General Approach to Genetic Testing

There are numerous commercially available genetic tests, including those used to guide intervention in symptomatic or asymptomatic individuals, to identify individuals at risk for future disorders, to predict the prognosis of diagnosed disease and to predict treatment response. The concept of this policy offers a framework for evaluating the utility of genetic tests, by classifying the types of genetic tests into clinically relevant categories and developing criteria that can be used for evaluating tests in each category.

The purpose of this policy is to provide assistance in evaluating the utility of genetic tests. In providing a framework for evaluating genetic tests, this policy will not attempt to determine the clinical utility of genetic testing for specific disorders. Rather, it provides guidelines that can be applied to a wide range of different tests.

This policy applies only if there is not a separate Blue Cross Blue Shield of North Carolina (BCBSNC) medical policy that outlines specific criteria for testing. If a separate BCBSNC policy does exist, then the criteria for medical necessity in that policy supersedes the guidelines in this policy. Please see the list of Related Policies below.

This policy does not include cytogenetic testing (karyotyping), biochemical testing, or molecular testing for infectious disease.

This policy does not address reproductive genetic testing. There are separate corporate medical policies for genetic testing in the reproductive setting as outlined in the Related Policies section.

Definitions:

**Genetic testing:** Genetic testing involves the analysis of chromosomes, DNA (deoxyribonucleic acid), RNA (ribonucleic acid), genes or gene products to detect inherited (germline) or non-inherited (somatic) genetic variants related to disease or health.

**Carrier testing:** A carrier of a genetic disorder has one abnormal allele for a disorder. When associated with an autosomal recessive or X-linked disorder, carriers of the causative variant are typically unaffected. When associated with an autosomal dominant disorder, the individual has one normal and one mutated copy of the gene, and may be affected with the disorder, may be unaffected but at high risk of developing the disease later in life, or the carrier may remain unaffected because of the sex-limited nature of the disease.

Carrier testing may be offered to individuals: A) who have family members with a genetic condition; B) who have family members who are identified carriers; and C) who are members of ethnic or racial groups known to have a higher carrier rate for a particular condition.
General Approach to Genetic Testing

**Germline variants:** These variants are present in the DNA of every cell of the body, from the moment of conception. These include cells in the gonads (testes or ova) and could therefore be passed on to offspring.

**Somatic variants:** Somatic variations that occur with the passage of time, and are restricted to a specific cell or cells derived from it. If these variants are limited to cells that are not in the gonads, these variations will not be passed on to offspring.

**Pharmacogenomics:** The study of how an individual’s genetic makeup affects the body’s response to drugs.

**Related Policies:**

- Assays of Genetic Expression to Determine Prognosis of Breast Cancer
- BRAF Gene Mutation Testing to Select Melanoma or Glioma Patients for Targeted Therapy
- Cardiovascular Disease Risk Tests
- Carrier Testing for Genetic Diseases
- Circulating Tumor DNA for Cancer Management (Liquid Biopsy)
- Common Genetic Variants to Predict Risk of Nonfamilial Breast Cancer
- DNA Based Testing for Adolescent Idiopathic Scoliosis
- Fetal RHD Genotyping Using Cell-Free Fetal DNA
- Gene Expression Testing in the Evaluation of Patients With Stable Ischemic Heart Disease
- Gene Expression Profiling for Uveal Melanoma
- Genetic and Protein Biomarkers for Diagnosis and Risk Assessment of Prostate Cancer
- General Approach to Evaluating the Utility of Genetic Panels
- Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
- Genetic Testing for Alpha-1 Antitrypsin Deficiency
- Genetic Testing for Alpha Thalassemia
- Genetic Testing for Alzheimer's Disease
- Genetic Testing for Breast and Ovarian Cancer
- Genetic Testing for CADASIL Syndrome
- Genetic Testing For Cardiac Ion Channelopathies
- Genetic Testing for Colon Cancer
- Genetic Testing for Cutaneous Malignant Melanoma
- Genetic Testing for Dilated Cardiomyopathy
- Genetic Testing for Duchenne and Becker Muscular Dystrophy
- Genetic Testing for Epilepsy
- Genetic Testing for Evaluation of Developmental Delay/Autism Spectrum Disorder
- Genetic Testing for Fanconi Anemia
- Genetic Testing for FMR1 Mutations Including Fragile X Syndrome
- Genetic Testing for Hereditary Hearing Loss
- Genetic Testing for Hereditary Hemochromatosis
- Genetic Testing for Hereditary Pancreatitis
- Genetic Testing for Heterozygous Familial Hypercholesterolemia
- Genetic Testing for Lactase Insufficiency
- Genetic Testing for Macular Degeneration
- Genetic Testing for Myeloproliferative Neoplasms
- Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy
- Genetic Testing for PTEN Hamartoma Tumor Syndrome
- Genetic Testing for Rett Syndrome
- Genetic Testing for Statin Induced Myopathy
- Genetic Testing for the Diagnosis of Inherited Peripheral Neuropathy
- Laboratory and Genetic Testing for Use of 5-Fluorouracil in Patients with Cancer
- Laboratory Tests For Heart Transplant Rejection
General Approach to Genetic Testing

