Clinical Use Guidelines

Investigational and Experimental Laboratory Testing

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Introduction

Investigational and experimental (I&E) molecular and genomic testing is addressed by this guideline.

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures address by this guideline	Procedure codes
4q25-AF Risk Genotype	81479
9p21 Genotype	81479
Accelerate PhenoTest BC kit	0086U
Accelerate PhenoTest BC kit, AST configuration	0311U
AlloSure Heart	81479
AlloSure Lung	81479
AmHPR Helicobacter pylori Antibiotic Resistance Next Generation Sequencing Panel	0008U
Apolipoprotein E Genotype (APOE)	81401
Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping	0355U
ARISk Autism Risk Assessment Test	81479
AssureMDx	81479
Augusta Hematology Optical Genome Mapping	0331U
Augusta Optical Genome Mapping	0260U
Bacterial Typing by Whole Genome Sequencing	0010U
Bartonella ddPCR and Digital ePCR	0301U, 0302U

Procedures address by this guideline	Procedure codes
BBDRisk Dx	0067U
BluePrint Molecular Subtyping Profile	81479
Bridge Urinary Tract Infection Detection and Resistance Test	0321U
Bridge Women's Health Infectious Disease Detection Test	0330U
Cardiac DNA Insight	81225, 81226, 81227, 81240, 81241, 81291, 81355, 81400, 81401, 81479
ChemoFX	81535 81536
Clarava	0319U
Clarifi ASD	0170U
clonoSeq	81479
CNGnome	0209U
ColonSentry	81479
Colvera	0229U
Crohn’s Prognostic Test	81401
Decipher Bladder TURBT	0016M
DecisionDx Cutaneous Melanoma	81529
DecisionDx DiffDx - Melanoma	0314U
DecisionDx - SCC	0315U
DEPArray	0009U
DetermaRx	0288U
Digitization of pathology slides	0760T, 0761T, 0762T, 0763T

Procedures address by this guideline	Procedure codes
Envisia Genomic Classifier	81554
EpiSign Complete	0318U
EpiSwitch CiRT	0332U
ERA (Endometrial Receptivity Analysis)	0253U
EsoGuard	0114U
ExoDx Prostate (IntelliScore)	0005U
FM/a fibromyalgia	81599
GPS Cancer	81479
HelioLiver Test	0333U
HERmark Breast Cancer Assay	84999
IBD sgi Diagnostic	81479, 82397, 83520, 86140, 86255, 88346, 88350
Insight TNBCtype	0153U
Invitae PCM MRD Monitoring	0307U
Invitae PCM Tissue Profiling and MRD Baseline Assay	0306U
IriSight Prenatal Analysis – Proband	0335U
IriSight Prenatal Analysis – Comparator	0336U
Johns Hopkins Metagenomic Next Generation Sequencing Assay for Infectious Disease Diagnostics	0323U
Karius Test	0152U
KIF6 Genotype	81479
Know error	81479, 84999, 81265, 81266
LactoTYPE	81400
LPA-Aspirin Genotype	81479
LPA-Intron 25 Genotype	81479

Procedures address by this guideline	Procedure codes
LungLB	0317U
Lymph2Cx Lymphoma Molecular Subtyping Assay	0017M
Lymph3Cx Lymphoma Molecular Subtyping Assay	0120U
Mammostrat Breast Cancer Recurrence Assay	84999, S3854
MicroGenDX qPCR & NGS For Infection	0112U
Mind.Px	0258U
MindX Blood Test - Longevity	0294U
MindX Blood Test - Memory/Alzheimer's	0289U
MindX Blood Test - Mood	0291U
MindX Blood Test - Pain	0290U
MindX Blood Test - Stress	0292U
MindX Blood Test - Suicidality	0293U
miR-31now	0069U
miR Sentinel Prostate Cancer Test	0343U
Molecular Microscope MMDx—Heart	0087U
Molecular Microscope MMDx—Kidney	0088U
mRNA CancerDetect	0296U
MycoDART Dual Amplification Real Time PCR Panel for 4 Aspergillus species	0109U
myPath Melanoma	0090U
MyProstateScore (MPS, MIPS, previously Mi-Prostate Score)	81599 or 0113U
myPRS Myeloma Prognostic Risk Signature	81479
myTAIHEART	0055U
NavDx	0356U
Oncomap ExTra	0329U
OncoSignal 7 Pathway Signal	0262U
OncoTarget/OncoTreat	0019U
OncotypeDx AR-V7 Nucleus Detect	81479

