

Genetic and Genomic Testing (Disease Specific)

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Disclaimer	Refer to the member's specific benefit plan and <i>Schedule of Benefits</i> to determine coverage. This may not be a benefit on all plans or the plan may have broader or more limited benefits than those listed in these criteria.
Description	<p>Genetic testing is the use of specific assays to determine the genetic status of individuals already suspected to be at high risk for a particular inherited condition. High risk means that the individual has a known family history or classic symptoms of the disorder. Genetic testing includes a variety of techniques that test for genetic diseases and analyzes genetic risk factors that may contribute to disease. Techniques involve the examination of a blood sample, or other body fluid, or tissue to indicate the presence, absence, or alteration (mutation) of genes linked to specific diseases or conditions.</p> <p>The main difference between genetic and genomic tests is that genetic tests look at sequence variants in single genes while genomic tests look at the expression of multiple genes in a single assay. Genetic testing typically refers to inherited disorders. Genomic testing usually refers to tests that look at expression profiles of multiple genes in a particular tissue affected by an acquired disease (e.g., a tumor), and in many cases, are cancer tests.¹</p> <p>Recognizing the differences as described above, for the purposes of this Medical Policy, the term "genetic testing" is considered interchangeable with "genomic testing" and is used throughout.</p>
Coverage Determination	<p>Prior Authorization is required for the following tests: Allomap, BRCA 1, BRCA 2, Colaris®, Colaris AP®, and Oncotype DX. Guidelines for these tests are located on pages 7, 8 and 9. For Benefit Certification and billing purposes, S codes should be utilized (see pages 12 and 13). Log on to Pres Online to submit a request: https://ds.phs.org/preslogin/index.jsp</p> <p>Prior Authorization is not required for all other testing listed under "Covered Diagnoses." However, all claims are subject to retrospective review.</p> <p>Genetic testing may not be a benefit on all plans. Refer to the member's specific benefit plan and <i>Schedule of Benefits</i> to determine coverage.</p>

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The following basic guidelines apply:

General population screening using genetic testing is not covered unless specified in this Policy or the member's contract. If there is a conflict between this Policy and the member's contract, the contract will govern.

Metabolic disease/Genetic inborn errors of metabolism testing is covered for newborn screening for genetic disorders as mandated by state guidelines.²

Genetic testing is covered for certain diagnoses when **all** of the following criteria have been met. (See pages 4-9 for a list of diagnoses and the type of genetic testing covered.)

- Genetic testing should be ordered by specialized physicians and/or certified genetic counselor qualified to interpret the testing results. Appropriate documentation of patient consent should be obtained.
- After physical examination and routine testing, the diagnosis remains uncertain. The member is at risk for a genetic disease, either with a direct risk factor for the development of an inheritable disease (known family history), or demonstrating signs/symptoms of a genetic disease.
- The genetic test result has a potential to affect the course of treatment for the member.
- Consultations with qualified genetic counselors and physicians should be part of the treatment plan in order for the patient to receive the appropriate interpretation of the genetic testing. Unless otherwise stated, a printed three generation pedigree should be part of the genetic consultation and should be available for review.⁵¹
- The genetic test is considered a proven method to
 1. identify or rule out an inheritable disease, **or**
 2. to detect an inherited or acquired disease-related genotype, mutation, phenotype or karyotype for clinical purposes.
- Genetic testing for a specific disease is only covered once in a person's lifetime. Coverage will be extended if additional tests are developed that expand the ability to find mutations in patients who have been previously tested, **and** if the test is considered a proven method.

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- Carrier and predictive testing is covered for certain genetic diseases when there is an affected family member of first or second-degree relation who has an identified mutation or genetic disease, and the information will help with medical or reproductive decision-making. In some circumstances, testing may also be covered when the patient is the reproductive partner of a person with a positive genetic test and the couple intends to have a baby.
- Prenatal or preimplantation genetic testing is covered for certain genetic diseases if there is an increased risk (known family history) that an offspring will have a genetic or chromosomal disorder. (Please note: Preimplantation genetic testing, as part of assisted reproductive techniques such as in-vitro fertilization, may not be a covered benefit. Refer to the member's specific benefit plan to determine coverage.)

Exclusions

Genetic testing of PHP members is not covered when the test is performed primarily for the medical management of other family members.

Additional expenses for banking of genetic material is not covered.

