BlueCross BlueShield Minnesota

Blue Cross Blue Shield of Minnesota Medical Policy

Medical Policy:	VI-09-015
Topic:	Genetic Testing for Inherited Non-Cancer Conditions
Section:	Laboratory
Effective Date:	January 27, 2025
Issued Date:	January 27, 2025
Last Revision Date:	May 2023
Annual Review:	May 2024

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.

Definitions

Compound Heterozygous: The presence of 2 different mutant alleles (alternate versions of a gene) at a particular gene locus, one on each chromosome of a pair.

Family History refers to the presence of a genetic disorder in 1 or more close blood relatives. Close blood relatives may include:

- **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.

Homozygous: Having the same alleles at a particular gene locus on homologous chromosomes (chromosome pairs).

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.

Carrier Screening (Panethnic Panels): Testing parents (or prospective parents) for variants in many genes associated with a variety of genetic disorders simultaneously in order to identify carriers who have an increased risk of having a child with a genetic condition. This testing is performed in a panethnic approach without regard to race or ethnicity.

This policy is designed to address medical guidelines that are appropriate for the majority of individuals with a particular disease, illness, or condition. Each person's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.

Policy Position *Coverage is subject to the specific terms of the member's benefit plan.*

Note: This policy does not include preimplantation genetic testing, fetal aneuploidy testing, or universal newborn screening. Please see related policies II-02 Preimplantation Genetic Testing and VI-43 Testing of Fetal Nucleic Acids in Maternal Blood for Detection of Fetal Aneuploidy.

The following criteria apply to circumstances in which there is no Blue Cross Blue Shield of Minnesota medical policy that addresses genetic testing for a specific condition.

NOTE: Coverage may be subject to legislative mandates, including but not limited to the following, which applies prior to the policy statements:

- Minnesota Statute 62Q.473 Biomarker Testing.

I. Genetic Counseling

Genetic testing for inherited non-cancer conditions may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria for genetic counseling are met along with criteria in sections II-IV below:

- A recommendation for testing is confirmed by **ONE** of the following:

    - A physician who is certified by the American Board of Medical Genetics and Genomics or has active candidate status for certification who has no financial relationship with the testing laboratory* **OR**
    - An American Board of Medical Genetics or American Board of Genetic Counseling certified or certification eligible Genetic Counselor who has no financial relationship with the testing laboratory***; OR**
    - A nurse credentialed as either a Genetic Clinical Nurse (GCN) or an Advanced Practice Nurse in Genetics (APNG) by either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing Center (ANCC) who has no financial relationship with the testing laboratory***; OR**
    - Board certified or board eligible medical specialist who is trained in the treatment of the genetic condition that is being tested, who has no financial relationship with the testing laboratory*;
- **AND**
- Content of counseling includes **BOTH** of the following:
    - Evaluation of a 3-generation pedigree; **AND**
    - Discussion of ALL of the following with the individual who is considering testing or parent/guardian of individual:
        - When clinically appropriate, options for surveillance and risk reduction (e.g., reproductive decision-making, lifestyle, preventive measures) for individuals with positive results, individuals with negative results, and key differences between the two; **AND**
        - Potential for uninformative or uncertain test results; **AND**
        - Potential that test results may provide health information regarding the risk of disease for other family members.

*Genetics professionals are not excluded if they are employed by or contracted with a laboratory that is part of an Integrated Health System which routinely delivers health care services beyond the laboratory test itself.

II. <u>Preconception or Prenatal Carrier Screening for Genetic Diseases</u>

- Single-gene or multigene panel screening of a parent or prospective parent to determine carrier status may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for the following conditions:
    - Cystic fibrosis, common variants (the current standard includes 23 of the more common gene mutations);
    - Spinal muscular atrophy (the current standard includes testing of SMN1 and SMN2).
- Single-gene or multigene panel screening of a parent or prospective parent to determine carrier status for other conditions may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when ALL of the following criteria are met:
    - Genetic counseling criteria in section I have been met; **AND**
    - At least one of the following:
        - One or both individuals is known to be a carrier of a clinically significant hereditary condition; **OR**
        - One or both individuals have a previously affected child with either an autosomal recessive disorder, an x-linked disorder, or an inherited disorder with variable penetrance; **OR**
        - One or both individuals have a first- or second-degree relative who is affected with an autosomal recessive disorder, an x-linked disorder, or an inherited disorder with variable penetrance; **OR**
        - One or both individuals are members of a population known to have a carrier prevalence for a particular condition that is higher than the prevalence found in the general population. These include, but are not limited to:
            - Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia, Gaucher disease, Mucolipidosis IV, Niemann-Pick (type A) and Tay-Sachs disease in individuals of Ashkenazi Jewish descent
            - Hemoglobinopathies, such as alpha thalassemia, beta thalassemia and hemoglobin E thalassemia, in individuals of African American, Southeast Asian and Mediterranean descent.
    - **AND**
    - **ALL** of the following criteria are met:
        - The natural history of the disease is well understood and there is a reasonable likelihood that the disease is one with high morbidity in the homozygous or compound heterozygous state; **AND**
        - A clinical association between the genetic marker and the disorder has been established; **AND**
        - Genetic testing is performed to facilitate decisions surrounding reproduction. **AND**
        - Alternative biochemical or other clinical tests to definitively diagnose carrier status are not available, or if available, provide an indeterminate result or are individually less efficacious than genetic testing;
- Carrier screening panels (panethnic panels) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for a parent or prospective parent when ALL of the following criteria are met:
    - ALL of the criteria in either of the 2 subsections above are met; **AND**
    - Testing will be used to identify autosomal recessive and X-linked genetic disorders; **AND**
    - As an alternative to testing of individual genes (e.g, SMN1 gene and CFTR gene).
- All other uses of carrier screening for genetic conditions, including but not limited to population screening (e.g., 23andMe test), are considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