Procedures address by this guideline	Procedure codes
PAI-1 Testing for Cardiovascular Disease Risk Assessment	81400, 85415
PancreaSeq Genomic Classifier	0313U
PanGIA Prostate	0228U
Pathway Fit	81291, 81401, 81479
PCR Fungal Screen for Onychomycosis	87481, 87798
Percepta Genomic Sequencing Classifier	81479
POC (Products of Conception)	0252U
Praxis Optical Genome Mapping	0264U
Praxis Somatic Combined Whole Genome Sequencing and Optical Genome Mapping	0300U
Praxis Somatic Optical Genome Mapping	0299U
Praxis Somatic Transcriptome	0298U
Praxis Somatic Whole Genome Sequencing	0297U
Praxis Transcriptome	0266U
PreciseDx Breast Cancer Test	0220U
PredictSURE IBD Test	0203U
PrismRA	81479 or 81599
ProMark Proteomic Prognostic Test	81479
Prospera	81479
Prostate Cancer Risk Panel	0053U
RadTox cfDNA test	0285U
RetnaGene AMD	81401, 81405, 81408, 81479, 81599
ROMA Risk of Ovarian Malignancy Algorithm	81500
Signatera	0340U

Procedures address by this guideline	Procedure codes
Single Cell Prenatal Diagnosis (SCPD) Test	0341U
SMART PGT-A (Pre-implantation Genetic Testing - Aneuploidy)	0254U
SMASH	0156U
Statin Induced Myopathy Genotype (SLCO1B1)	81328
Targeted genomic sequence analysis panel, solid organ neoplasm, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, MET, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis	81449
Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis	81456
Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NOTCH1, NPM1, NRAS), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis	81451
Thyroid GuidePx	0362U
ToxLok	0079U
TruGraf Kidney	81479
Tuteva	0320U
Twin Zygosity, cell free fetal DNA	0060U
Viracor TRAC dd-cfDNA	0118U
Vectra	81490
Vita Risk	0205U
Investigational and experimental tests that make use of molecular and genomic technologies	81479, 84999, 81599, and others

What Is I&E Molecular and Genomic Testing?

Definition

An investigational and experimental (I&E) procedure is the use of a service, supply, drug, or device that is not recognized as standard medical care for the condition, disease, illness, or injury. Treatment is determined by the health plan based on an independent, peer review of literature and scientific data. I&E molecular and genomic tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact.

Investigational and Experimental Determinations

Molecular and genomic tests are routinely released to market that make use of novel technologies or have a novel clinical application. These tests are often available on a clinical basis long before the required evidence to support clinical validity and clinical utility are established. Typically, there is insufficient data to support that the test

- accurately assesses the outcome of interest, analytical and clinical validity
- significantly improves health outcomes, clinical utility, and
- performs better than an existing standard of care medical management option.

Because these tests are often proprietary, there may be no independent test evaluation data available in the early stages to support the laboratory's claims regarding test performance and utility.

As new molecular and genomic tests become commercially available, the evidence base is reviewed. Tests determined to be I&E by the Health Plan are addressed by this guideline or a test-specific guideline and are not eligible for reimbursement.

Food and Drug Administration (FDA) clearance

In the case of laboratory testing, FDA clearance is not a suitable standard given that the clearance assessment does not require evidence to support clinical utility. In addition, while the FDA has stated that it has the discretion to regulate laboratory developed tests (LDTs), it is currently only selectively exercising that discretion to take action against egregious practices.

Criteria

Introduction

This section catalogues some, but not all, molecular and genomic tests that have

been determined to be investigational and experimental (I&E). I&E tests may also be addressed in test-specific guidelines and the reader is referred to those documents for additional information. New I&E tests may not yet be specifically listed in this guideline, but such decisions will be made using the following criteria.

Criteria: General Coverage Guidance

Molecular and genomic tests are only eligible for reimbursement when ALL of the following conditions are met:

- **Technical and clinical validity: The test must be accurate, sensitive and specific, based on sufficient, quality scientific evidence to support the claims of the test.**
- **Clinical utility: Healthcare providers can use the test results to provide significantly better medical care for the individual.**
- **Reasonable use: The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social or ethical challenges.**

Novel Oncology Molecular and Genomic Tests

The following tests used in the screening, diagnosis, prognostication, and treatment decision-making for various neoplasms do not meet the above criteria and are not eligible for reimbursement.