The following testing is **not covered** by PHP:

- *APOE* testing for use as adjunct test in clinical evaluation of patients with dementia of unknown etiology or for risk assessment of Alzheimer Disease in asymptomatic individuals.^{87, 96}
- *CDKN2A* Testing (Melaris®) (test for familial melanoma)¹²
- *CYP2D6* Genotyping (for dose management of Tamoxifen during treatment for breast cancer)⁶⁵
- deCODE Prostate Cancer™ (for assessment of prostate cancer risk or prostate cancer aggressiveness)⁸⁵
- Epidermal Growth Factor Receptor (EGFR) Gene Amplification Analysis by FISH (for predicting response to non-small cell lung cancer drug therapy). EGFR Sequence Variant Analysis is a covered benefit for this diagnosis (see page 6)⁶⁶
- eXagen BC™ (breast cancer prognostic test)
- eXagen/BD™ (inflammatory bowel disease expression profile)
- eXagen/BS™ (irritable bowel syndrome expression profile)
- Familion® (for Brugada syndrome, short QT syndrome, or catecholaminergic polymorphic ventricular tachycardia. Familion® is covered for long QT syndrome; see page 6)⁶⁸
- H/I™ (HOXB13:1L17BR) Gene Expression Ratio (used for breast cancer recurrence risk)³²
- *JAK2* testing (for chronic myeloproliferative disorders for children. *JAK2* testing is covered for adults.)¹⁸

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- Mammostrat® (used for breast cancer recurrence risk)³²
- Methylenetetrahydrofolate reductase (*MTHFR*) C677T (used for risk assessment for venous thromboembolism or obstetric complications)²⁰
- Methylenetetrahydrofolate reductase (*MTHFR*) (to predict response to anti-folate chemotherapy (includes Methotrexate)⁵⁶
- Mitochondrial DNA (mtDNA) Whole Genome Scanning/Sequencing (See “Mitochondrial Disorders” under “Covered Diagnoses” for diagnoses covered)^{97,103}
- PathFinder TG® (RedPath Integrated Pathology) (wide scope of application in cancer diagnosis)^{80, 98}
- PGxPredict™: Rituximab (for prediction of response to treatment of follicular non-Hodgkin’s lymphoma)⁷³
- PreGen-Plus™
- ProOncTumorSourceDX™ (to identify tissue or origin for metastatic tumor)⁸⁹
- TargetNow® by Caris DX (to identify biological markers in an individual’s cancer that are associated with targets for certain drugs)
- TheraGuide 5-FU™ (used to determine risk of adverse reaction to 5-FU related chemotherapy)²⁹

Covered Diagnoses and types of genetic testing covered for each diagnosis

Genetic testing may be covered when any of the following diagnoses are suspected, either because of symptomatology and/or family history. The basic guidelines on page 2 must be met. The results of the genetic testing must have potential to impact medical and reproductive decision making. Please see “Background” section on pages 10 and 11 for a list of the different types of genetic tests. In some instances, more specific criteria are required for coverage of a genetic test. See pages 7 through 10 for those.

- Newborn Screening for genetic disorders, as mandated by state guidelines. Guidelines can be accessed at the following web site²: <http://legis.state.nm.us/Sessions/05%20Regular/final/HB0479.pdf>
- Adrenoleukodystrophy, X-linked (includes adrenomyeloneuropathy) (diagnostic, carrier, prenatal or preimplantation)⁸³
- AlloMap® (used to determine cardiac transplant rejection)⁵⁷. See page 7 for specific guidelines. To be used in lieu of biopsy. Prior Authorization **is required**.
- Angelman syndrome (diagnostic testing for children)⁵⁸
- Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C). Genetic testing for sequence variants (*DSG2*, *DSP* and *PKP2*) are covered for diagnostic and predictive purposes as stated below:
 - Members with confirmed diagnosis (using International Task

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- Force diagnostic criteria) to facilitate genetic screening for ARVD/C in at-risk relatives; **or**
- Members who are at-risk relatives (meaning first-degree or second-degree relative) or of a proband with a confirmed diagnosis of ARVD/C (as defined above).¹⁰²
 - Azoospermia or severe oligozoospermia (Y chromosome microdeletions) (diagnostic).⁷⁹
 - Breast and ovarian cancer *BRCA1* and *BRCA2*: see pages 7 and 8 for specific guidelines.^{13,54,60,101} **Prior Authorization is required.**
 - Breast cancer recurrence: see page 8 for specific guidelines for *Oncotype DX*.³² **Prior Authorization is required.**
 - Breast cancer, invasive: Invitrogen SPOT_Light® HER2 CISH™ covered to predict response to trastuzumab treatment.⁸⁶
 - Canavan disease (diagnostic, carrier, prenatal or preimplantation testing)^{33,59}
 - Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) (diagnostic, predictive, prenatal and preimplantation)^{61,84}
 - Charcot-Marie-Tooth, Type 1A (diagnostic, prenatal or preimplantation testing)^{11,34}
 - Chromosomal imbalances for patients, see page 8 for specific guidelines for Comparative Genomic Hybridization (CGH) Microarray Testing.⁶⁴
 - Chromosome 22q11.2 deletion syndrome (diagnostic, prenatal and preimplantation)⁶²
 - Chronic myelogenous leukemia (CML), *BCR-ABL* Testing (Diagnostic and monitoring response to therapy)¹⁰
 - Chronic Myeloproliferative Disorders (polycythemia vera, essential thrombocytopenia and primary Myelofibrosis), *JAK2* testing for adults (diagnostic testing)¹⁸
 - Colorectal Cancer Drug Therapy (*KRAS* Sequence Variant Analysis) (predictive)⁷¹
 - Cystic Fibrosis (diagnostic, carrier, prenatal or preimplantation testing)^{6,59}
 - Deafness (Congenital) (diagnostic, carrier or prenatal testing)³⁵
 - Ehlers-Danlos syndrome (diagnostic, predictive, prenatal or preimplantation testing)^{30,49}
 - Familial adenomatous polyposis (diagnostic, predictive, prenatal or preimplantation testing): see page 9 for guidelines.^{7,47}
 - Familial dysautonomia (diagnostic, carrier, prenatal or preimplantation)⁵⁹
 - Fanconi's anemia (diagnostic testing)⁴⁷
 - Fragile X syndrome (diagnostic, carrier, prenatal or preimplantation testing)^{15,26}
 - Gaucher disease (carrier, prenatal or preimplantation testing)³⁶
 - *HLA* associated diseases (diagnostic)⁶⁹

