



Status

Active

## Medical and Behavioral Health Policy

Section: Laboratory

Policy Number: VI-09

Effective Date: 03/17/2014

Blue Cross and Blue Shield of Minnesota medical policies do not imply that members should not receive specific services based on the recommendation of their provider. These policies govern coverage and not clinical practice. Providers are responsible for medical advice and treatment of patients. Members with specific health care needs should consult an appropriate health care professional.

## GENETIC TESTING AND COUNSELING FOR HERITABLE DISORDERS

**Description:** Genetic testing is the process of assessing changes in genes, proteins, or chromosomes. This includes analysis of DNA to detect potential heritable disorders, genetic mutations related to disorders that may be passed from parent to child. Genetic testing may also be applied to somatic mutations, which are genetic mutations that occur in cells during a person's lifetime.

This policy addresses analysis of genetic mutations for heritable disorders. Routine prenatal and newborn testing for abnormalities of whole chromosomes, such as trisomy 21, trisomy 13 and trisomy 18, are not within the scope of this policy. Please refer to the cross-reference section for a list of policies regarding genetic testing for specific disorders.

**Definitions:** **Genetic counseling** is a process through which a professional with specialized training in genetics evaluates family history to determine whether a condition in the family may be genetic and estimates the chances that another relative may be affected. Genetic counselors also offer and interpret genetic tests that may help to estimate risk of disease and guide a patient and his/her family in understanding the utility of testing and the potential impacts of positive or negative test results. Counseling is provided by clinical geneticists or certified genetic counselors. Clinical geneticists are physicians who are board certified or eligible for certification by the American Board of Medical Genetics (ABMG). Genetic counselors are master's or PhD level health care professionals who have completed certification or are eligible for certification by the American Board of Genetic Counseling (ABGC). Genetic counseling may also be performed by physicians with training, skill, and expertise in genetic counseling. Nurse practitioners and physician's assistants under the supervision of a medical geneticist may provide counseling and order tests.

Genetic risk assessment is a process by which a genetic counselor reviews the medical and family history of an individual to determine the likelihood that the individual has a mutation or mutations associated with an inherited risk for a given condition and to determine whether a DNA test would identify or reduce that risk.

Genetic counseling should include sharing information with the patient prior to testing to ensure access to appropriate testing and/or information posttest. Information generally includes:

- A description of the test and the specific purposes for analyzing the mutation(s) or chromosomal variant(s) included in the test.
- Clinical implications of positive and negative test results and communication that the test results include information only on the mutations analyzed. Mutations in other genes not included in the test or mutations not yet identified as risk factors may confer risk of being a carrier of a heritable disorder or of being at increased risk of a disease despite a negative result on a given test.
- Potential for uninformative results or incorrect results such as false positives or false negatives.
- Potential physical or emotional risks associated with the test
- Potential that test results may provide information regarding the health or risk of disease of other family members or their children.
- Whether the results will be used for research purposes.
- Circumstances under which results can be disclosed and who will receive the results.
- What will happen to the test specimen after completion of the test

**Pedigree:** Genetic counseling often includes development of a pedigree, which is a diagram of genetic relationships and medical history of a family to determine inheritance patterns of genetic conditions.

**First degree relative:** A family member who shares about 50 percent of their genes with a particular individual in a family. First degree relatives include parents, offspring, and siblings.

**Second degree relative:** A family member who shares about 25 percent of their genes with a particular individual in a family. Second degree relatives include grandparents, grandchildren, uncles, aunts, nephews, nieces, and half-siblings.

**Third degree relative:** A family member who shares about one-eighth of their genes, such as first cousins, great-grandparents, great-aunts, great-uncles.

**Chromosomal DNA Inheritance Patterns:**

Genes are units of DNA. They may be located on chromosomes, the thread-like structures in a cell's nucleus, or in mitochondrial DNA. Mitochondria are structures outside the nucleus of a cell that generate much of the cell's energy. This policy deals primarily with chromosomal

DNA.

