Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Joint Medical Policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and is therefore subject to change.

***Current Policy Effective Date: 11/1/22**
(See policy history boxes for previous effective dates)

Title: Genetic, Molecular and Other Tests- Experimental/Investigational Status

Description/Background

The Health and Human Services (HHS) Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) defined genetic or genomic testing as testing that "involves an analysis of human chromosomes, deoxyribonucleic acid, ribonucleic acid, genes, and/or gene products (e.g., enzymes and other types of proteins), which is predominately used to detect heritable or somatic mutations, genotypes, or phenotypes related to disease and health.[1] The purpose of genetic tests includes predicting risk of disease, screening newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations." They are also performed to screen fetuses or embryos used prior to implantation after in vitro fertilization for genetic defects.

Genetic testing searches for alterations or mutations in a person's chromosomes or genes as well as changes in the level or structure of key proteins coded for by specific genes. Genetic tests can also be used to look at levels of RNA that play a role in certain conditions. Abnormal results on these tests could mean that someone has a genetic disorder or may have a propensity to develop certain diseases later in life.

Genetic tests have been developed for more than 2,200 diseases, of which about 2,000 are currently available for use in clinical settings. Most tests look at single genes and are used to diagnose rare genetic disorders, such as Fragile X Syndrome and Duchenne Muscular Dystrophy. In addition, some genetic tests look at rare inherited mutations of otherwise protective genes, such as *BRCA1* and *BRCA2*, which are responsible for some hereditary breast and ovarian cancers. However, a growing number of tests are being developed to look at multiple genes that may increase or decrease a person's risk of common diseases, such as cancer or diabetes. Such tests and other applications of genomic technologies have the potential to help manage (MBB- tests don't prevent disease) common disease and improve the health of individuals and populations.

Many disease entities arise from errors or defects in our genes and/or how genetic information is processed. Through the proteins they encode, genes determine how efficiently we process foods, how effectively we detoxify poisons and how vigorously we respond to infections. A large number of diseases are thought to stem from genetic mutations that arise in a de novo fashion (sporadically) or are inherited from one (dominant) or both (recessive) parents. Common disorders such as heart disease and most cancers arise from a complex interplay among multiple genes and between genes and factors in the environment.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of these tests.

Medical Policy Statement

The tests listed in this policy have been determined to be Investigational/Experimental. They are not a covered benefit for all contracts that exclude reimbursement for investigational services.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Exclusions:

Table 1. Tests determined by BCBSM to be Investigational/Experimental

Test Name	Code(s)	FDA Approved	Medical Policy
4Kscore Test	81313, 81479, 0010M	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Adenosine Triphosphate Bioluminescence Assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
AdMark CSF Analysis	83520,84999	No	Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer's Disease
AlzheimAlert	83520,84999	No	Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer's Disease
Ambry Genetic Panel	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
2ntegr IFX	84999	No*	Measurement of Serum Antibodies to Selected Biologic Agents
2ntegr ADA	84999	No*	Measurement of Serum Antibodies to Selected Biologic Agents