Gene Expression Assays

- **BluePrint Molecular Subtyping Profile [Proprietary 80-gene expression signature to classify Basal-type, Luminal-type and ERBB2-type breast cancers from Agendia] CPT: 81479**
- **ColonSentry [Proprietary 7-gene signature to detect colorectal cancer from StageZero Life Sciences] CPT: 81479**
- **Decipher Bladder TURBT [Oncology (bladder), mRNA, microarray gene expression profiling of 219 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as molecular subtype (luminal, luminal infiltrated, basal, basal claudin-low, neuroendocrine-like)] CPT: 0016M**
- **DecisionDx - Cutaneous Melanoma assay [Proprietary 31-gene signature to assess melanoma metastatic risk from Castle Biosciences] CPT: 81529**
- **DecisionDx DiffDx - Melanoma [Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 35 genes (32 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical result (ie, benign, intermediate, malignant) from Castle Biosciences, Inc] CPT: 0314U**

- DecisionDx - SCC [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) from Castle Biosciences, Inc] CPT: 0315U
- Envisia Genomic Classifier [Proprietary gene expression assay designed to aid in the diagnosis of idiopathic pulmonary fibrosis from Veracyte] CPT: 81554
- EpiSwitch CiRT (Checkpoint-inhibitor Response Test) [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 from Next Bio-Research Services, LLC] CPT: 0332U
- ExoDx Prostate (IntelliScore) [Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score from Exosome Diagnostics, Inc.] CPT: 0005U
- Insight TNBCtype [Oncology (breast), mRNA, gene expression profiling by next-generation sequencing of 101 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a triple negative breast cancer clinical subtype(s) with information on immune cell involvement from Insight Molecular Labs] CPT: 0153U
- Lymph2Cx Lymphoma Molecular Subtyping Assay, [Oncology (diffuse large B-cell lymphoma [DLBCL]), mRNA, gene expression profiling by fluorescent probe hybridization of 20 genes, formalin-fixed paraffin embedded tissue, algorithm reported as cell of origin from Mayo Clinic] CPT: 0017M
- Lymph3Cx Lymphoma Molecular Subtyping Assay, [Oncology (B-cell lymphoma classification), mRNA, gene expression profiling by fluorescent probe hybridization of 58 genes (45 content and 13 housekeeping genes), formalin-fixed paraffin-embedded tissue, algorithm reported as likelihood for primary mediastinal B-cell lymphoma (PMBCL) and diffuse large B-cell lymphoma (DLBCL) with cell of origin subtyping in the latter from Mayo Clinic] CPT: 0120U
- miR-31now [Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin fixed paraffin-embedded tissue, algorithm reported as an expression score from GoPath Laboratories] CPT: 0069U
- mRNA CancerDetect [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 from Viome Life Sciences, Inc] CPT: 0296U

- **Myeloma Prognostic Risk Signature (myPRS) [Proprietary gene expression assay that is designed to predict an individual's risk of early relapse of multiple myeloma from Quest Diagnostics] CPT: 81479**
- **myPath Melanoma [Proprietary 23-gene expression assay to assess the risk of malignant melanoma when a result cannot be obtained by clinical assessment and/or histopathology alone from Castle Biosciences, Inc] CPT: 0090U**
- **OncoSignal 7 Pathway Signal [Oncology (solid tumor), gene expression profiling by real-time RT-PCR of 7 gene pathways (ER, AR, PI3K, MAPK, HH, TGFB, Notch), formalin-fixed paraffin-embedded (FFPE), algorithm reported as gene pathway activity score from Protean BioDiagnostics] CPT: 0262U**
- **OncoTarget/OncoTreat [Oncology, RNA, gene expression by whole transcriptome sequencing, formalin-fixed paraffin embedded tissue or fresh frozen tissue, predictive algorithm reported as potential targets for therapeutic agents from Columbia University Department of Pathology and Cell Biology, Darwin Health] CPT: 0019U**
- **PancreaSeq Genomic Classifier [Oncology (pancreas), DNA and mRNA next-generation sequencing analysis of 74 genes and analysis of CEA (CEACAM5) gene expression, pancreatic cyst fluid, algorithm reported as a categorical result (ie, negative, low probability of neoplasia or positive, high probability of neoplasia) from Molecular and Genomic Pathology Laboratory, University of Pittsburgh Medical Center] CPT: 0313U**
- **Percepta Genomic Sequencing Classifier [Proprietary gene expression assay designed to assess the risk of malignancy of lung nodules from Veracyte] CPT: 81479**
- **Thyroid GuidePx [Oncology (papillary thyroid cancer), gene-expression profiling via targeted hybrid capture-enrichment RNA sequencing of 82 content genes and 10 housekeeping genes, formalin-fixed paraffin embedded (FFPE) tissue, algorithm reported as one of three molecular subtypes from Protean BioDiagnostics] CPT: 0362U**

