analysis (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (e.g., BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
	81320	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)

	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)
	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)
	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 1 exon)
	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
	81404	Molecular pathology procedure, level 5 (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
	81405	Molecular pathology procedure, level 6 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)
	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)
	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)
	81408	Molecular pathology, level 9 (e.g., analysis of >50 exons in a single gene by DNA sequence analysis)
	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
	81413	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A
	81414	Cardiac ion channelopathies (eg, 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
	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)
	81434	Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A
	81437	Hereditary neuroendocrine tumor related disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, 5 or more genes, interrogation for sequence variants and copy number variants
	81439	Hereditary cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (eg, DSG2, MYBPC3, MYH7, PKP2, TTN)
	81442	Noonan spectrum disorders (eg, Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic 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
	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)
	81448	Hereditary peripheral neuropathies (eg, Charcot-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (eg, BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)
	81479	Unlisted Molecular Pathology
	81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores
	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
	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-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype
	81599	Unlisted multianalyte assay with algorithmic analysis
	84999	Unlisted chemistry procedure

HCPCS	S3844	DNA analysis of the connexin 26 gene (GJB2) for susceptibility to congenital, profound deafness
	S3870	Comparative genomic hybridization (cgh) microarray testing for developmental delay, autism spectrum disorder and/or intellectual disability

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Robson ME, Bradbury AR, Arun B, et al. American Society of Clinical Oncology Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2015;33(31):3660-3667.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
4/2023	Q2 2023 Code set update
7/2023	Annual review. Panels and codes already addressed on another policy removed and criteria denial changed from investigational to not medically necessary
10/2023	Q4 code set update. Revised code
12/2023	Annual update. List of non-covered panels updated.
1/2024	Q1 2024 code set update.
7/2024	Q3 2024 code set update.
1/2025	Q1 2025 code set update. Updated "not medically necessary" list.
4/2025	Q2 2025 code set update.
7/2025	Q3 2025 code set update. Code added.
10/2025	Annual update. Updated "not medically necessary" list. Q4 2025 code set update.
2/2026	Interim update. Remove panels from non-covered panel table.
4/2026	Q2 2026 code set update.
7/2026	Q3 2026 code set update.