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- Hemochromatosis, hereditary (diagnostic or carrier testing)^{16,37}
- Hemoglobinopathies (thalassemias and sickle cell anemia) (diagnostic or carrier testing)^{43,44}
- Hemophilias (diagnostic, carrier, prenatal or preimplantation testing)^{38,39}
- Hereditary non-polyposis colorectal cancer (HNPCC) – Lynch syndrome: See pages 8 and 9 for colorectal cancer screening guidelines (diagnostic, predictive, prenatal or preimplantation testing)^{8, 47,81,100} **Prior Authorization is required.**
- Huntington Chorea/Disease (diagnostic, predictive, prenatal or preimplantation testing)¹⁷
- Long QT syndrome (Familion®) (diagnostic or predictive testing)^{3,68}
- Lung cancer, non-small cell. Epidermal Growth Factor Receptor (EGFR) Sequence Variant Analysis and *KRAS* Sequence Variant Analysis (for predicting response to non-small cell lung cancer drug therapy) (predictive)^{67,70,82}
- *MYH* associated polyposis (diagnostic, predictive, prenatal or preimplantation testing)^{47,88} See page 9 for guidelines. **Prior Authorization is required.**
- Mitochondrial disorders: Leber hereditary optic neuropathy (LHON), Leigh syndrome, neurogenic muscle weakness with ataxia and retinitis pigmentosa (NARP), mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS), myoclonic epilepsy with ragged-red fibers (MERRF) (diagnostic, prenatal or preimplantation testing)^{19, 97, 103}
- Myotonic dystrophy (diagnostic, predictive, prenatal or preimplantation testing)^{27,72}
- Niemann-Pick disease (diagnostic, carrier, prenatal or preimplantation testing)⁴⁰
- Neurofibromatosis (diagnostic, prenatal and preimplantation testing)^{47, 52}
- Osteogenesis Imperfecta Types 1 to IV (diagnostic, prenatal, preimplantation testing)⁶³
- *PTEN* hamartoma tumor syndrome (diagnostic, predictive, prenatal or preimplantation testing) for patients at high risk of breast, thyroid, endometrial and renal cancers.⁹⁹
- Prader-Willi syndrome (diagnostic, prenatal and preimplantation testing)²¹
- Primary dystonia Type 1 (diagnostic, prenatal or preimplantation testing)^{22,28}
- Retinoblastoma (diagnostic, predictive and prenatal testing)⁴¹
- *RET* Proto-Oncogene Point Mutations (diagnostic or predictive testing)⁴²
- Rett syndrome (diagnostic, prenatal or preimplantation)⁵³
- Spinal Muscular Atrophy (diagnostic, carrier, prenatal or preimplantation)⁷⁴

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- Spinocerebellar Ataxia (diagnosis, predictive)^{75,76,77, 90-95}
- Tay-Sachs disease (diagnostic, carrier, prenatal or preimplantation testing)^{9,59}
- Thrombosis panel for risk assessment for venous thromboembolism (VTE) or obstetric complications: see page 6 for specific guidelines.^{14,20,23,24}
- von Hippel-Lindau disease (diagnostic, predictive, prenatal or preimplantation testing)⁴⁵
- Uniparental disomy (UPD) for Chromosomes 7,11,14 or 15 (diagnostic, prenatal or preimplantation). See page 8 for specific guidelines.⁷⁸
- Warfarin, Pharmacogenetic Testing: This test has been reviewed by the Technology Assessment Committee and the Medical Policy Committee. The practical value of this testing is limited or yet to be determined; therefore, the TAC and MPC do not endorse this testing for widespread use. A small volume of clinically appropriate testing is already occurring and will be continue to be covered.¹⁰⁴

