# Non-Covered Genetic Panel Tests

**MEDICAL POLICY NUMBER:** 213

**Effective Date:** 10/1/2024

**Last Review Date:** 9/2024

**Next Annual Review:** 9/2025



**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 Heart** | CareDx | None |
| **AlloSure Kidney** | CareDx | None |
| **Bacteria, Viruses, Fungus, and Parasite Metagenomic Sequencing, Spinal Fluid (MSCSF)** | MayoClinic | 0480U |
| **Bridge Urinary Tract Infection Detection and Resistance Test** | Bridge Diagnostics | 0321U |
| **CancerTYPE ID®** | Biotheranostics | None |
| **Cardiomyopathy Panel** | GeneDx | None |
| **Clarava** | Verici Dx | 0319U |
| **Colvera** | Clinical Genomics | None |
| **Common Hereditary Cancers Panel** | Invitae | 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 |
| **DCMNext** | Ambry Genetics | None |
| **DetermaRx** | Oncocyte Corporation | 0288U |
| **Developmental Eye Disease Panel** | Molecular Vision Laboratory | None |
| **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** | CareDx | None |
| **Hemiplegic Migraine Panels** | GeneDx | None |
| **Infantile Epilepsy Panel** | GeneDx | None |
| **Invitae Arrhythmia and Cardiomyopathy Comprehensive Panel** | Invitae | None |
| **Invitae Comprehensive Neuromuscular Disorders Panel** | Invitae | None |

| | | |
|---|---|---|
| **Invitae Comprehensive Neuropathies Panel** | Invitae | None |
| **Invitae Connective Tissue Disorders Panel** | Invitae | None |
| **Invitae Dystonia Comprehensive Panel** | Invitae | None |
| **Invitae Ehlers-Danlos Syndrome Panel** | Invitae | None |
| **Invitae Epilepsy 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 |
| **Megalencephaly Panel** | Seattle Children's Hospital | 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 |
| **PrismaRA** | Scipher Medicine | 0456U |
| **Prospera™** | Natera™ | 0493U |
| **PurISTSM** | Tempus AI, Inc. | 0510U |
| **+RNAinsight for CancerNext** | Ambry Genetics | 0134U |
| **+RNAingight for ATM** | Ambry Genetics | 0136U |
| **Tempus xT Gene Panel** | Tempus | None |
| **Tissue of Origin (TOO)** | Cancer Genetics Inc. | None |

| | | |
|---|---|---|
| **Tuteva** | Verici Dx | 0320U |
| **UriFind® Urothelial Carcinoma 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 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.

## *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), 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 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 | 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 |
| | 0456U | Autoimmune (rheumatoid arthritis), next-generation sequencing (NGS), gene expression testing of 19 genes, whole blood, with analysis of anticyclic citrullinated peptides (CCP) levels, combined with sex, patient global assessment, and body mass index (BMI), algorithm reported as a score that predicts nonresponse to tumor necrosis factor inhibitor (TNFi) therapy |
| | 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 |
| | 0480U | Infectious disease (bacteria, viruses, fungi, and parasites), cerebrospinal fluid (CSF), metagenomic next-generation sequencing (DNA and RNA), bioinformatic analysis, with positive pathogen identification |
| | 0493U | Transplantation medicine, quantification of donor-derived cell-free DNA (cfDNA) using next-generation sequencing, plasma, reported as percentage of donor-derived cell-free DNA |
| | 0510U | Oncology (pancreatic cancer), augmentative algorithmic analysis of 16 genes from previously sequenced RNA whole-transcriptome data, reported as probability of predicted molecular subtype |
| | 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 disorders (eg, 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 |
| | 81438 | Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL |
| | 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. |
| 10/2024 | Annual review and Q4 2024 code set update. Updated policy names in cross reference section. Additional tests added to noncovered list. |