Other Novel Assays

- **AssureMDx [Proprietary non-invasive assay that analyzes tumor markers in the urine of individuals with hematuria to identify those at low risk and high risk for bladder cancer by MDx Health] CPT: 81479**
- **Augusta Hematology Optical Genome Mapping [Oncology (hematolymphoid neoplasia), optical genome mapping for copy number alterations and gene rearrangements utilizing DNA from blood or bone marrow, report of clinically significant alternations from Georgia Esoteric and Molecular Labs] CPT: 0331U**

- BBDRisk Dx [Oncology (breast), immunohistochemistry, protein expression profiling of 4 biomarkers (matrix metalloproteinase-1 [MMP-1], carcinoembryonic antigen-related cell adhesion molecule 6 [CEACAM6], hyaluronoglucosaminidase [HYAL1], highly expressed in cancer protein [HEC1]), formalin-fixed paraffin-embedded precancerous breast tissue, algorithm reported as carcinoma risk score from Silbiotech, Inc] CPT: 0067U
- ChemoFX [Proprietary test from Helomics to assess chemosensitivity] CPT: 81535, 81536
- clonoSEQ [Proprietary test that determines measurable residual disease (MRD) in the form of residual clonal cells to monitor changes in the disease burden during and post-treatment from Adaptive Biotechnologies] CPT: 81479
- Colvera [BCAT1 (Branched chain amino acid transaminase 1) and IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis from Colvera] CPT: 0229U
- DEPArray [Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin fixed paraffin embedded tissue isolated using image-based dielectrophoresis (DEP) sorting, reported as ERBB2 gene amplified or non-amplified from PacificDx] CPT: 0009U
- DetermaRx [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 from Oncocyte Corporation] CPT: 0288U
- Digitization of pathology slides CPT: 0760T, 0761T, 0762T, 0763T
- GPS Cancer [Proprietary test using a tissue block sample of the highest carcinoma grade of a tumor and a sample of blood to compare an individual's normal DNA to the tumor DNA to be used as part of a precision medicine approach for individuals with cancer from NantHealth] CPT: 81479
- HelioLiver Test [Oncology (liver), surveillance for hepatocellular carcinoma (HCC) in high-risk patients, analysis of methylation patterns on circulating cell-free DNA (cfDNA) plus measurement of serum of AFP/AFP-L3 and oncoprotein des-gamma-carboxy prothrombin (DCP), algorithm reported as normal or abnormal result from Fulgent Genetics] CPT: 0333U
- HERmark Breast Cancer Assay [Proprietary test designed to evaluate Her-2 total proteins in formalin-fixed, paraffin-embedded (FFPE) tissue specimens from LabCorp] CPT: 84999
- Invitae PCM MRD Monitoring [Oncology (minimal residual disease [MRD]), next-generation targeted sequencing analysis of a patient-specific panel, cell-free DNA, subsequent assessment with comparison to previously analyzed patient specimens to evaluate for MRD from Invitae Corporation] CPT: 0307U

