Genetic Testing

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Medical Coverage Policy

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Description

Deoxyribonucleic acid (DNA) is a molecule that carries instructions for the characteristics and functions of living organisms, including humans, and are transmitted from one generation to the next. An individual's complete set of genetic instructions is referred to as the genome.

Sometimes variants (mutations) take place and can disrupt an individual's usual processes. This happens during DNA replication. The interference leads to a permanent alteration in the DNA sequence.

Chromosomes, a single gene or multiple genes can mutate in a number of ways including substitutions, insertions (additions), deletions, duplications (copied at least one time) and repeat expansions (repetition of short DNA sequences). Variants can be insignificant or even beneficial; others are pathogenic (disease-causing).

Variants can be detected with genetic testing by analyzing DNA with sequencing (sometimes referred to as next-generation sequencing [NGS]) or by analyzing deletions/duplications analysis and large genomic rearrangements. Some laboratories combine these methods, which is known as comprehensive testing.

Germline (inherited) genetic testing refers to the identification of variants associated with inherited risk of disease which can be detected by evaluating an individual's entire genome at a single time (referred to as whole genome sequencing [WGS]) or by targeting chromosomes, genes, gene regions or gene products within an individual's genome that may play a role in the development or progression of an associated disease. An individual's germline DNA is present at birth, is constant and is identical in all body tissue types. Almost any sample (eg, blood, saliva, buccal [cheek] smear, fresh or frozen tissues, formalin-fixed paraffin-embedded [FFPE] tissues, hair follicles and prenatal specimens) is suitable for germline testing. In general, germline testing for a particular disorder is performed once per lifetime; however, there are rare instances when repeat testing is appropriate.

When an inherited pathogenic variant has been detected in an affected relative, unaffected family members may be eligible for examination of that variant, referred to as known familial variant (KFV) analysis. Ideally, genetic testing begins with the affected relative. In the situation where an appropriate affected family member is unavailable for testing, testing based on family history can be considered. However, a benign (negative) result for the unaffected individual does not provide the same level of information as when the pathogenic variant is known. Therefore, significant limitations may exist when interpreting benign test results.

Multigene panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene) and have been proposed to evaluate the DNA of an individual with a personal and/or family history of more than one hereditary condition or syndrome. Panels often include medically actionable genes but may also include those with unclear medical management.

Genetic testing may be used for a variety of purposes:

- Carrier screening is performed on prospective parents to identify genetic risks that can be passed to offspring. Carriers are themselves unaffected but at risk for producing affected children.

- Diagnostic testing is utilized to identify or rule out a suspected genetic condition in an individual who exhibits signs and symptoms of the disorder.

- Pharmacogenomics testing analyzes an individual's unique genetic makeup to help determine response to a specific medication.

- Predictive testing may be used for an individual who does not exhibit signs or symptoms of a disorder but may be at increased risk for developing the disorder due to family history. There are two types of

predictive testing: presymptomatic (development of symptoms is certain in the presence of a gene mutation [eg, hereditary hemochromatosis, Huntington disease]) or predispositional (development of symptoms is likely, but not certain, in the presence of a gene mutation [eg, breast cancer]).

- Preimplantation genetic testing is used as an adjunct to assist in reproductive technology (ART). Testing is performed on embryos following in vitro fertilization (IVF) to detect genetic disorders prior to implantation into the uterus.

- Prenatal genetic testing is performed during pregnancy to identify genetic disorders in fetuses.

DNA banking or preservation is the long-term storage of an individual's genetic material and can be obtained using a variety of samples such as blood, saliva or other tissues. (**Refer to Coverage Limitations section**)

Polygenic risk score (PRS) has been suggested as a tool to aid in the assessment of an individual's risk for a disease. PRS are groups of single nucleotide polymorphism (SNPs) that are associated with a condition. The number, or score, provides an estimated effect of many genetic variants that may be used to predict risk. Some genetic reports include PRS. AmbryScore is an example of PRS testing. (**Refer to Coverage Limitations section**)

SNPs are variations that occur in a single nucleotide (adenine, guanine, thymine or cytosine), the basic building blocks of DNA or ribonucleic acid (RNA). Most of these genetic differences have no health effect; however, some SNPs can influence an individual's physical appearance, vulnerability to disease and drug responses. SNP testing measures these alterations and has been suggested to aid in the prediction of disease risk. Examples include, but may not be limited to, BREVAGen and OncoVue. **(Refer to Coverage Limitations section)**

Coverage Determination

General Criteria for Genetic Tests
Apply General Criteria for Genetic Testing when disease- or gene-specific criteria are not available on a medical coverage policy.