III. <u>Genetic Testing to Determine Risk of a Non-Cancer Conditions</u>

- Genetic testing of an asymptomatic adult (age 18 or above) to determine future risk of a non-cancer condition may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:
    - Genetic counseling criteria in section I have been met; **AND**
    - One of the following:
        - A familial disease-causing mutation has been identified in a 1st or 2nd degree blood relative who is affected; OR
        - First-degree relative (parent, sibling, or child) is affected by or is known to be a carrier of a genetic disease;
    - **AND**

- Results of the genetic test will impact disease prevention, surveillance, or medical management of the individual.

- Genetic testing of an asymptomatic minor (age < 18) to determine future risk of a **non-cancer** condition may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:
  - Genetic counseling criteria in section I have been met; **AND**
  - A familial disease-causing mutation has been identified in at least one 1st or 2nd degree blood relative who is affected with an adult onset autosomal dominant or X-linked condition; **AND**
  - One of the following:
    - The condition may have onset in childhood or adolescence; **OR**
    - The condition has recommendations for surveillance that begin in childhood or adolescence.
- Presymptomatic genetic testing to predict risk of a non-cancer condition in an adult or minor using multigene panels that include genes with no established clinical association between the genetic markers and the disorder being addressed are considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of clinical evidence demonstrating an impact on improved health outcomes. Examples of these tests include but are not limited to:
  - 23andMe
  - ARISk Autism Risk Assessment Test
  - ARUP Aortopathy Sequencing Panels
  - deCODE T2™
  - deCODE AF™
  - deCODE MI™
  - deCODE Glaucoma™
  - GeneDX Childhood-onset Epilepsy panel
  - Invitae Genetic Health Screen
  - MNG Laboratories Comprehensive Epilepsy NextGen DNA Sequencing Panel
  - Pathway Genomics® Cardiac DNA Insight®, Healthy Weight DNA Insight®, Healthy Woman DNA Insight®, PathwayFit®, SkinFit™
  - RetnaGene AMD

IV. Genetic Testing for Diagnosis or Disease Prognosis of Non-Cancer Conditions

- Single-gene or multigene panel testing may be considered **MEDICALLY NECESSARY AND APPROPRIATE** to diagnose a genetic disorder in an individual with signs or symptoms of a specific inherited condition who meets **ALL** of the following criteria:
  - Genetic counseling criteria in section I have been met; **AND**
  - One of the following is met:
    - A condition listed below is suspected (related genes in parentheses):
      - Alpha thalassemia and beta thalassemia (HBA1/HBA2)
      - Alpha-1 Antitrypsin Deficiency (SERPINA1)
      - Ataxia-telangiectasia (ATM)
      - Bloom syndrome (BLM)
      - Canavan disease (ASPA)
      - CHARGE syndrome (CHD7)
      - Cystic fibrosis (CFTR)
      - Factor V Leiden thrombophilia (F5)
      - Familial dysautonomia (IKBKAP)
      - Familial hyperinsulinism (ABCC8)
      - Gaucher disease (GBA)
      - Hemoglobin E thalassemia (Glu26Lys mutation in beta-globin)
      - Hirschsprung disease (ECE1)
      - Joubert syndrome (TMEM216)
      - Maple syrup urine disease (BCKDHB)
      - Mucolipidosis IV (MCOLN1)
      - Myotonic dystrophy (DPMK, CCHC or ZNF9)
      - Muscular dystrophy including Becker and Duchenne types (DMD)
      - Niemann-Pick Type A (SMPD1)
      - Phenylketonuria (PAH)
      - Retinoblastoma (RB1)
      - Sickle cell anemia (HBB)
      - Spinal muscular atrophy (SMN1, SMN2)
      - Tay-Sachs disease (HEXA)
      - Von Hippel-Lindau syndrome (VHL);
    - **OR**
    - Condition is not listed immediately listed above and **all** of the following are met:
      - Biochemical or radiologic testing is indeterminate, nondiagnostic, or not applicable; **AND**
      - Genes included in the testing are directly associated with the individual's symptoms or presumptive diagnosis; **AND**
      - Results of the genetic test will impact medical management of the individual (e.g., initiation or withdrawal of treatment, increased screening or surveillance)
- Genetic testing using multigene panels that include genes with no established clinical association between the genetic markers and the disorder for which the test is intended are considered E**XPERIMENTAL/INVESTIGATIVE** due to a lack of clinical evidence demonstrating an impact on

improved health outcomes. Examples of these tests include but are not limited to:

- Ambry Genetics Pan Cardio Panel
- Ambry Genetics Marfan, Aneurysm and Related Disorders Panel
- Baylor College of Medicine Low Bone Mass Panel
- Emory Genetic Arrythmias Sequencing Panel and Deletion/Duplication Panel
- Inheritest® Carrier Screen Comprehensive Panel
- Invitae Arrhythmia Comprehensive Panel
- Macula Risk®
- Prometheus IBD sgi Diagnostic®
- Versiti Comprehensive Bleeding Disorder Panel

Procedure Codes
Multiple codes apply

Documentation Submission

Link to Pre-Authorization Form: **https://www.bluecrossmn.com/sites/default/files/DAM/2021-12/BCBSMN-Pre-Auth-Request-fillable-X18509R07.pdf**

Denial Statements

No additional statements.

Links

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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. When determining coverage, reference the member's specific benefit plan, including exclusions and limitations.

Medicaid products may provide different coverage for certain services, which may be addressed in different policies. For Minnesota Health Care Program (MHCP) policies, please consult the MHCP Provider Manual website.

Medicare products may provide different coverage for certain services, which may be addressed in different policies. For Medicare National Coverage Determinations (NCD), Local Coverage Determinations (LCD), and/or Local Coverage Articles, please consult CMS, National Government Services, or CGS websites.

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.

Blue Cross and Blue Shield of Minnesota reserves the right to revise, update and/or add to its medical policies at any time without notice. Codes listed on this policy are included 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.

These guidelines are the proprietary information of Blue Cross and Blue Shield of Minnesota. Any sale, copying or dissemination of the medical policies is prohibited; however, limited copying of medical policies is permitted for individual use.

Acknowledgements:

ATTENTION: If you speak English, language assistance services, free of charge, are available to you. Call the number on the back of your ID card (TTY: 711).

ATENCIÓN: Si usted habla español, servicios de asistencia lingüística, de forma gratuita, están disponibles para usted. Llame al número en la parte posterior de su tarjeta de identificación (TTY: 711).

请注意：如果您说中文，可向您提供免费语言协助服务。

请拨打您的身份证背面的号码（TTY：711）。

CHÚ Ý: Nếu quý vị nói tiếng Việt, chúng tôi cung cấp dịch vụ hỗ trợ ngôn ngữ miễn phí cho quý vị. Xin gọi số điện thoại ở mặt sau thẻ ID của quý vị (TTY: 711).

알림: 한국어를 사용하시는 분들을 위해 무료 통역이 제공됩니다. ID 카드 뒷면에 있는 번호로 전화하십시오 (TTY: 711).

ATENSYON: Kung nagsasalita ka ng Tagalog, may makukuha kang mga libreng serbisyong tulong sa wika. Tawagan ang numero sa likod ng iyong ID card (TTY: 711).

ВНИМАНИЕ: Если вы говорите по-русски, вы можете воспользоваться бесплатными услугами языковой поддержки. Позвоните по номеру, указанному на обороте вашей идентификационной карты (номер для текст-телефонных устройств (TTY): 711).

تنبيه: إذا كنت تتحدث اللغة العربية، فهناك خدمات المعاونة في اللغة المجانية متاحة لك. اتصل بالرقم الموجود خلف بطاقة هويتك (جهاز الاتصال لذوي صعوبات السمع والنطق: 711).

ATTENTION: Si c'est créole que vous connaissez, il y a un certain service de langues qui est gratis et disponible pour vous-même. Composez le numéro qui est au dos de votre carte d'identité. (TTY: 711).

ATTENTION: Si vous parlez français, les services d'assistance linguistique, gratuitement, sont à votre disposition. Appelez le numéro au dos de votre carte d'identité (TTY: 711).

UWAGA: Dla osób mówiących po polsku dostępna jest bezpłatna pomoc językowa. Zadzwoń pod numer podany na odwrocie karty ubezpieczenia zdrowotnego (TTY: 711).

ATENÇÃO: Se a sua língua é o português, temos atendimento gratuito para você no seu idioma. Ligue para o número no verso da sua identidade (TTY: 711).

ATTENZIONE: se parla italiano, per lei sono disponibili servizi di assistenza linguistica a titolo gratuito. Contatti il numero riportato sul retro della sua carta d'identità (TTY: 711).

ACHTUNG: Wenn Sie Deutsch sprechen, steht Ihnen unsere fremdsprachliche Unterstützung kostenlos zur Verfügung. Rufen Sie dazu die auf der Rückseite Ihres Versicherungsausweises (TTY: 711) aufgeführte Nummer an.

注：日本語が母国語の方は言語アシスタンス・サービスを無料でご利用いただけます。ID カードの裏に明記されている番号に電話をおかけください (TTY: 711)。

توجه : اگر شما به زبان **فارسی** صحبت می کنید، خدمات کمک زبان، به صورت رایگان، در دسترس شماست. با شماره واقع در پشت کارت شناسایی خود (TTY: 711) تماس بگیرید.