Additional criteria for specific genetic testing:

- AlloMap® is a noninvasive option to monitor cardiac transplant rejection, and is used in lieu of biopsy.⁵⁷ AlloMap® testing protocols will vary with facilities. PHP covers AlloMap® when **ALL** of the following criteria are met. **Prior Authorization is required.**
 - Member is age 15 years or older
 - Member is >55 days post-cardiac transplant with stable allograft function and low probability of moderate/severe acute cellular rejection at the time of testing.
- *BRCA1* and *BRCA2* for breast or ovarian cancer: **Prior Authorization is required.** Basic guidelines for *BRCA1* and *BRCA2* testing are listed below. Refer to NCCN® Practice Guidelines in Oncology for Hereditary Breast and/or Ovarian Cancer for greater detail. Genetic testing criteria for *BRCA1* and *BRCA2* is located on page 6 at the following web address.^{13,54,60,101}
http://www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf

BRCA1 and *BRCA2* are covered per NCCN guidelines in the following circumstances:

- Member from a family with a known *BRCA1/BRCA2* mutation
- Personal history of breast cancer **and one** of the following:
 - Diagnosed at ≤ 45 years of age
 - Diagnosed at ≤ 50 years of age with at least one close blood

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- relative with breast cancer \leq 50 years of age and/or \geq 1 close blood relative with epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
- Two breast primaries when first breast cancer diagnosis occurred before age 50
- Diagnosed age $<$ 60 with a triple negative breast cancer
- Diagnosed age $<$ 50 with a limited family history (Individuals with limited family history, such as fewer than 2 first or second degree female relatives surviving beyond 45 years in either lineage may have underestimated probability of a familial mutation)
- Diagnosed at any age, when \geq 2 close blood relatives with breast and/or epithelial ovarian, fallopian tube or primary peritoneal cancer at any age
- Close male blood relative with breast cancer
- No additional family history required for an individual of ethnicity associated with higher mutation frequency (e.g., Ashkenazi Jewish, Icelandic, Swedish, Hungarian or other).
- Personal history of epithelial ovarian, fallopian tube or primary peritoneal cancer
- Personal history of male breast cancer
- Personal history of breast and/or ovarian cancer at any age with \geq 2 close blood relatives with pancreatic cancer at any age
- Personal History of pancreatic cancer at any age with \geq 2 close blood relatives with breast and/or ovarian and/or pancreatic cancer at any age

Family history only:

First or second degree blood relative meeting any of the above criteria

Third degree blood relative with breast cancer and/or ovarian/fallopian tube/ primary peritoneal cancer with \geq 2 close blood relatives with breast cancer (at least one with breast cancer \leq 50 y) ovarian cancer

- Predicting breast cancer recurrence: Oncotype DX Recurrence Score Assay is a genomic test. **Prior Authorization is required.** Oncotype DX is covered in the following circumstances:
 - Woman newly diagnosed with Stage I or II breast cancer
 - Node negative, estrogen receptor positive³²
 - Pedigree and genetic counseling not necessary for this test
- Colorectal cancer (CRC) screening is covered for patients meeting the requirements below. **Prior Authorization is required.**
 - PHP covers genetic testing for Lynch syndrome. **Prior Authorization is required.** Lynch syndrome (HNPCC) is the most common of the familial colon cancer syndromes and the

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identification of individuals with Lynch syndrome and their relatives leads to reduced cancer mortality. The Amsterdam Criteria II and the revised Bethesda guidelines were developed to improve identification of individuals with Lynch syndrome who will benefit from genetic testing. However, these criteria are stringent and difficult to use in a clinical practice setting. The following requirements must be met:

1. Familial adenomatous polyposis has been excluded as a diagnosis; **and**
2. Before gene sequencing is ordered for a member who has been identified as potentially having Lynch Syndrome, the following requirements should be met and available for review:
 - A three generation pedigree
 - The person being initially tested in a family with suspected Lynch syndrome should have the diagnosis of colorectal cancer or endometrial cancer. If a person with endometrial cancer is the first family member with an HNPCC-related cancer, there must also be a first-degree relative with documented colon cancer. HNPCC or Lynch-related tumors refer to colorectal, endometrial, gastric, ovarian, pancreas, ureter, renal pelvis, biliary tract, small bowel CA, as well as brain and sebaceous skin tumors.
 - The person to be tested should have had immunohistochemistry (IHC) testing of the four *MMR* proteins (*MSH1*, *MSH6*, *MLH1*, *PMS2*) and one of the *MMR* proteins should be absent by IHC. There are exceptions that may need to be reviewed with peer consultants. IHC stains for *MMR* are available at TriCore Reference Laboratories, and are typically obtained post-operatively on colon tumor pathologies.
 - If *MLH1* is absent by IHC prior to gene sequencing, testing for *b-RAF* is recommended. If testing for *b-RAF* is negative, then promoter methylation assay is recommended.
3. Genetic counseling and testing is also available to PHP members who have a first or second-degree relative in which a deleterious Lynch syndrome mutation has been identified.
4. All other requests for testing should be referred to the Medical Directors who will utilize the Amsterdam II and revised Bethesda guidelines in determination of coverage for genetic testing. A three-generation pedigree demonstrating a family history of colon cancer or other HNPCC/Lynch-related cancers should be submitted with the request.