- **Invitae PCM Tissue Profiling and MRD Baseline Assay [Oncology (minimal residual disease [MRD]), next-generation targeted sequencing analysis, cell-free DNA, initial (baseline) assessment to determine a patient specific panel for future comparisons to evaluate for MRD from Invitae Corporation] CPT: 0306U**
- **Know error [Proprietary test for DNA based specimen provenance confirmation from Strand Diagnostics] CPT: 81479, 84999, 81265, 81266**
- **LungLB [Oncology (lung cancer), four-probe FISH (3q29, 3p22.1, 10q22.3, 10cen) assay, whole blood, predictive algorithm generated evaluation reported as decreased or increased risk for lung cancer from LungLife AI] CPT: 0317U**
- **Mammostrat Breast Cancer Recurrence Assay [Proprietary immunohistochemical (IHC) assay of 5 proteins in individuals with early stage breast cancer to assess recurrence risk from Clarient, Inc.] CPT: 84999, S3854**
- **miR Sentinel Prostate Cancer Test [Oncology (prostate), exosome-based analysis of 442 small noncoding RNAs (sncRNAs) by quantitative reverse transcription polymerase chainreaction (RT-qPCR), urine, reported as molecular evidence of no-, low-, intermediate- or high-risk of prostate cancer from miR Scientific, LLC] CPT: 0343U**
- **Mitomic Prostate Test [Proprietary test using mitochondrial DNA to detect prostate cancer not identified by standard biopsy pathology from MDNA Life Sciences] CPT: none; research use only**
- **MyProstateScore (MPS, MIPS, previously Mi-Prostate Score) [urine analysis of TMPRSS2:ERG and PCA3 genes combined with blood PSA levels for early detection of prostate cancer from Lynx Dx] CPT: 81599 or 0113U**
- **NavDx [Oncology (oropharyngeal), evaluation of 17 DNA biomarkers using droplet digital PCR (ddPCR), cell-free DNA, algorithm reported as a prognostic risk score for cancer recurrence from Naveris] CPT: 0356U**
- **Oncomap ExTra [Oncology (neoplasia), exome and transcriptome sequence analysis for sequence variants, gene copy number amplifications and deletions, gene rearrangements, microsatellite instability and tumor mutational burden utilizing DNA and RNA from tumor with DNA from normal blood or saliva for subtraction, report of clinically significant mutation(s) with therapy associations from Exact Sciences] CPT: 0329U**
- **OncotypeDx AR-V7 Nucleus Detect [Proprietary test designed to detect AR-V7 proteins in the nucleus of CTCs to determine response to AR-targeted therapies from Genomic Health] CPT: 81479**
- **PanGIA Prostate [Oncology (prostate), multianalyte molecular profile by photometric detection of macromolecules adsorbed on nanosponge array slides with machine learning, utilizing first morning voided urine, algorithm**

reported as likelihood of prostate cancer from Genetics Institute of America] CPT: 0228U

- PAULA [Proprietary panel of four proteins designed to detect lung cancer in asymptomatic individuals at high risk from Genesys Biolabs] CPT: none; no insurance billing
- Praxis Somatic Combined Whole Genome Sequencing and Optical Genome Mapping [Oncology (pan tumor), whole genome sequencing and optical genome mapping of paired malignant and normal DNA specimens, fresh tissue, blood, or bone marrow, comparative sequence analyses and variant identification from Praxis Genomics LLC] CPT: 0300U
- Praxis Somatic Optical Genome Mapping [Oncology (pan tumor), whole genome optical genome mapping of paired malignant and normal DNA specimens, fresh frozen tissue, blood, or bone marrow, comparative structural variant identification from Praxis Genomics LLC] CPT: 0299U
- Praxis Somatic Transcriptome [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 from Praxis Genomics LLC] CPT: 0298U
- Praxis Somatic Whole Genome Sequencing [Oncology (pan tumor), whole genome sequencing of paired malignant and normal DNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and variant identification from Praxis Genomics LLC] CPT: 0297U
- PreciseDx Breast Cancer Test [Oncology (breast cancer), image analysis with artificial intelligence assessment of 12 histologic and immunohistochemical features, reported as a recurrence score from PreciseDx] CPT: 0220U
- ProMark Proteomic Prognostic Test [Proprietary proteomic assay designed to assess the risk of aggressive prostate cancer from Metamark] CPT: 81479
- Prostate Cancer Risk Panel [FISH analysis of 4 genes (ASAP1, HDAC9, CHD1 and PTEN), needle biopsy specimen, algorithm reported as probability of higher tumor grade from Mayo Clinic] CPT: 0053U
- RadTox cfDNA test [Oncology, response to radiation, cell-free DNA, quantitative branched chain DNA amplification, plasma, reported as a radiation toxicity score from DiaCarta Inc] CPT: 0285U
- ROMA Risk of Ovarian Malignancy Algorithm [Proprietary test using the combination of CA125 + HE4 antigens to assess the likelihood of malignancy before surgery; test kit from Fujirebio Diagnostics, Inc. and offered by several reference laboratories] CPT: 81500

- Signatera [Oncology (pan-cancer), analysis of minimal residual disease (MRD) from plasma, with assays personalized to each patient based on prior next generation sequencing of the patient's tumor and germline DNA, reported as absence or presence of MRD, with disease-burden correlation, if appropriate from Natera, Inc] CPT: 0340U
- Targeted genomic sequence analysis panel, solid organ neoplasm, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, MET, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis CPT: 81449
- Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis CPT: 81456
- Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NOTCH1, NPM1, NRAS), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis CPT: 81451
- ToxLok [Comparative DNA analysis using multiple selected single-nucleotide polymorphisms (SNPs), urine and buccal DNA, for specimen identity verification from InSource Diagnostics] CPT: 0079U

Cardiovascular Molecular and Genomic Tests

The following tests used to predict cardiovascular disease and/or direct therapy do not meet the above criteria and are not eligible for reimbursement.