Apifiny	0021U	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
ARCHITECT HE4	86305	Yes	Serum Biomarker Human Epididymis Protein 4 (HE4)
ATM Variants (Ataxia-telangiectasia mutated)	81408	No	Genetic Testing Moderate Penetrance Variants Associated with Breast Cancer
Avise MTX	84999	No*	Methotrexate (MTX) Polyglutamate Testing To Measure Response To Methotrexate Therapy
Axis-Shield HoloTC Assay	84999	Yes	Holotranscobalamin as a Marker of Vitamin B12 (Cobalamin) Status
BD-MAX™ Vaginal Panel	81514	No	Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis
BGM Galectin-3 InVitro Diagnostic Assay	82777	Yes	Galectin-3 Testing in the Management of Chronic Heart Failure
Blue Print	81599	No*	Genetic Testing – Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
Boston Heart Cardiovascular Risk Panel	84999, 81599	No*	Cardiovascular Risk Panels
BRACAPlus	81479	No*	Genetic Testing for Hereditary Breast and/or Ovarian Cancer, Including Multigene Panels
Breast Next	81479	No*	Genetic Testing for Hereditary Breast and/or Ovarian Cancer, Including Multigene Panels Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
BROCA Cancer Risk Panel	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing Genetic Testing for Hereditary Breast and/or Ovarian Cancer Syndrome (BRCA1/BRCA2), Including Multigene Panels
CanerIntercept® Detect	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
Candidate Gene Panels	81313, 81479, 0010M	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Cardiac Panel	84999, 81599	No*	Cardiovascular Risk Panels
Cardiac Risk Panel	84999, 81599	Yes	Cardiovascular Risk Panels
Cardiovascular Risk Panel	84999, 81599	No*	Cardiovascular Risk Panels
Cancer Next	81479	No	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
Cancer TYPE ID	81504, 81540	No	Genetic Testing-Microarray Testing for Cancers of Unknown Primary (CUP) Origin
Caris Life Sciences Panel	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing
Celiac PLUS	81382, 82784, 83520, 86255	No	Miscellaneous Genetic and Molecular Diagnostic Tests
CellMax-CRC Colorectal Cancer Early Detection Test	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
Cellsearch® CTC	86152, 86153		Genetic Testing for KRAS, NRAS and BRAF Mutation Analysis in Metastatic Colorectal Cancer.

Noninvasive prenatal screening for microdeletions using cell-free fetal DNA (cfDNA)	81422	No	Genetic Testing-Noninvasive Prenatal Screening For Fetal Aneuploidies and Microdeletions Using Cell-Free Fetal DNA
CHEK2	G0452, 81479	No	Genetic Testing for CHEK2 Mutations for Breast Cancer
Chemo FX	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
ClearID Solid Tumor Panel	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
ColoNext	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
ColoPrint	81525, 81599, 84999, 88299	No*	Genetic Testing-Multigene Expression Assay for Predicting Recurrence in Colon Cancer (e.g., Coloprint, Colon PRS, GeneFx, OncoDefender, Oncotype Dx® Colon Cancer Test)
Colon PRS	81525, 81599, 84999, 88299	No*	Genetic Testing-Multigene Expression Assay for Predicting Recurrence in Colon Cancer (e.g., Coloprint, Colon PRS, GeneFx, OncoDefender, Oncotype Dx® Colon Cancer Test)
ColoSentry	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
ColoSeq Gene Panel	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
Colosure	81528	No*	Analysis of Human DNA in Stool Samples as a Technique for Colorectal Cancer Screening
Colvera	0229U	No	Gene Expression Profile Testing and Circulating Tumor DNA Testing for Predicting Recurrence in Colon Cancer
ConfirmMDX	S3721, 81313 81551	No	Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer
Correct Chemo Assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
CorusCAD	81599, 84999	No	Gene Expression Testing to Predict Coronary Artery Disease
Courtagan epiSEEK	81401, 81403, 81404, 81405, 81406, 81407, 81479	No	Genetic Testing for Epilepsy (not related to infantile or early childhood onset)
Crohn's Prognostic	81401, 83520, 86021, 86255	No	Miscellaneous Genetic and Molecular Diagnostic Tests
CSTB (cystatin B)	0234U	No	Genetic Testing for Rett Syndrome
CVD Inflammatory Profile	84999, 81599	No*	Cardiovascular Risk Panels
CV Health Plus Panel	84999, 81599	Yes	Cardiovascular Risk Panels
Cxbladder™	81479	No	Urinary Tumor Markers for Bladder Cancer
Cytoprint (Fluorescence Assay)	81599	No	Chemosensitivity and Chemoresistance Assay, In Vitro

DCP (des-gamma-carboxy-prothrombin)	83591	No	Oncoprotein Des-gamma-carboxy Prothrombin Immunoassay
DecisionDx-Melanoma	81479, 81599, 84999, 81529	No	Gene Expression Profiling for Cutaneous Melanoma
Des-gamma-carboxy-prothrombin	83591	No*	Oncoprotein Des-gamma-carboxy Prothrombin (DCP) Immunoassay