Note: Gene sequencing for the 4 *MMR* proteins are carried out at a

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number of reference laboratories. It is best to order the specific gene which shows an abnormal IHC. It is not necessary to sequence all genes at the same time. The majority of mutations occur in either *MLH1* or *MSH2*.¹⁰⁰

- Gene sequencing, including Colaris AP®, is covered for the detection of mutations in the *APC* and *MYH* genes which cause adenomatous polyposis syndromes, including familial adenomatous polyposis (FAP), attenuated FAP (AFAP) and *MYH*-associated polyposis (MAP). **Prior Authorization is required.** The following criteria must be met:
 - Member has a personal history of suspected FAP, AFAP or MAP; **or**
 - Member has a first- or second-degree relative with disease causing mutation for FAP, AFAP or MAP.^{7,47,55, 88}
- Comparative Genomic Hybridization (CGH) Microarray Testing for Chromosomal Imbalances is covered as an adjunct to a conventional karyotype analysis for members suspected of having a genetic syndrome (i.e., have congenital anomalies, dysmorphic features, mental retardation, developmental delays or disabilities), when the test results will impact medical or reproductive decision making.⁶⁴
- Thrombosis panel for risk assessment for venous thromboembolism (VTE) or obstetric complications -- Factor V Leiden and Prothrombin *G20210A* are covered in the following circumstances:
 - Patients with obstetric complications of abnormal placenta vasculature
 - Patients with VTE with a personal or family history of recurrent VTE.^{14,20,23,24}
- Uniparental disomy (UPD) for Chromosomes 7, 11, 14, 15
 - For neonates, infants, children or adults symptomatic for Beckwith-Wiedemann syndrome for UPD for chromosome 11
 - For prenatal testing among fetuses with inherited Robertsonian translocations, supernumerary marker chromosomes, or level III mosaicism involving chromosomes 7, 14 or 15 for UPD for chromosomes 7, 14 or 15.⁷⁸

Background

Genetics refers to the study of genes and their role in inheritance – the way certain traits or conditions are passed down from one generation to another. Genetics involves scientific studies of single genes and their effects. Genes (units of heredity) carry the instructions for making proteins, which direct the activities of cells and functions of the body. Genes influence traits such as hair and eye color as well as health and

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disease development. Genetics determines much (but not all) of a person's health status; environmental differences also play a part.⁴⁸

A **genome** is defined as all the genetic material in the chromosomes of a particular organism. **Genomics** is a relatively new term describing the study of multiple genes from the same person, including interactions of those genes with each other and the person's environment. Genomics involves the scientific study of complex diseases such as heart disease, asthma, diabetes and cancer because they are caused more by a combination of genetic and environmental factors. Genomics is offering new possibilities for therapies and treatment of some diseases, as well as new diagnostic methods. The major tools and methods related to genomics studies are bioinformatics, genetic analysis, measurement of gene expression, and determination of gene function.⁴⁸

Types of genetic tests:

- Newborn screening: Used just after birth to identify genetic disorders that can be treated early in life.
- Diagnostic testing: Used to identify or rule out a specific genetic or chromosomal condition. In many cases, genetic testing is used to confirm a diagnosis when a particular condition is suspected based on physical signs and symptoms. Diagnostic testing can be performed before birth or at any time during a person's life, but is not available for all genes or all genetic conditions. The results of a diagnostic test can influence a person's choices about health care and the management of the disorder.
- Carrier testing: Used to identify people who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder. This type of testing is offered to individuals who have a family history of a genetic disorder and to people in certain ethnic groups with an increased risk of specific genetic conditions. If both parents are tested, the test can provide information about a couple's risk of having a child with a genetic condition.
- Prenatal testing: Used to detect changes in a fetus' genes or chromosomes before birth. This type of testing is offered during pregnancy if there is an increased risk that the baby will have a genetic or chromosomal disorder. In some cases, prenatal testing can lessen a couple's uncertainty or help them make decisions about a pregnancy. It cannot identify all possible inherited disorders and birth defects.

