Genetic testing: general approach to genetic and molecular testing

These services may or may not be covered by your HealthPartners plan. Please see your plan documents for your specific coverage information. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage.

Administrative Process

Prior authorization is not required for the following services:

- Transplant-related testing for chimerism (81265-81268).
- Targeted carrier screening, except when associated with a code in Box A below
- Prenatal diagnosis for single-gene disorders via amniocentesis, CVS, or PUBS, except when associated with a code in Box A below

Prior authorization is required for known familial variant analysis of a genetic condition, single gene analysis of a genetic condition, and multigene panel analysis of a genetic condition.

Prior authorization is required for all genetic testing, unless otherwise noted in this policy, or one of the other policies listed in the Related Content section.

Prior authorization is required for testing that is associated with a procedure code listed in "Box A", below.

Box A: Genetic testing procedure codes that require prior authorization
Molecular pathology procedures, Tier 2 or unlisted (CPT 81400-81408, 81479)
Unlisted multianalyte assays (CPT 81599)
Any other listed or unlisted laboratory/pathology CPT code when it is used in association with a genetic test.

Tests that require prior authorization will be reviewed for medical necessity of the testing as a whole. That is, a single coverage decision will apply to all of the tests, services, and/or procedure codes associated with the genetic test, whether they are requested/billed together or separately.

Coverage

General Approach to Genetic Testing

General Criteria for Known Familial Variant Analysis for a Genetic Condition

The criteria below are intended for the evaluation of genetic testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

1. Targeted mutation analysis for a known familial variant for a genetic condition is considered **medically necessary** when:
   - A. The member is 18 years or older (if the condition is adult-onset), **and**
   - B. The member has a close relative with a known pathogenic or likely pathogenic variant causing the condition, **and**
   - C. An association between the gene and disease has been established.
2. Targeted mutation analysis for a known familial variant of uncertain significance is considered **investigational**.
3. Targeted mutation analysis for a known familial variant for a genetic condition is considered **investigational** for all other indications.

General Criteria for Targeted Carrier Screening

The criteria below are intended for the evaluation of genetic testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

Targeted carrier screening is defined as a test that screens via full gene sequencing or targeted mutation analysis for a pathogenic or likely pathogenic variant in a gene associated with a specific genetic condition.

1. Carrier screening for a genetic disorder may be considered **medically necessary** when:
   - A. The member is considering pregnancy or is currently pregnant, **and**
   - B. The genetic disorder is a recessive condition with a childhood onset, **and**
   - C. One of the following:

i. The member has a close relative with a known pathogenic or likely pathogenic variant associated with the disorder, **or**
ii. The member's reproductive partner is a carrier for the genetic disorder, **or**
iii. The member or the member's reproductive partner are members of a population known to have a carrier rate of 1% or higher for the genetic condition, **or**
iv. The member or the member's reproductive partner has a first- or second-degree relative who is affected with the genetic disorder.

2. Carrier screening for a genetic disorder is considered **investigational** for all other indications.

General Criteria for Single Gene or Multigene Panel Analysis

The criteria below are intended for the evaluation of genetic testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

1. Genetic testing for a genetic condition via single-gene or multigene panel analysis may be considered **medically necessary** when:
   A. The member displays clinical features of the suspected genetic condition, **and**
   B. The diagnosis remains uncertain after appropriate clinical evaluation and other standard laboratory tests/imaging/etc. have been performed, **and**
   C. The test has clinical validity, as demonstrated by accurately determining diagnostic, prognostic or clinical information for a disease, **and**
   D. The test has clinical utility, as demonstrated by at least one of the following:
      i. The test will determine if a particular therapeutic intervention is effective (or ineffective) in the member, or if a particular intervention may be harmful, **or**
      ii. The test will directly impact the member's clinical management, **or**
      iii. The test will determine prognosis, **or**
      iv. The test will provide or refine estimates of the natural history, recurrence risk, or the predicted course of the genetic condition, **and**
   E. There is no known pathogenic or likely pathogenic familial variant for the genetic condition for which targeted variant analysis would be more appropriate, **and**
   F. Non-genetic causes for the member's clinical features have been ruled out (e.g., pathogens, drug toxicity, environmental factors, etc.), **and**
   G. An association with the gene or multigene panel and disease has been established.
2. Genetic testing via single-gene or multigene panel analysis is considered **investigational** for all other indications.

Prenatal Diagnosis for Single Gene Disorders

The criteria below are intended for the evaluation of genetic testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

1. Prenatal diagnosis for single-gene disorders via amniocentesis, CVS (chorionic villus sampling), or PUBS (percutaneous umbilical blood sampling), may be considered **medically necessary** when:
   A. The member meets any of the following:
      i. At least one biological parent has a known pathogenic variant for an autosomal dominant condition, **or**
      ii. Both biological parents are known carriers of an autosomal recessive condition, **or**
      iii. One biological parent is suspected or known to be a carrier of an X-linked condition, **or**
      iv. The member has a history of a previous child with a genetic condition and the member is suspected to have germline mosaicism, **and**
   B. The natural history of the disease is well-understood, and there is a high likelihood that the disease has high morbidity, **and**
   C. The genetic test has adequate sensitivity and specificity to guide clinical decision making and residual risk is understood.
2. Prenatal diagnosis for single-gene disorders via amniocentesis, CVS, or PUBS, for adult onset single-gene disorders (examples: hereditary cancer syndromes such as *BRCA1/2*, etc.) is considered **not medically necessary**.
3. Prenatal diagnosis for single-gene disorders, via amniocentesis, CVS, or PUBS, is considered **investigational** for variants of unknown significance (VUS).
4. Prenatal diagnosis for single-gene disorders, via amniocentesis, CVS, or PUBS, is considered **investigational** for all other indications.