Dimension MPO Flex Reagent Cartridge	83876	Yes	Myeloperoxidase (MPO) Immunoassay for Cardiac Disease Risk
DiSC Assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
Emory Gentetics Epilesy and Seizure Disorder Panel	81401, 81403, 81404, 81405, 81406, 81407, 81479	No	Genetic Testing for Epilepsy (not related to infantile or early childhood onset)
Envisia™	81554	No	Miscellaneous Genetic and Molecular Diagnostic Tests
Eq-PRC LightCycler Warfarin Genotype Kit	G9143, 81227, 81355	Yes	Genetic Testing for Warfarin Dosing
EVA/PCD	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
eSensor Warfarin Sensitivity Testing	G9143, 81227, 81355	Yes	Genetic Testing for Warfarin Dosing
Extreme Drug Resistant Assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
Fluorometric microculture cytotoxicity assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
FMR2 (AFF2) variant testing	81171, 81172	No*	Genetic Testing for FMR1 and FMR2 Variants (including Fragile X and Fragile XE Syndromes)
Foundation One Liquid (previously FoundationAct)	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
Foundation One CDX, mRNA breast cancer	81522	No	Genetic Testing—Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
Genecept Assay	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
Gene DX Comprehensive Epilepsy Panel	81401, 81403, 81404, 81405, 81406, 81407, 81479	No	Genetic Testing for Epilepsy (not related to infantile or early childhood onset)
GeneFX Colon	81525, 81599, 84999, 88299	No*	Genetic Testing-Multigene Expression Assay for Predicting Recurrence in Colon Cancer (e.g., Coloprint, Colon PRS, GeneFx, OncoDefender, Oncotype Dx® Colon Cancer Test)
GeneSight Analgesic	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management
GeneSight Psychotropic Panel	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
GeneSight pharmacogenomics	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
GeneSight RX	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
Gen-Probe PROGENSA PCA3 Assay	S3721, 81313	Yes	Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer
Gene Trails Solid Tumor Panel	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing
GI Effects Stool Test	84999	No	Miscellaneous Genetic and Molecular Diagnostic Tests

Guardant360® Liquid Biopsy	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
GYN Plus	81479	No	Genertic Cancer Susceptibility Panels Using Next Generation Sequencing
Heart's Breath	0085T, 88299, 86849, 81495	Yes	Laboratory Tests for Heart Transplant Rejection
HE4 EIA	86305	Yes	Serum Biomarker Human Epididymis Protein 4 (HE4)
Histoculture Drug Resistant Assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
Human ST2/IL-1 R4 DuoSet	83006	No	ST2 Assay for Chronic Heart Failure
IBD sgi Diagnostic	83520, 82397, 86140, 88347, 81479	No	Miscellaneous Genetic and Molecular Diagnostic Tests and Serum Markers for the Diagnosis of IBD
Idgenetix Panel	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
Illumina TruSight	81445, 81450, 81460, 81465	No*	Genetic Testing-Molecular Panel Testing of Cancers to Identify Targeted Therapies
ImmunoGenomic Profile	81479	No	Miscellaneous Genetic and Molecular Diagnostic Tests
Infiniti 2C9-VKORC1 Multiplex Assay for Warfarin	G9143, 81227, 81355	Yes	Genetic Testing for Warfarin Dosing
iGene Cancer Panel	81479	No*	Genetic Testing for Hereditary Breast and/or Ovarian Cancer, Including Multigene Panels
Innotest for T-tau/P-tau & AB-42	81445, 81450, 81460, 81465, 83520, 84999	No	Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer's Disease
Ion AmpliSeq Panel	81445, 81450, 81460, 81465	No*	Genetic Testing-Molecular Panel Testing of Cancers to Identify Targeted Therapies
Ion AmpliSeq Cancer Hotspot Panel v2	81445, 81450, 81460, 81465	No*	Genetic Testing-Molecular Panel Testing of Cancers to Identify Targeted Therapies
Ion AmpliSeq Comprehensive Cancer Panel	81445, 81450, 81460, 81465	No*	Genetic Testing-Molecular Panel Testing of Cancers to Identify Targeted Therapies
Know Error DNA test	81479	No	Miscellaneous Genetic and Molecular Diagnostic Tests
Macula Risk	81401, 81405, 81408	No	Genetic Testing for Macular Degeneration
MBL ST2 ELISHA Kit	83006	No	ST2 Assay for Chronic Heart Failure
Melaris	81404	Yes	Genetic Testing for Familial Cutaneous Malignant Melanoma (CDKN2A)
Memorial Sloan Kettering – 6ntegrated Mutation Profiling of Actionable Caner Targets	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing
Mental Health DNA Insight panel	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
Methotrexate	80204	No	Methotrexate Polyglutamate Testing to Measure Response to Methotrexate Therapy
Microculture Kinectic Assay	89240, 81535,81536	No*	Chemosensitivity and Chemoresistance Assay, In Vitro
Millennium PGT (Pain Management) panel	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management
MI Profile	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing

miRInform® Thyroid	81599	No	Genetic Testing-Molecular Markers in Fine Needle Aspirates (FNA) of the Thyroid
miReview	81504, 81540	No	Genetic Testing-Microarray Testing for Cancers of Unknown Primary (CUP) Origin
Molecular Testing Labs™ Pain Management Panel	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management
MTHFR gene analysis	81291	No*	Genetic Testing for Inherited Thrombophilias
My5 FU	84999, S3722, 81400, 81401	Yes	Genetic and Laboratory Testing for Use of 5-Fluorouracil in Patients with Cancer
Multitarget Polymerase Chain Reaction Testing 711 for bacterial vaginosis	81513	No	Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis
myPath Melanoma	81479, 81599, 84999	No	Gene Expression Profiling for Cutaneous Melanoma
MyTAI Heart	0055U	No	Laboratory Tests for Heart and Kidney Transplant Rejection
Myriad myRisk	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
Noonan Syndrome Genetic Testing	81442	No*	Genetic Testing for Noonan Spectrum Disorder
OncoBEAM	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
Onco DX DCIS	S3854	No*	Genetic Testing – Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer

OncoDefender	81525, 81599, 84999, 88299	No*	Genetic Testing-Multigene Expression Assay for Predicting Recurrence in Colon Cancer (e.g., Coloprint, Colon PRS, GeneFx, OncoDefender, Oncotype Dx® Colon Cancer Test)
Oncoprotein DCP	83591	No	Oncoprotein Des-gamma-carboxy Prothrombin Immunoassay
Oncotype Dx Colon	81525, 81599, 84999, 88299	No*	Genetic Testing-Multigene Expression Assay for Predicting Recurrence in Colon Cancer (e.g., Coloprint, Colon PRS, GeneFx, OncoDefender, Oncotype Dx® Colon Cancer Test)
OnkoMatch	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing
OvaNext	81479	No*	Genetic Testing for Hereditary Breast and/or Ovarian Cancer, Including Multigene Panels
Pain Medication DNA Insight	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management
Panc Next	81479	No	Genertic Cancer Susceptibility Panels Using Next Generation Sequencing
PanGIA Prostate	0228U	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Paradigm Cancer Diagostic Panel	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing
PathFinder TG Barrett	84999, 89240	No*	Genetic Testing-Molecular Anatomic Pathology (PathFinder TG®)
PathFinder TG Biliary	84999, 89240	No*	Genetic Testing-Molecular Anatomic Pathology (PathFinder TG®)
Pathfinder TG Glioma	84999, 89240	No*	Genetic Testing-Molecular Anatomic Pathology (PathFinder TG®)
PathFinder Metastasis	84999, 89240	No*	Genetic Testing-Molecular Anatomic Pathology (PathFinder TG®)
PathFinder TG Molecular Test	84999, 89240	No*	Genetic Testing-Molecular Anatomic Pathology (PathFinder TG®)
PathFinder TG Pancreas	84999, 89240	No*	Genetic Testing-Molecular Anatomic Pathology (PathFinder TG®)
Pathway Genomics Pain Medication DNA Insight panel	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management
PathWork Tissue of Origin	81504, 81540	Yes	Genetic Testing-Microarray Testing for Cancers of Unknown Primary (CUP) Origin
PathWork Tissue of Origin FFPE	81504, 81540	Yes	Genetic Testing-Microarray Testing for Cancers of Unknown Primary (CUP) Origin
PCA3 Assay	S3721, 81313	Yes	Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer
PGL Next	81479	No	Genertic Cancer Susceptibility Panels Using Next Generation Sequencing
Pigmented Lesion Assay	81479, 81599, 84999	No	Gene Expression Profiling for Cutaneous Melanoma
PLAC Test	83698, 0423T	Yes	Lipoprotein-Associated Phospholipase A2 (Lp-PLA2) in the Assessment of Cardiovascular Risk