- 4q25-AF Risk Genotype Test (rs2200733 allele) CPT: 81479
- 9p21 Genotype Test (rs10757278 and rs1333049 alleles) CPT: 81479
- Apolipoprotein E Genotype (APOE) CPT: 81401
- KIF6 Genotype Test CPT: 81479
- LPA-Aspirin Genotype Test (4399Met allele) CPT: 81479
- LPA-Intron 25 Genotype Test CPT: 81479
- myTAIHEART CPT: 0055U
- PAI-1 Testing for Cardiovascular Disease Risk Assessment CPT: 81400, 85415
- Statin Induced Myopathy Genotype (SLCO1B1) CPT: 81328

Gene Variant or Marker Risk Assessment Tests

The following tests that make use of inherited genomic information to assess disease risk, prognosis, or subtyping do not meet the above criteria and are not eligible for reimbursement.

- **AlloSure Heart [Proprietary non-invasive assay to screen for organ injury and rejection in heart transplant recipients through measurement of donor-derived cell-free DNA in recipient blood sample from CareDx] CPT: 81479**
- **AlloSure Lung [Proprietary non-invasive assay to screen for organ injury and rejection in lung transplant recipients through measurement of donor-derived cell-free DNA in recipient blood sample from CareDx] CPT: 81479**
- **Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping [APOL1 (apolipoprotein L1) (eg, chronic kidney disease), risk variants (G1, G2) from Quest Diagnostics] CPT: 0355U**
- **ARISk Autism Risk Assessment Test [Proprietary test from IntegraGen] CPT: 81479**
- **Augusta Optical Genome Mapping [Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping from Bionano Genomics, Inc] CPT: 0260U**
- **Cardiac DNA Insight [Proprietary test from Pathway Genomics that assesses genetic markers for cardiac-related conditions] CPT: 81225, 81226, 81227, 81240, 81241, 81291, 81355, 81400, 81401, 81479**
- **Clarifi ASD [Neurology (autism spectrum disorder [ASD]), RNA, next-generation sequencing, saliva, algorithmic analysis, and results reported as predictive probability of ASD diagnosis from Quadrant Biosciences] CPT: 0170U**
- **CNGnome [Cytogenomic constitutional (genome-wide) analysis, interrogation of genomic regions for copy number, structural changes and areas of homozygosity for chromosomal abnormalities from PerkinElmer Genomics] CPT: 0209U**
- **Crohn's prognostic test [NOD2/CARD15 gene variant testing] CPT: 81401**
- **EpiSign Complete [Pediatrics (congenital epigenetic disorders), whole genome methylation analysis by microarray for 50 or more genes, blood from Greenwood Genetic Center] CPT: 0318U**
- **ERA (Endometrial Receptivity Analysis) [Reproductive medicine (endometrial receptivity analysis), RNA gene expression profile, 238 genes by next-generation sequencing, endometrial tissue, predictive algorithm reported as endometrial window of implantation (eg, pre-receptive, receptive, post-receptive) from Igenomix] CPT: 0253U**

- **EsoGuard [Gastroenterology (Barrett's esophagus), VIM and CCNA1 methylation analysis, esophageal cells, algorithm reported as likelihood for Barrett's esophagus from Lucid Diagnostics] CPT: 0114U**
- **FM/a fibromyalgia [interleukin-6, interleukin-8, macrophage inflammatory protein-1 alpha and macrophage inflammatory protein-beta (IL-6, IL-8, MIP-1a and MIP-1b, supernatant of stimulated cell culture, immunoassay, multianalyte assay with algorithmic analysis, reported as a score from EpicGenetics, Inc] CPT: 81599**
- **IBD sgi Diagnostic [Proprietary test from Prometheus with genomic components including ATG16L1, STAT3, NKX2-3, and ECM1 gene variants.] CPT: 81479, 82397, 83520, 86140, 86255, 88346, 88350**
- **IriSight Prenatal Analysis – Proband [Rare diseases (constitutional/heritable disorders), whole genome sequence analysis, including small sequence changes, copy number variants, deletions, duplications, mobile element insertions, uniparental disomy (UPD), inversions, aneuploidy, mitochondrial genome sequence analysis with heteroplasmy and large deletions, short tandem repeat (STR) gene expansions, fetal sample, identification and categorization of genetic variants from Variantyx, Inc] CPT: 0335U**
- **IriSight Prenatal Analysis – Comparator [Rare diseases (constitutional/heritable disorders), whole genome sequence analysis, including small sequence changes, copy number variants, deletions, duplications, mobile element insertions, uniparental disomy (UPD), inversions, aneuploidy, mitochondrial genome sequence analysis with heteroplasmy and large deletions, short tandem repeat (STR) gene expansions, blood or saliva, identification and categorization of genetic variants, each comparator genome (eg, parent) from Variantyx, Inc] CPT: 0336U**
- **LactoTYPE [Proprietary test from Prometheus that assesses the hypolactasia C/T genetic variant] CPT: 81400**
- **MethylDetox Profile [The MethylDetox Profile test is a testing panel that assesses genes in the methylation pathway to provide "more actionable information than MTHFR testing alone" and provides "suggestions for specific nutrient needs" based on test findings from Cell Science Systems] CPT: none; no insurance billing**
- **MindX Blood Test - Longevity [Longevity and mortality risk, mRNA, gene expression profiling by RNA sequencing of 18 genes, whole blood, algorithm reported as predictive risk score from MindX Sciences Inc] CPT: 0294U**
- **MindX Blood Test - Memory/Alzheimer's [Neurology (Alzheimer disease), mRNA, gene expression profiling by RNA sequencing of 24 genes, whole blood, algorithm reported as predictive risk score from MindX Sciences Inc] CPT: 0289U**