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- Preimplantation testing: A specialized technique that can reduce the risk of having a child with a particular genetic or chromosomal disorder. It is used to detect genetic changes in embryos created using assisted reproductive techniques such as in-vitro fertilization. Only embryos without certain genetic changes are implanted in the uterus to initiate a pregnancy.
- Predictive and presymptomatic testing: Used to detect gene mutations associated with disorders that appear after birth, often later in life. These tests can be helpful to people who have a family member with a genetic disorder, but who have no features of the disorder themselves at the time of testing. The results of the testing can provide information about a person's risk of developing a specific disorder and help with making decisions about medical care.⁴⁶

Medical Terms

Assay: A laboratory test to find and measure the amount of a specific substance.

First-degree relative: Parents, children, siblings (blood relatives).

Gene expression: The process by which proteins are made from the instructions encoded in DNA.

Second-degree relative: Grandparents, aunts and uncles, nieces and nephews, grandchildren, half-sibling (blood relatives)

Third-degree relative: Great-grandparents, great-aunts, great-uncles, and first cousins (blood relatives)

Three-Generation Pedigree: A pictorial representation of diseases within a family to assess hereditary influences on disease or to help identify relatively rare conditions that may not be considered in a differential diagnosis.⁵¹

Coding

The coding listed in this Medical Policy is for reference only. Covered and noncovered codes are included in this list.

HCPSC® Codes	Description
S0265	Genetic counseling, under physician supervision, each 15 minutes
S3800	Genetic testing for amyotrophic lateral sclerosis (ALS)

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S3818	Complete gene sequence analysis; BRCA1 gene
S3819	Complete gene sequence analysis; BRCA2 gene
S3820	Complete BRCA1 and BRCA2 gene sequence analysis for susceptibility to breast and ovarian cancer
S3822	Single mutation analysis (in individual with a known BRCA1 or BRCA2 mutation in the family) for susceptibility to breast and ovarian cancer
S3823	Three-mutation BRCA1 and BRCA2 analysis for susceptibility to breast and ovarian cancer in Ashkenazi individuals
S3828	Complete gene sequence analysis; MLH1 gene (Colaris®)
S3829	Complete gene sequence analysis; MSH2 gene (Colaris®)
S3830	Complete MLH1 and MLH2 gene sequence analysis for hereditary nonpolyposis colorectal cancer (HNPCC) genetic testing (Colaris®)
S3831	Single-mutation analysis (in an individual with known MLH1 and MLH2 mutation in the family) for hereditary nonpolyposis colorectal cancer (HNPCC) genetic testing (Colaris®)
S3833	Complete APC gene sequence analysis for susceptibility to familial adenomatous polyposis (FAP) and attenuated FAP (Colaris AP®)
S3834	Single-mutation analysis (in individuals with a known APC mutation in the family) for susceptibility to familial adenomatous polyposis (FAP) and attenuated FAP (Colaris AP®)
S3835	Complete gene sequence analysis for cystic fibrosis
S3837	Complete gene sequence analysis for hemochromatosis genetic testing
S3840	DNA analysis for germline mutations of the RET proto-oncogene for susceptibility to multiple endocrine neoplasia type 2
S3841	Genetic testing for retinoblastoma
S3842	Genetic testing for von Hippel-Lindau disease
S3843	DNA analysis of the F5 gene for susceptibility to Factor V Leiden thrombophilia
S3844	DNA analysis of the connexin26 gene (GJB2) for susceptibility to congenital, profound deafness
S3845	Genetic testing for alpha-thalassemia
S3846	Genetic testing for hemoglobin E beta-thalassemia
S3847	Genetic testing for Tay-Sachs disease
S3848	Genetic testing for Gaucher disease
S3849	Genetic testing for Niemann-Pick disease
S3850	Genetic testing for sickle cell anemia
S3851	Genetic testing for Canavan disease
S3852	DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease
S3853	Genetic testing for myotonic muscular dystrophy
S3854	Genetic expression profiling panel for use in the management of breast cancer treatment (Oncotype DX)
S3855	Genetic testing for detection of mutations in the presenilin, 1 gene

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S3860	Genetic testing, comprehensive cardiac ion channel analysis, for variants in 5 major cardiac ion channel genes for individuals with high index of suspicion for familiar long QT syndrome (LQTS) or related syndromes
S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada syndrome
S3862	Genetic testing, family-specific ion channel analysis, for blood-relatives of individuals (index case) who have previously tested positive for a genetic variant of a cardiac ion channel syndrome using either one of the above test configurations or confirmed results from another laboratory
S3890	DNA analysis, fecal, for colorectal cancer screening