Humana members may be eligible under the Plan for **genetic testing** when the following criteria are met:

- Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations and views of physicians practicing in relevant clinical areas; **AND**

- Individual exhibits clinical features or signs/symptoms of an inherited condition or is at significant risk of an inherited condition based on family history; **AND**

- Laboratory tests or other diagnostics such as imaging are unavailable or a definitive diagnosis is not possible due to equivocal results; **AND**

- Pre- and post-test genetic counseling; **AND**

- Results of genetic testing will change clinical management based on specialty society recommendations and directly impacts the individual being tested who is a covered member

Known Familial Pathogenic or Likely Pathogenic Variant
Refer to **Coverage Limitations section** for multigene panel analysis for KFV.

Humana members may be eligible under the Plan for **KFV genetic testing** when the individual to be tested has a first- second-or third-degree relative with a pathogenic or likely pathogenic variant. Genetic testing should be limited to the KFV.

Repeat Germline Genetic Testing
Humana members may be eligible under the Plan for **repeat germline genetic testing** when technological advancements for genetic testing may detect previously missed pathogenic variants (eg, evaluation of deletions and large genomic rearrangement has become available and initial testing included sequencing only or new methods for capturing and sequencing DNA)

Examination and selection of retrieved archival tissue(s) for molecular analysis is considered integral to the primary molecular pathology procedure/laboratory testing and not separately reimbursable.

Physician interpretation and reporting for molecular pathology procedures, cytogenetics and molecular cytogenetics is considered integral to the primary pathology procedure/laboratory testing and is not separately reimbursable.

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **genetic testing** for any indications other than those listed above including, but may not be limited to:

- Deletion/duplication information is obtained as part of the sequencing procedure but submitted as an independent analysis

- General population screening

- Genetic testing for an adult-onset condition in an individual 17 years of age or younger including prenatal genetic testing unless testing changes medical management

- Individual to be tested is unaffected and has an affected first-, second- or third-degree relative with an uninformative (negative or variant of unknown significance [VUS]) genetic test result for the associated condition

- Individual to be tested is unaffected and an affected first-, second- or third-degree relative is available for genetic testing

- KFV detection analysis if the individual to be tested previously received KFV testing, single gene analysis or multigene panel testing that would have detected the KFV

- Role of the gene to be analyzed has no known disease relationship

- Sequencing, deletion/duplication analysis or large genomic rearrangement analysis (conducted individually, as comprehensive testing or sequentially without KFV results of a first, second- or third-degree relative

These are considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

Humana members may **NOT** be eligible under the Plan for **genetic testing** for any of the following:

- Multigene panels unless specifically outlined in a medical coverage policy and meets disease- or gene-specific criteria (refer to applicable medical coverage policy)

- PRS (eg, AmbryScore)

- SNPs (eg, BREVAGen, OncoVue)

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for **DNA banking or preservation**. In the absence of contractual provisions for these services, these are considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
88291	Cytogenetics and molecular cytogenetics, interpretation and report	**Physician interpretation and reporting for cytogenetics and molecular cytogenetics is considered integral to the primary pathology procedure/laboratory testing and is not separately reimbursable**
88363	Examination and selection of retrieved archival (ie, previously diagnosed) tissue(s) for molecular analysis (eg, KRAS mutational analysis)	**Examination and selection of retrieved archival tissue(s) for molecular analysis is considered integral to the primary molecular pathology procedure/laboratory testing and not separately reimbursable**
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
G0452	Molecular pathology procedure; physician interpretation and report	**Physician interpretation and reporting for molecular pathology procedures is considered integral to the primary molecular pathology procedure/laboratory testing and not separately reimbursable**

S0265	Genetic counseling, under physician supervision, each 15 minutes	

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Appendix

Appendix A
Pre- and Post-Test Genetic Counseling Criteria

Pre- and post-test genetic counseling performed by any of the following qualified medical professionals
Genetic counselor who is board-certified or board-eligible by the American Board of Medical Genetics and Genomics (ABMGG) or American Board of Genetic Counseling, Inc (ABGC) and is not employed by a commercial genetic testing laboratory; **OR**
Genetic clinical nurse (GCN) or advanced practice nurse in genetics (APNG) who is credentialed by the Genetic Nursing Credentialing Commission (GNCC) or the American of Nurses Credentialing Center (ANCC) and is not employed by a commercial genetic testing laboratory; **OR**
Medical geneticist who is board-certified or board-eligible by ABMGG; **OR**
Treating physician who has evaluated the individual to be tested and has completed a family history of three generations

Appendix B
Family Relationships

Degree of Relationship	Relative of the Individual to be Tested
First-degree	Child, full-sibling, parent
Second-degree	Aunt, uncle, grandchild, grandparent, nephew, niece, half-sibling
Third-degree	First cousin, great aunt, great-uncle, great-grandchild, great-grandparent, half-aunt, half-uncle

Change Summary

- 03/28/2024 Update, Coverage Change.