PlasmaSELECT	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
PreGen Plus	81528	No	Analysis of Human DNA in Stool Samples as a Technique for Colorectal Cancer Screening
Presage ST2 Assay	83006	Yes	ST2 Assay for Chronic Heart Failure
Pre-DX Diabetes Risk Score	81506	No*	Multianalyte Assays with Algorithmic Analysis for Predicting Risk of Type 2 Diabetes
Progensa PCA3 Assay	S3721, 81313	Yes	Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer
PrognostiX CardioMPO	83876	Yes	Myeloperoxidase (MPO) Immunoassay for Cardiac Disease Risk
Prometheus Anser IFX	84999	No*	Measurement of Serum Antibodies to Selected Biologic Agents
Prometheus Crohn's Prognostic Test	84999	No*	Serum Markers for the Diagnosis of Inflammatory Bowel Disease
Prometheus IBD sgi Diagnostic	84999	No*	Serum Markers for the Diagnosis of Inflammatory Bowel Disease
Proove Opiod Risk Panel	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels Genetic Testing for Pharmacogenetic Testing for Pain Management
Proove Narcotic Risk and Pain Perception panel	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management
Prosigna	S3854	No*	Genetic Testing – Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
Prospera™	81479	No	Laboratory Test Post Transplant and for Heart Failure
Prostarix	81313, 81479. 0010M	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Prostate Health Index	86316	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Prostrate Core Mitomics Test	81313, 81479. 0010M	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Rapid Genotyping Assay	G9143, 81227, 81355	Yes	Genetic Testing for Warfarin Dosing
RenalNext	81479	No*	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
ResponseDX: Colon	81479	No	Miscellaneous Genetic and Molecular Diagnostic Tests
Retna Gene AMD	81401, 81405, 81408	No	Genetic Testing for Macular Degeneration
Rosetta Cancer Origin	81504, 81540	No	Genetic Testing-Microarray Testing for Cancers of Unknown Primary (CUP) Origin
Salivary Hormone Testing	S3650, S3652	No*	Salivary Testing for Hormone Levels
Scoliscore AIS	0004M	No	Genetic Testing – DNA Based Testing for Adolescent Idiopathic Scoliosis
SelectMDx	81313	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
SensiGene Fetal RHD	81403	No*	Genetic Testing – Fetal RHD Genotyping Using Maternal Plasma