CPT Codes	Description
83891	Molecular diagnostics; isolation or extraction of highly purified nucleic acid
83894	Molecular diagnostics; separation by gel electrophoresis (e.g. agarose, polyacrylamide)
83898	Molecular diagnostics; amplification of patient nucleic acid, each nucleic acid sequence
83904	Molecular diagnostics; mutation identification by sequencing, single segment, each segment
83908	Molecular diagnostics; signal amplification of patient nucleic acid, each nucleic acid sequence
83909	Molecular diagnostics; separation and identification by high resolution technique (eg, capillary electrophoresis)
83912	Molecular diagnostics; interpretation and report
83913	Molecular diagnostics; RNA stabilization
83914	Mutation identification by enzymatic ligation or primer extension, single segment, each segment (eg, oligonucleotide ligation assay (OLA), single base chain extension (SBCE), or allele-specific primer extension (ASPE))
88245-88249	Chromosome analysis for breakage syndromes
88261-88264	Chromosome analysis
88271-88275	Molecular cytogenetics
88280-88291	Chromosome analysis
88384-88386	Array-based evaluation of multiple molecular probes

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[MPMPPC011003]

Genetic and Genomic Testing (Disease Specific)
MPM 7.1

ICD-9© Diagnosis Codes	Description
151.0 – 151.9	Malignant neoplasm of stomach
152.0 – 152.9	Malignant neoplasm of small intestine, including duodenum
153.0 – 154.9	Malignant neoplasm of colon
155.0 – 155.2	Malignant neoplasm of liver and intrahepatic bile ducts
162	Malignant neoplasm of trachea, bronchus and lung
171.9	Malignant neoplasm of connective and other soft tissue site unspecified
174.0 – 175.9	Malignant neoplasm of female breast
179	Malignant neoplasm of uterus, part unspecified
182.0	Malignant neoplasm of body of uterus
182.8	Malignant neoplasm of other specified sites of body of uterus
183.0	Malignant neoplasm of ovary and other uterine adnexa [
183.2	Malignant neoplasm of Fallopian tube
188.0 – 188.9	Malignant neoplasm of bladder
189.1	Malignant neoplasm of renal pelvis
189.2	Malignant neoplasm of ureter
190.5	Malignant neoplasm of retina
193	Malignant neoplasm of thyroid gland
202.0, 202.8	Lymphoma (malignant), follicular
203.00	Multiple myeloma and immunoproliferative neoplasms (without remission)
203.1	Multiple myeloma and immunoproliferative neoplasms (in remission)
204.00	Acute lymphoid leukemia, without mention of having achieved remission
204.10	Chronic lymphoid leukemia, without mention of having achieved remission
205.00	Acute myeloid leukemia, without mention of having achieved remission
205.10	Chronic myeloid leukemia, without mention of having achieved remission
211.3	Benign neoplasm of colon
227.0	Benign neoplasm of adrenal gland
233.0	Carcinoma in situ of breast
237.71	Neurofibromatosis, type I
237.72	Neurofibromatosis, type II
238.4	Polycythemia vera
238.71	Essential thrombocythemia
238.75	Myelodysplastic syndrome, unspecified
238.76	Myelofibrosis with myeloid metaplasia
238.79	Other lymphatic and hematopoietic tissues

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[MPMPPC011003]

Genetic and Genomic Testing (Disease Specific)
MPM 7.1

ICD-9© Diagnosis Codes	Description
253.4	Other anterior pituitary disorders
258.01	Multiple endocrine neoplasia [MEN] type 1
259.4	Dwarfism, not elsewhere classified
270.2	Other disturbances of aromatic amino-acid metabolism
272.7	Lipidoses
275.0	Disorders of iron metabolism
277.0 – 277.09	Cystic Fibrosis
277.39	Other amyloidosis
277.5	Mucopolysaccharidosis
277.85	Disorders of fatty acid oxidation
277.87	Disorders of mitochondrial metabolism
282.3	Other hemolytic anemias due to enzyme deficiency
282.4	Thalassemias
282.5	Sickle-cell trait
282.7	Other hemoglobinopathies
284.0	Constitutional aplastic anemia
286.0	Congenital factor VIII disorder
286.1	Congenital factor IX disorder
286.3	Congenital deficiency of other clotting factors
288.01	Congenital neutropenia
288.02	Cyclic neutropenia
289.81	Primary hypercoagulable state
299.00 – 299.01	Infantism autism, current or active state or residual state
317 – 319	Mental retardation
330.0	Leukodystrophy
330.1	Cerebral lipidoses
330.8	Other specified cerebral degenerations in childhood
333.4	Huntington's chorea
333.6	Genetic torsion dystonia
334.0	Friedreich's ataxia
334.1	Hereditary spastic paraplegia
334.3	Other cerebellar ataxia
334.8	Other spinocerebellar diseases
335.10 – 335.19	Spinal muscular atrophy
345.10 – 345.11	Generalized convulsive epilepsy
356.1	Peroneal muscular atrophy

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[MPMPPC011003]