General Criteria for Tumor Biomarker Analysis

The criteria below are intended for the evaluation of genetic testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

1. General tumor biomarker analysis* is considered **medically necessary** when:
   - A. The member has a confirmed neoplasm and/or malignancy, **and**
   - B. The test has clinical validity, as demonstrated by accurately determining diagnostic, prognostic or clinical information for a disease, **and**
   - C. The test has clinical utility, as demonstrated by at least one of the following:
     - i. The test will determine if a particular therapeutic intervention is effective (or ineffective) in the member, or if a particular intervention may be harmful, **or**
     - ii. The test will directly impact the member's clinical management, **or**
     - iii. The test will determine prognosis, **or**
     - iv. The test will provide or refine estimates of the natural history, recurrence risk, or the predicted course of the genetic condition, **and**
   - D. Testing is being performed in a Clinical Laboratory Improvement Amendments (CLIA) approved laboratory.
2. General tumor biomarker analysis is considered **investigational** for all other indications.

*See the Oncology: Molecular Analysis of Solid Tumors and Hematologic Malignancies policy for criteria regarding common mutation analysis for tumor testing.

General Criteria for Oncology Algorithmic Tests

The criteria below are intended for the evaluation of genetic testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

1. Oncology algorithmic testing* is considered **medically necessary** when:
   - A. The member has a suspected or confirmed neoplasm and/or malignancy, **and**
   - B. The test has clinical validity, as demonstrated by accurately determining diagnostic, prognostic or clinical information for a disease, **and**
   - C. The test has clinical utility, as demonstrated by at least one of the following:
     - i. The test will determine if a particular therapeutic intervention is effective (or ineffective) in the member, or if a particular intervention may be harmful, **or**
     - ii. The test will directly impact the member's clinical management, **or**
     - iii. The test will determine prognosis, **or**
     - iv. The test will provide or refine estimates of the natural history, recurrence risk, or the predicted course of the genetic condition.
2. Oncology algorithmic testing is considered **investigational** for all other indications.

*See the Oncology: Algorithmic testing policy for criteria regarding common algorithmic tests.

General Criteria for Other Tests

The criteria below are intended for the evaluation of testing that has not been more specifically addressed by coverage criteria in another policy or another section of this policy.

1. Other tests are considered **medically necessary** when:
   - A. The member displays relevant clinical features consistent with the intended use of the test, **and**
   - B. The test has clinical validity, as demonstrated by accurately determining diagnostic, prognostic or clinical information for a disease, **and**
   - C. The test has clinical utility, as demonstrated by at least one of the following:
     - i. The test will determine if a particular therapeutic intervention is effective (or ineffective) in the member, or if a particular intervention may be harmful, **or**
     - ii. The test will directly impact the member's clinical management, **or**
     - iii. The test will determine prognosis, **or**
     - iv. The test will provide or refine estimates of the natural history, recurrence risk, or the predicted course of the disease or genetic condition, **and**
   - D. Testing is being performed in a Clinical Laboratory Improvement Amendments (CLIA) approved laboratory.
2. Other tests are considered **investigational** for all other indications.

Definitions

An **adult-onset condition** is one in which the signs, symptoms, or manifestations of a disease typically begin after a person is age 18 years or older.

An **algorithmic test** is one that combines biomarkers and clinical data into an algorithm to generate a disease risk assessment, prognostic result, or clinical recommendation for treatment.

Amniocentesis is a procedure in which a sample of amniotic fluid is removed from the uterus for prenatal diagnostic testing.

Chorionic Villi Sampling (CVS) is a procedure where a sample of chorionic villi is removed from the placenta for prenatal diagnostic testing.

Clinical validity, according to the National Institutes of Health-Department of Energy (NIH-DOE) Task Force on Genetic Testing, describes the accuracy with which a test identifies a particular clinical condition. The components of measuring clinical validity are:

- **Sensitivity**: among people with a specific condition, the proportion who have a positive test result
- **Specificity**: among people who do not have the condition, the proportion who have a negative test result
- **Positive predictive value**: among people with a positive test result, the proportion of people who have the condition
- **Negative predictive value**: among people with a negative test result, the proportion who do not have the condition

Clinical utility refers to the risks and benefits resulting from genetic test use. The most important considerations in determining clinical utility are: (1) whether the test and any subsequent interventions lead to an improved health outcome among people with a positive test result; and (2) what risks occur as a result of testing.

Close relatives include first-, second-, and third-degree blood relatives on the same side of the family:

- **First-degree** relatives are parents, siblings, and children
- **Second-degree** relatives are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
- **Third-degree** relatives are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

Germline pathogenic or likely pathogenic variants are mutations that occur in the egg and sperm cells, also known as the germ cells. These variants are inherited; that is, passed down in families by blood relatives. Most germline mutations do not result in disease.

Multifactorial conditions are complex conditions that are inherited and may be caused by a combination of the effects of multiple genes or by interactions between genes and the environment.

Percutaneous Umbilical Cord Blood Sampling (PUBS) is a procedure where a sample of fetal blood is extracted from the vein in the umbilical cord.

A **recessive condition** is one in which both copies of a gene have a mutation (autosomal recessive inheritance), or an individual with one X chromosome is hemizygous for a mutation, resulting in an X-linked recessive condition.

Products

This information is for most, but not all, HealthPartners plans. Please read your plan documents to see if your plan has limits or will not cover some items. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage. These coverage criteria do not apply to Medicare Products. For more information regarding Medicare coverage criteria or for a copy of a Medicare coverage policy, contact Member Services at 952-883-7272 or 1-877-778-8384.

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