Septin9 (Sept9) DNA methylation assay	81327	No	Miscellaneous Genetic and Molecular Diagnostic Tests
Signatera	81479	No	Gene Expression Profile Testing and Circulating Tumor DNA Testing for Predicting Recurrence in Colon Cancer
Singulex Cardiac Related Test Panels	84999, 81599	Yes	Cardiovascular Risk Panels
SLCO1B1 Testing for statin-induced myopathy	81328	No	Genetic Testing for Statin-Induced Myopathy
SmartGenomics	81445, 81450, 81460, 81465	No*	Genetic Testing – Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies and Genetic Cancer Sensibility Panels Using Next Generation Sequencing
SMART PGT-A (Igenomix®)	0254U	No	Genetic Testing-Preimplantation
SPOT-Light HER2 CISH	88299	Yes	HER-2/neu and TOP2A FISH Testing for Patients with Breast Cancer
STA2R test	81225, 81226, 81291, 81401, 81479	No*	Genetic Testing for Specified Conditions Using Testing Panels
Target Print	81479	No*	Genetic Testing – Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
Target Selector ctDNA EGFR Kit	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
Telomerase Reverse Transcriptase (TERT)	81479	No*	Genetic Testing-Molecular Markers in Fine Needle Aspirates (FNA) of the Thyroid
TGFBI Gene Analysis	81333	No	Gene Analysis for Corneal Dystrophy
TheraGuide	84999, S3722, 81400, 81401	No*	Genetic and Laboratory Testing for Use of 5-Fluorouracil in Patients with Cancer
Theranostics	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
ThX ID-BRAF Kit	81599	Yes**	Genetic Testing-Molecular Markers in Fine Needle Aspirates (FNA) of the Thyroid
ThyGenX Thyroid OncoGene Panel	81599	No	Genetic Testing-Molecular Markers in Fine Needle Aspirates (FNA) of the Thyroid
Thyroid Mutation Panel	81599	No	Genetic Testing-Molecular Markers in Fine Needle Aspirates (FNA) of the Thyroid
TMPRSS Fusion Genes	81313, 81479, 0010M	No	Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
TOP2A FISH Testing	88299	FDA Pre-market approval	HER-2/neu and TOP2A FISH Testing for Patients with Breast Cancer
TransPredict Fc gamma 3A	81479	No	Miscellaneous Genetic and Molecular Diagnostic Tests
TruGenome Predisposition Screen	81415, 81416, 81417, 81425, 81426, 81427	No*	Genetic Testing – Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders
TruGenome Technical Sequence Data	81415, 81416, 81417, 81425, 81426, 81427	No*	Genetic Testing – Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders
TruGenome Undiagnosed Disease Test	81415, 81416, 81417, 81425, 81426, 81427	No*	Genetic Testing – Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders
TruSeq Amplicon Panel	81445, 81450, 81460, 81465	No*	Genetic Testing-Molecular Panel Testing of Cancers to Identify Targeted Therapies

Velox™	86152, 86153, 0091U	No	Genetic Testing For Kras, Nras And Braf Mutation Analysis In Metastatic Colorectal Cancer
Verigene Warfarin Metabolism Nucleic Acid	G9143, 81227, 81355	Yes	Genetic Testing for Warfarin Dosing
Veristrat	84999, 81538	No	Proteomic Testing for Targeted Therapy in Non Small-Cell Lung Cancer (NSCLC), e.g., VeriStrat®
Vetra DA	81490	No	Multi-Biomarker Disease Activity (MBDA) Laboratory Testing (e.g., Vectra DA Blood Test) for Rheumatoid Arthritis
Viracor Trac™	00118U	No	Laboratory Tests Post Transplant
VKOR1 gene analysis	G1943, 81227, 81355	Yes	Genetic Testing for Warfarin Dosing
YouScript® Analgesic Panel	81225, 81226, 81227, 81291, 81401, 81479	No*	Genetic Testing for Pharmacogenetic Testing for Pain Management

No* - Commercially available panels are laboratory-developed tests that are not subject to FDA approval. Clinical laboratories may develop and validate tests in-house ("home-brew") and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act.

Yes** - review policy

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

Multiple – Refer to table under the exclusionary guidelines

Note: Code(s) may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

Rationale

ACCE Model Project

The Centers for Disease Control and Prevention (CDC) Office of Public Health Genomics helped to establish and support the ACCE Model Project that became the standard for evaluating scientific data on new genetic tests.[2] (ACCE takes its name from the four main criteria for evaluating a genetic test—analytic validity, clinical validity, clinical utility and associated ethical, legal and social implications.) The ACCE model process is composed of a standard set of 44 targeted questions that address disorder, testing, and clinical scenarios, as well as analytic validity, clinical validity, clinical utility, and associated ethical, legal, and social issues.