- **Autosomal recessive**

The term “autosomal” refers to genes that are located on chromosomes other than the X or Y sex chromosomes. An autosomal recessive inheritance pattern means that two copies of a gene mutation – one from the mother and one from the father are required in order for the child to be affected with the condition. Some autosomal recessive diseases occur with greater frequency in specific racial or ethnic groups. Cystic fibrosis, for example, is an autosomal recessive disease that occurs more frequently in Caucasian populations. Beta thalassemia is an autosomal recessive inherited blood disorder that occurs most frequently in people from Mediterranean countries, North Africa, the Middle East, India, Central Asia, and Southeast Asia. Sickle cell disease is another hereditary blood disorder that occurs most frequently in African American and Hispanic American populations. A number of autosomal recessive diseases occur more frequently in Ashkenazi Jewish individuals. These diseases include Bloom syndrome, Canavan disease, cystic fibrosis, Fanconi anemia group C, Gaucher disease Type 1, mucopolysaccharidosis IV, Niemann-Pick disease Type A, and Tay-Sach's disease.

- **Autosomal dominant**

Some mutations need only be passed from one parent to a child to cause a condition in that child. These are referred to as autosomal dominant mutations. Examples of dominant diseases include Huntington's disease and myotonic dystrophy. In some situations, a gene may have a dominant inheritance pattern but does not always result in disease. This is referred to as autosomal dominant inheritance with reduced penetrance.

- **X-linked**

Inheritance patterns of X-linked recessive disorders are complex. Because only the mother passes the X-chromosome to sons, her sons may inherit the disorder. Her daughters may either be carriers of the mutation or inherit an X-chromosome with no genetic mutation. In most instances, a daughter is not affected by the disease or may experience a milder form of the disease if an X-linked mutation is inherited from a father with the disease and a mother who is a carrier of the mutation. However, exceptions to this general principle exist and as such, a formal genetics evaluation is beneficial for a female who is potentially affected with an X-linked condition.

## **Types of Genetic Testing Addressed in this Policy**

### **Carrier status:**

Carrier testing refers to DNA analysis for mutations that may be passed from either one or both parents to a child. Carrier status generally refers to those conditions that follow an autosomal recessive

or X-linked inheritance pattern.

- **Genetic testing panels** for carrier screening include targeted genes with well-defined inheritance patterns based on ethnicity as recommended by the American Congress of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomic (ACMG). Examples of these panels include carrier testing in Ashkenazi Jewish individuals for carrier frequency of conditions that exceed the threshold for population screening. These include Tay-Sachs disease, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia (group C), Niemann-Pick (type A), Bloom syndrome, and Gaucher disease. Panels of tests for genes associated with inherited hemoglobinopathies may be recommended for carrier testing in individuals of African, Southeast Asian and Mediterranean descent who are at risk for being carriers of hemoglobinopathies such as alpha thalassemia, beta thalassemia, sickle cell disease and others.
- **Expanded carrier screening panels** may include conditions that are routinely assessed in carrier testing along with many conditions that are not routinely evaluated and for which the patient is not at risk of being a carrier. No existing specialty guidelines recommend which disease-related genetic mutations to include in expanded panels. Examples of expanded carrier screening panels include but are not limited to 23andMe, Counsyl™ GoodStart Select™, Inherigen™, Inheritest™ and NateraOne™.

**Presymptomatic genetic risk assessment** may be considered in an individual with family members who have been affected by a disorder linked to a specific genetic mutation or set of mutations, but the individual is not experiencing signs or symptoms of the genetic disorder. Presymptomatic risk assessment may be useful in certain autosomal dominant conditions such as Huntington's disease or conditions which are inherited through mitochondrial DNA rather than through chromosomal DNA. An example of the latter is Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS syndrome), a mitochondrial cytopathy that affects multiple body systems.

**Diagnostic genetic testing** refers to testing of an individual who is experiencing signs or symptoms of a genetic disorder. Testing is used to diagnose or rule out a specific genetic or chromosomal condition and the results are used to guide treatment.