- **MindX Blood Test - Mood [Psychiatry (mood disorders), mRNA, gene expression profiling by RNA sequencing of 144 genes, whole blood, algorithm reported as predictive risk score from MindX Sciences Inc] CPT: 0291U**
- **MindX Blood Test - Pain [Pain management, mRNA, gene expression profiling by RNA sequencing of 36 genes, whole blood, algorithm reported as predictive risk score from MindX Sciences Inc] CPT: 0290U**
- **MindX Blood Test - Stress [Psychiatry (stress disorders), mRNA, gene expression profiling by RNA sequencing of 72 genes, whole blood, algorithm reported as predictive risk score from MindX Sciences Inc] CPT: 0292U**
- **MindX Blood Test - Suicidality [Psychiatry (suicidal ideation), mRNA, gene expression profiling by RNA sequencing of 54 genes, whole blood, algorithm reported as predictive risk score from MindX Sciences Inc] CPT: 0293U**
- **Pathway Fit [Proprietary test from Pathway Genomics that focuses on metabolism, diet, and exercise traits] CPT: 81291, 81401, 81479**
- **POC (Products of Conception) [Fetal aneuploidy short tandem–repeat comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy from Igenomix] CPT: 0252U**
- **Praxis Optical Genome Mapping [Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping from Praxis Genomics, LLC] CPT: 0264U**
- **Praxis Transcriptome [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 from Praxis Genomics, LLC] CPT: 0266U**
- **PrismRA [Molecular signature predicting likelihood of non-response to TNF inhibitor therapies from Scipher Medicine] CPT: 81479 or 81599**
- **Prospera [Proprietary non-invasive assay that uses a single-nucleotide polymorphism (SNP)-based technology to evaluate active allograft rejection by measuring the DNA derived from transplanted donor kidneys; from Natera] CPT: 81479**
- **RetnaGene AMD [Proprietary test from Sequenom CMM to predict risk of wet AMD progression] CPT: 81401, 81405, 81408, 81479, 81599**
- **Single Cell Prenatal Diagnosis (SCPD) Test [Fetal aneuploidy DNA sequencing comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploid from Luna Genetics, Inc] CPT: 0341U**

- SMART PGT-A (Pre-implantation Genetic Testing - Aneuploidy) [Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy, per embryo tested from Igenomix] CPT: 0254U
- SMASH [Copy number (eg, intellectual disability, dysmorphology), sequence analysis from Marvel Genomics] CPT: 0156U
- Twin zygosity [genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood from Natera] CPT: 0060U
- Viracor TRAC dd-cfDNA [Transplantation medicine, quantification of donor-derived cell-free DNA using whole genome next-generation sequencing, plasma, reported as percentage of donor-derived cell-free DNA in the total cell-free DNA from Viracor Eurofins] CPT: 0118U
- Vita Risk [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 from Arctic Medical Laboratories] CPT: 0205U