Genetic and Genomic Testing (Disease Specific)
MPM 7.1

ICD-9© Diagnosis Codes	Description
356.2	Hereditary sensory neuropathy
359.1	Hereditary progressive muscular dystrophy
359.2	Myotonic disorders
362.74	Pigmentary retinal dystrophy
377.39	Other optic neuritis
389.00 - 389.9	Hearing loss
426.82	Long QT syndrome
427.9	Cardiac dysrhythmia, unspecified (use for ARVD/C)
453.0	Budd-Chiari syndrome
555.0 - 555.9	Regional enteritis
556.0 – 556.9	Ulcerative colitis
577.0	Acute pancreatitis
577.1	Chronic pancreatitis
581.0 – 581.9	Nephrotic syndrome
606.0	Azoospermia
606.1	Oligospermia
728.87	Muscle weakness
742.2	Reduction deformity of brain
742.8	Other specified anomalies of nervous system (familial dysautonomia)
753.14	Polycystic kidney, autosomal recessive
755.55	Acrocephalosyndactyly
756.0	Anomalies of skull and face bones
756.4	Chondrodystrophy [achondroplasia]
756.51	Osteogenesis imperfecta
756.83	Ehlers-Danlos syndrome
756.89	Other specified anomalies of muscle, tendon, fascia, and connective tissue
757.1	Ichthyosis congenita
758.32	Velo-cardio-facial syndrome
759.6	Other hamartoses, not elsewhere classified
759.81	Prader-Willi syndrome
759.82	Marfan syndrome
759.83	Fragile X syndrome
759.89	Other specified anomalies
781.3	Lack of coordination
783.43	Short stature
790.5	Other nonspecific abnormal serum enzyme levels [hyper-amylasemia]

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[MPMPPC011003]

Genetic and Genomic Testing (Disease Specific)
MPM 7.1

ICD-9© Diagnosis Codes	Description
996.83	Complications of transplanted organ, heart
V10.05	Personal history of malignant neoplasm of large intestine
V10.06	Personal history of malignant neoplasm of rectum, rectosigmoid junction, and anus
V10.3	Personal history of malignant neoplasm of breast
V10.42	Personal history of malignant neoplasm of other parts of uterus
V10.43	Personal history of malignant neoplasm of ovary
V12.72	Personal history of colonic polyps
V13.69	Personal history of other congenital malformations
V16.0	Family history of malignant neoplasm of gastrointestinal tract
V17.2	Family history of neurological diseases
V17.41 – V17.49	Family history of sudden cardiac death, other cardiovascular diseases
V18.4	Family history of mental retardation
V18.51	Family history, colonic polyps
V18.59	Family history of other digestive disorders
V18.9	Family history of genetic disease carrier
V19.5	Family history of congenital anomalies
V26.31	Testing of female for genetic disease carrier status
V26.32	Other genetic testing of female
V26.33	Genetic counseling
V26.34	Testing of male for genetic disease carrier status
V26.39	Other genetic testing of male
V28.0	Screening for chromosomal anomalies by amniocentesis
V29.3	Observation for suspected genetic or metabolic condition
V42.1	Organ or tissue replaced by transplant, heart
V77.0	Special screening for thyroid disorders
V77.6	Special screening for cystic fibrosis
V77.7	Special screening for other inborn errors of metabolism
V77.91	Screening for lipid disorders
V77.99	Special screening for other and unspecified endocrine, nutritional, metabolic, and immunity disorders
V78.1	Special screening for other and unspecified deficiency anemia
V78.2	Special screening for sickle-cell disease or trait
V78.3	Special screening for other hemoglobinopathies
V78.8	Special screening for other disorders of blood and blood-forming organs
V80.0	Special screening for neurological conditions
V80.3	Special screening for ear diseases
V82.4	Maternal postnatal screening for chromosomal anomalies
V83.01	Asymptomatic hemophilia A carrier
V83.02	Symptomatic hemophilia A carrier

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[MPMPPC011003]

Genetic and Genomic Testing (Disease Specific)
MPM 7.1

ICD-9© Diagnosis Codes	Description
V83.81	Cystic fibrosis gene carrier
V83.89	Other genetic carrier status
V84.09	Genetic susceptibility to other malignant neoplasm
V84.81 – V84.89	Genetic susceptibility to other disease

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This Medical Policy is intended to represent clinical guidelines describing medical appropriateness and is developed to assist Presbyterian Health Plan and Presbyterian Insurance Company, Inc. (Presbyterian) Health Services staff and Presbyterian medical directors in determination of coverage. The Medical Policy is not a treatment guide and should not be used as such.

For those instances where a member does not meet the criteria described in these guidelines, additional information supporting medical necessity is welcome and may be utilized by the medical director in reviewing the case. Please note that all Presbyterian Medical Policies are available on the Internet at:

<http://www.phs.org/phs/healthplans/providers/healthservices/Medical/index.htm>

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[MPMPPC011003]