Genetic risk assessment may also be performed for an individual who already has developed a genetic disease to determine the specific mutation or mutations involved to guide decision-making by family members about genetic testing or health screening.

### **Whole genome or whole exome sequencing**

The development of next generation sequencing, which allows rapid sequencing of many DNA segments, has made it possible to evaluate the sequence the entire genome (whole genome sequencing) for an individual. Whole exome sequencing (WES) involves determination of the DNA sequence of protein-encoding exons and may include some DNA regions that encode RNA molecules that are not involved in protein synthesis.

#### **Policy:**

#### **I. Testing for Carrier Status**

A. Carrier testing in a parent or prospective parent may be considered **MEDICALLY NECESSARY** when the parent or prospective parent is at high risk of being a carrier of a specific genetic disorder based upon family history as **defined by meeting one or more of the following conditions in section I.A and all of the criteria in section IB**

1. An affected child is identified with an autosomal recessive or X-linked disorder and genetic testing is performed to guide subsequent reproductive decisions;  
**OR**
2. One or both parents or prospective parents have a first or a second degree relative who is affected by a specific genetic disorder, or the first degree relative has an affected child with an autosomal recessive or X-linked disorder and genetic testing is performed to guide subsequent reproductive decisions or to guide medical management;  
**OR**
3. One parent or prospective parent is known to be a carrier of a clinically significant autosomal recessive condition;  
**OR**
4. The parents or prospective parents are members of a racial or ethnic group with a high risk of a specific genetic disorder with an autosomal recessive pattern of inheritance.

B. If one or more of the criteria in Section A (above) are met , parents or prospective parents must meet **ALL** of the following criteria:

1. For each disorder, a specific causative mutation, or set of mutations, has been established in the population being tested;  
**AND**
2. A clinical association between the mutation detected and the severity of the disorder has been validated in the peer-reviewed medical literature;  
**AND**
3. The test will identify or rule out heritability of the condition and will provide information that established biochemical or other testing cannot provide;  
**AND**
4. Genetic testing is performed to facilitate decisions surrounding reproduction;

**AND**

5. Testing is accompanied by genetic counseling.
- C. Genetic testing for carrier status is considered **INVESTIGATIVE** when the criteria above are not met. There is a lack of clinical evidence demonstrating its impact on improved health outcomes.
- D. Expanded carrier screening panels are considered **INVESTIGATIVE**. These include but are not limited to the following:
  - 23andMe
  - Counsyl™
  - GoodStart Select™
  - Inherigen™
  - InherigenPlus™
  - Inheritest™
  - NateraOne™

**II. Presymptomatic Genetic Testing to Predict Risk of a Disorder**

- A. Presymptomatic genetic testing may be considered **MEDICALLY NECESSARY** in individuals with a reasonable expectation that the condition exists or may arise based on family history and a pedigree analysis and who have no signs or symptoms of a genetic disorder when **ALL** of the following criteria are met:
  1. A specific causative mutation, or set of mutations, has been established for the disorder being evaluated;  
**AND**
  2. A clinical association between the mutation detected and the severity of the disorder has been validated in the peer-reviewed medical literature;  
**AND**
  3. The results of the genetic test will impact disease prevention, surveillance, or medical management of the individual;  
**AND**
  4. Testing is accompanied by genetic counseling.
- B. Presymptomatic genetic testing to predict risk of a disorder is considered **INVESTIGATIVE** when the criteria above are not met. There is a lack of clinical evidence demonstrating its impact on improved health outcomes. Examples of these tests include but are not limited to the following:
  - 23andMe
  - deCODE T2™
  - deCODE AF™
  - deCODE MI™
  - deCODE Glaucoma™
- C. Genetic testing of children to predict adult onset of disease is considered **NOT MEDICALLY NECESSARY** unless test results will guide current decisions concerning prevention and this benefit would be lost by waiting until the child has reached

adulthood.