- **Analytical validity**: Measures the specific genotypic test performance characteristics and whether the test accurately and reliably detects the gene marker(s) of interest. This refers to how well a test performs in the laboratory and how well the test measures the property or

characteristic it is intended to measure. If the test does what its maker's claim, it must produce the same results repeatedly and in different laboratories given the same set of procedures.

- **Clinical validity**: Refers to the associations of the test result(s) with patient outcomes of interest and may be expressed as clinical sensitivity, specificity, and predictive value for the outcome. Evidence is usually retrospective. This component refers to the accuracy with which a test predicts the presence or absence of a clinical condition or predisposition. Initially, the test must be conducted on individuals who are known to have the condition (as well as those who do not) to determine its success rate.
- **Clinical utility**: Clinical utility determines whether the use of genetic testing to modify medical management decisions improves patient outcomes. Best evidence is prospective, from randomized clinical trials of standard management procedures versus genetic test-directed management. Evidence may also be derived using banked samples from already-completed clinical trials, or by constructing an indirect chain of evidence linking test results to clinical outcome. If a test has utility, it means that the result (positive or negative) provides information that can be used in the formulation of an effective treatment or? Preventive strategy.
- **Ethical, Legal and Social Implications**: Determines what, if any, ethical, legal, or social implications may arise from the use of this test and its results.

The tests listed in Table 1 have not demonstrated definitive analytic validity, clinical validity and clinical utility. A definitive and consistent impact on clinical outcomes has not been demonstrated. While some tests may provide information of interest or involve technologies that are extremely interesting and useful, the information obtained with these tests has not been definitively demonstrated to affect clinical decision making or ultimate patient outcomes.

Government Regulations

Please refer to the MolDX: molecular diagnostic tests local coverage determination at the Wisconsin Physicians Service (WPS) site for specific test coverage for Medicare: https://www.wpsgha.com/wps/portal/mac/site/policies/guides-and-resources/lcds-and-coverage-articles/!ut/p/z1/tVPBjpswFPyVvcCN2MBCaCVUkTRpIlTuVlUC4RI5xjHOEkxsB9r9-prkVGkXVK2KxIHBb8Yz7z2QgRRkFWoYRYrxCpX6e5f5--fFwl_YAVw_OTGEUTzfurNgPYEzByQ9B5bjRw9k_fVbkIEMV6pWBdi1tXzAvFKkUg-koiWThQEVrxm2sMaIMGDNS4YZkQakV5YTaaEqtwSR_Cpwh5Y4v2OYN0QgSiwkFMMlkZ1QjVkOdnngORi5yMr9HFqPtu9Zn_wgsFxICMS25-X2odfY7eadMfjOE8Heehd-c4eCudf3CAzWZz1H7jcY8rAEGS354T4HUXVwAwoyQY5EEDG6Cg0XStXyswEN2LbtiHJOSzLC_GxA_fuLRKEyBVbhybyEJpECh9K8typsycHEeWibDclDiIrNatae7Ovz63y8SrOoSCayfFkt0mQ_PeEfc0qrOIpMzRreNA3bjQzbmXdvJ61HhxboJq0R8yppGD01W9Q61KVsWkZxyX24dZZNlXibNw0VXCqQ_u0D7HQbxu_nPAZJw0gLNhUXZ53Tz3-csgUcUNg4H1QYoPc-SL8cmkMdNDtdLlmk17xb7V9dxv91z7WiI-JprFtbI1VYrDpykL5FA9Iemvq8OQfub8asl2OsvINHz_uvk-_Wbtm8rkkS_QEaQWsx/dz/d5/L2dBISEvZ0FBIS9nQSEh/#d852ca3a-d6d0-4165-9688-30ee0c155d1b.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [BCBSM, formerly HCFA] are updated and/or revised periodically. Therefore, the most current BCBSM information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Genetic Testing and Counseling
- Above listed policies (Table 1) for each individual genetic test