Microarray-Based Gene Expression Profile Testing for Multiple Myeloma Risk Stratification
Microarray-based Gene Expression Testing for Cancers of Unknown Primary
Molecular Analysis for Targeted Therapy for Non-Small Cell Lung Cancer (NSCLC)
Molecular Markers in Fine Needle Aspirates of the Thyroid
Molecular Panel Testing of Cancers to Identify Targeted Therapies
Multigene Expression Assay for Predicting Recurrence in Colon Cancer
Noninvasive Prenatal Testing for Fetal Aneuploidies Using Cell Free Fetal DNA
PathFinderTG Molecular Testing
Pharmacogenetic Testing for Drug Metabolism
Proteomics-based Testing Related to Ovarian Cancer
Proteomic Testing for Targeted Therapy in Non-Small Cell Lung Cancer
Quantitative Assay for Measurement of HER2 Total Protein Expression and HER2 Dimers
Serum Biomarker Human Epididymis Protein 4 (HE4)
Urinary Tumor Markers for Bladder Cancer
Vectra® DA Blood Test for Rheumatoid Arthritis
Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

Genetic testing classified in one of the categories below may be considered medically necessary when all criteria are met for each category as outlined in the When Covered section.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Genetic Testing is covered

Genetic testing is considered medically necessary for a genetic or heritable disorder when the following are met:

1. Testing of an affected (symptomatic) individual germline DNA to benefit the individual (excluding reproductive testing)
   a. Diagnosis
   b. Prognostic
   c. Therapeutic

2. Testing of DNA from cancer cells of an affected individual to benefit the individual
   a. Diagnostic
   b. Prognostic
   c. Testing to predict treatment responses

3. Testing an asymptomatic individual to determine future risk of disease

4. Testing of an affected individual’s germline DNA to benefit family member(s)

When Genetic Testing is not covered

Genetic testing is considered not medically necessary when:
General Approach to Genetic Testing

1. Testing is not considered standard of care, such as the clinical diagnosis can be made without the use of a genetic test.

2. Testing is not clinically appropriate for the patient’s condition/disease, for example, when it will not change diagnosis and/or management. Other situations where testing is not clinically appropriate include, but are not limited to:
   - Testing is performed entirely for non-medical (e.g., social) reasons.
   - Testing is not expected to provide a definitive diagnosis that would obviate the need for further testing.

3. Testing is performed primarily for the convenience of the patient, physician or other health care provider.

4. Testing would result in outcomes that are equivalent to outcomes using an alternative strategy, and the genetic test is more costly.

Policy Guidelines

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual and their family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Limitations of genetic testing

- The testing methods may not detect all of the mutations that may occur in a gene.
- Genetic testing may identify variants of unknown clinical significance.
- Genetic testing may not necessarily determine the clinical outcome.
- Different genes can cause the same disease (genetic heterogeneity).
- A variant in a gene may cause different phenotypes (phenotypic heterogeneity).
- Some disease-causing genes may not be identified as of yet.
- Genetic testing is subject to laboratory error.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 0008U, 0013U, 0014U, 0060U, 81238, 81247, 81249, 81361, 81362, 81363, 81364

Effective in 2013, if the specific analyte is listed in codes 81200-81355 or 81400-81408, that CPT code would be reported. If the specific analyte is not listed in the more specific CPT codes, unlisted code 81479 would be reported.
General Approach to Genetic Testing

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

  Medical Director review 7/2013
  Specialty Matched Consultant Advisory Panel review 1/2014
  Specialty Matched Consultant Advisory Panel review 4/2015
  Medical Director review 4/2015
  Medical Director review 3/2016
  Specialty Matched Consultant Advisory Panel review 3/2017
  Medical Director review 3/2017
  Specialty Matched Consultant Advisory Panel review 3/2018
  Medical Director review 3/2018

Policy Implementation/Update Information
General Approach to Genetic Testing

8/27/13 New policy developed. Genetic testing classified in one of the following categories may be considered medically necessary when all criteria are met for each category. Diagnostic testing, Risk assessment, Prognostic testing, Genetic variants that alter response to treatment or to an environmental factor. Medical Director review 7/2013. (mco)


7/29/14 Related Policies list updated. References updated. No changes to Policy Statements. (mco)

5/26/15 Specialty Matched Consultant Advisory Panel review 4/2015. Description section updated to include the following statement, “This policy does not address reproductive genetic testing.” Related Policies section updated to reflect policy title changes and archived policies removed. References updated. Medical Director review 4/2015. Policy Statements revised to remove bulleted terms: Diagnostic testing, Risk assessment, Prognostic testing and Genetic variants that alter response to treatment or to an environmental factor. When Covered section revised for each new category of testing; for the category of testing an individual for the benefit of a family member, criteria are for clinical utility rather than medical necessity. Policy Guidelines section updated. (td)


7/28/17 Code section updated with addition of 0008U, 0013U, 0014U effective 8/1/17. (jd)

12/29/17 Code section updated with addition of 81238, 81247, 81248, 81249, 81361, 81362, 81363, 81364 effective 1/1/18. (jd)


6/29/18 Added code 0060U to Billing/Coding section, effective 7/1/18. (jd)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.