### III. Diagnostic Testing

- A. Genetic testing may be considered **MEDICALLY NECESSARY** to diagnose a genetic disorder in individuals with signs or symptoms who meet **ALL** of the following criteria:
1. The test used has been established in the peer-reviewed medical literature to reliably detect a specific causative mutation or set of mutations or a chromosome variant associated with a specific disease;  
**AND**
  2. A biochemical or other test is identified but the results are indeterminate, or the genetic disorder cannot be identified through biochemical or other testing (e.g. serum cholesterol testing for familial hypercholesterolemia or ultrasound screening for aortic disease in Marfan syndrome);  
**AND**
  3. The results of the genetic test will impact the medical management of the individual;  
**AND**
  4. Testing is accompanied by genetic counseling.
- B. Genetic testing for diagnostic purposes in individuals not meeting the above criteria is considered **INVESTIGATIVE**. There is a lack of clinical evidence demonstrating its impact on improved health outcomes.
- C. Genetic testing of an individual's entire genome or exome for any indication in the absence of genetic counseling with pedigree analysis as defined in this policy is considered **INVESTIGATIVE**. There is a lack of clinical evidence that this type of testing improves health outcomes.

**Coverage:** Blue Cross and Blue Shield of Minnesota medical policies apply generally to all Blue Cross and Blue Plus plans and products. Benefit plans vary in coverage and some plans may not provide coverage for certain services addressed in the medical policies.

Medicaid products and some self-insured plans may have additional policies and prior authorization requirements. Receipt of benefits is subject to all terms and conditions of the member's summary plan description (SPD). As applicable, review the provisions relating to a specific coverage determination, including exclusions and limitations. Blue Cross reserves the right to revise, update and/or add to its medical policies at any time without notice.

For Medicare NCD and/or Medicare LCD, please consult CMS or National Government Services websites.

Refer to the Pre-Certification/Pre-Authorization section of the Medical Behavioral Health Policy Manual for the full list of services, procedures, prescription drugs, and medical devices that require Pre-

certification/Pre-Authorization. Note that services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial of claims may result if criteria are not met.

**Coding:** *The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.*

**CPT:**

81228 Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)

81229 Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities

**HCPCS:**

G0452 Molecular pathology procedure; physician interpretation and report

**Deleted Codes:** 83890, 83891, 83892, 83893, 83894, 83896, 83897, 83898, 83900, 83901, 83902, 83903, 83904, 83905, 83906, 83907, 83908, 83909, 83912, 83913, 83914, 88384, 88385, 88386

**Policy History:** **Developed April 11, 1986**

**Most recent history:**

Reviewed November 9, 2011

Revised February 8, 2012

Reviewed February 13, 2013

Revised January 8, 2014

**Cross Reference:** Gene Expression Testing to Predict Coronary Artery Disease (CAD), VI-40  
Genetic Testing for Familial Alzheimer's Disease, VI-04  
Genetic Testing for Hereditary Breast and/or Ovarian Cancer Syndrome (BRCA1 and BRCA2 Genes), VI-16  
Genetic Testing for Congenital Long Qt Syndrome, VI-19  
Genetic-Based Tests for Screening, Detection, and/or Management of Prostate Cancer, VI-23  
Single-Nucleotide Polymorphism (SNP) Breast Cancer Risk Assessment, VI-32  
Cardiovascular Disease Risk Assessment and Management: Laboratory Evaluation of Non-Traditional Lipid and Nonlipid Biomarkers, VI-24

BRAF Mutation Analysis, VI-42  
KRAS Mutation Analysis, VI-20

*Current Procedural Terminology* (CPT®) is copyright 2013 American Medical Association. All Rights Reserved. No fee schedules, basic units, relative values, or related listings are included in CPT. The AMA assumes no liability for the data contained herein. Applicable FARS/DFARS restrictions apply to government use.

Copyright 2014 Blue Cross Blue Shield of Minnesota.

---