References

1. Department of Health and Human Services, Secretary's Advisory Committee on Genetic Testing. Request for public comment on a proposed classification methodology for determining level of review for genetic tests. Federal Register 2000;65(236):76643-76645.
2. Centers for Disease Control and Prevention. ACCE Model Process for Evaluating Genetic Tests. Last reviewed December 28, 2010, archived. https://www.cdc.gov/genomics/gtesting/acce/. (February 2018).

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through July 2022, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/1/18	4/17/18	4/17/18	Joint policy established
10/1/18	10/16/18	10/16/18	Added CxBladder™ to policy.
12/11/18	12/12/18	12/12/18	Added Pigmented Lesion Assay, myPath Melanoma and DecisionDx-Melanoma to policy.
2/19/19	2/19/19		Added Apifiny, ExoDX Prostate Intelliscore, myTAI Heart, Prostate Health Index and SelectMDx to policy. Removed Thyroseq and Mammaprint.
4/16/19	4/16/19		Added cfDNA, noninvasive prenatal screening for microdeletions using cfDNA.
6/18/19	6/18/19		Added FMR2 variant testing and TERT testing to policy.
8/20/19	8/20/19		No additions/deletions.
10/15/19	10/15/19		Added: Target Selector ctDNA kit, CellMax-CRC Early Detection, CellSearch, ClearID solid tumor panel, FoundationOne Liquid, Guardant360®, Velox™, CancerIntercept® Detect, PlasmaSELECT, OncoBEAM, Theranostics and ATM.
12/17/19	12/17/19		Added Tumor Mutational Burden testing as E/I.
2/18/20	2/18/20		Added TGFBI testing (81333), Adalimumab (80145), Infliximab (80230) and Vedolilzumab testing (80280) to the policy as E/I.
4/14/20	4/14/20		Added codes 81522 and 81542 to policy as E/I.
6/16/20	6/16/20		No new codes added/deleted.
8/18/20	8/18/20		No new codes added/deleted.
10/20/20	10/20/20		No new codes added/deleted.
12/15/20	12/15/20		No new codes added/deleted.

2/16/21	2/16/21		Added SLCO1B1 testing for statin-induced myopathy, code 81328. Added Colvera (0229U) and Signatera (no specific code).
4/20/21	4/20/21		Added codes: 80204, 81529 and 0234U.
6/15/21	6/15/21		Removed codes 80145, 80230 and 80280 now established. Removed Decipher, OncotypeDX Prostate, Prolaris and ProMark, now established. Added codes 81513, 81514, 0113U, 0228U as E/I. Added Foundation One CDx (F1CDx), Foundation One CDx Heme Test to table.
8/17/21	8/17/21		No new codes added/deleted.
10/19/21	10/19/21		No new codes added/deleted.
12/14/21	12/14/21		Added SMART PGT-A testing as E/I.
2/15/22	2/15/22		Added Envisia™ (Veracyte™) code 81554, removed TMB, removed code 81455 as is now established. Veristrat is now E/I for all indications.
4/19/22	4/19/22		Removed 0005U, 0113U and 0037U as they are now established under certain circumstances.
9/1/22	6/21/22		Removed code 0239U as it is established per policy, *Circulating Tumor DNA for Management of Non-Small-Cell Lung Cancer (Liquid Biopsy)*, EFD 9/1/22
11/1/22	8/16/22		Removed Mammostrat, BreastOncPX, NexCourse, Breast PRS tests from policy as they are no longer available.

Next Review Date: Every Qtr.

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN:	Revised:

BCBSM:	Revised:

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: GENETIC, MOLECULAR AND OTHER TESTS-EXPERIMENTAL/INVESTIGATIONAL STATUS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT – HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.