Non-cancer Gene Expression Assays

- Clarava [Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using pretransplant peripheral blood from Verici Dx, Inc] CPT: 0319U
- Mind.Px [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 from Mindera Corporation] CPT: 0258U
- Molecular Microscope MMDx—Heart [Transplantation medicine (heart allograft rejection), microarray gene expression profiling of 1283 genes, utilizing transplant biopsy tissue, algorithm reported as a probability score for rejection from Kashi Clinical Laboratories] CPT: 0087U
- Molecular Microscope MMDx—Kidney [Transplantation medicine (kidney allograft rejection), microarray gene expression profiling of 1494 genes, utilizing transplant biopsy tissue, algorithm reported as a probability score for rejection from Kashi Clinical Laboratories] CPT: 0088U
- PredictSURE IBD Test [Autoimmune (inflammatory bowel disease), mRNA, gene expression profiling by quantitative RT-PCR, 17 genes (15 target and 2 reference genes), whole blood, reported as a continuous risk score and

classification of inflammatory bowel disease aggressiveness from KSL Diagnostics, PredictImmune Ltd] CPT: 0203U

- TruGraf Kidney [gene expression profile of mRNA from 107 inflammatory pathway genes to rule out subclinical rejection in renal transplant patients from Eurofins Transplant Genomics] CPT: 81479
- Tuteva [Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using posttransplant peripheral blood, algorithm reported as a risk score for acute cellular rejection from Verici Dx, Inc] CPT: 0320U
- Vectra [Proprietary panel of 12 biomarkers that yields a rheumatoid arthritis disease activity score from LabCorp] CPT: 81490

Infectious Disease Assays

- Accelerate PhenoTest BC kit [Infectious disease (bacterial and fungal), organism identification, blood culture, using rRNA FISH, 6 or more organism targets, reported as positive or negative with phenotypic minimum inhibitory concentration (MIC)-based antimicrobial susceptibility from Accelerate Diagnostics, Inc] CPT: 0086U
- Accelerate PhenoTest® BC kit, AST configuration [Infectious disease (bacterial), quantitative antimicrobial susceptibility reported as phenotypic minimum inhibitory concentration (MIC)–based antimicrobial susceptibility for each organisms identified from Accelerate Diagnostics, Inc] CPT: 0311U
- AmHPR Helicobacter pylori Antibiotic Resistance Next Generation Sequencing Panel [Helicobacter pylori detection and antibiotic resistance, DNA, 16S and 23S rRNA, gyrA, pbp1, rdxA and rpoB, next generation sequencing, formalin-fixed paraffin embedded or fresh tissue, predictive, reported as positive or negative for resistance to clarithromycin, fluoroquinolones, metronidazole, amoxicillin, tetracycline and rifabutin from American Molecular Laboratories, Inc.] CPT: 0008U
- Bacterial Typing by Whole Genome Sequencing [Infectious disease (bacterial), strain typing by whole genome sequencing, phylogenetic-based report of strain relatedness, per submitted isolate from Mayo Clinic] CPT: 0010U
- Bartonella ddPCR and Digital ePCR [Droplet digital PCR-based assay for detection of multiple species of Bartonella from Galaxy Diagnostics] CPT 0301U, 0302U
- Bridge Urinary Tract Infection Detection and Resistance Test [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 from Bridge Diagnostics] CPT: 0321U

- **Bridge Women's Health Infectious Disease Detection Test [Infectious agent detection by nucleic acid (DNA or RNA), vaginal pathogen panel, identification of 27 organisms, amplified probe technique, vaginal swab from Bridge Diagnostics] CPT: 0330U**
- **Johns Hopkins Metagenomic Next Generation Sequencing Assay for Infectious Disease Diagnostics [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 from Johns Hopkins Medical Microbiology Laboratory] CPT: 0323U**
- **Karius Test [Infectious disease (bacteria, fungi, parasites, and DNA viruses), microbial cell-free DNA, plasma, untargeted next-generation sequencing, report for significant positive pathogens from Karius Inc] CPT: 0152U**
- **MicroGenDX qPCR & NGS For Infection, [Infectious agent detection and identification, targeted sequence analysis (16S and 18S rRNA genes) with drug-resistance gene from MicroGenDX] CPT: 0112U**
- **MycoDART Dual Amplification Real Time PCR Panel for 4 Aspergillus species [Infectious disease (Aspergillus species), real-time PCR for detection of DNA from 4 species (A. fumigatus, A. terreus, A. niger, and A. flavus), blood, lavage fluid, or tissue, qualitative reporting of presence or absence of each species from RealTime Laboratories, Inc/MycoDART, Inc] CPT: 0109U**
- **PCR Fungal Screen for Onychomycosis [Molecular tests for onychomycosis (e.g. Bako Diagnostics Onychodystrophy DNA Test)] CPT: 87481, 87798**

400 Buckwalter Place Boulevard, Bluffton, SC 29910 (800) 918-8924