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OVERVIEW

Genetic testing is a technique used to identify people at risk for a specific genetic disease, predict the possibility of future genetic disease, or to determine the risk for transmitting such a disease to their offspring. Testing may also be used as part of the process to identify, confirm, or predict the possibility of a specific medical condition and develop a treatment plan.

This policy indicates genetic testing services that

- require/recommend preauthorization via the online tool
- not medically necessary
- not covered
- covered

For information regarding Proprietary Laboratory Analyses Codes, please see the Proprietary Laboratory Analyses Policy.

MEDICAL CRITERIA

Generally, InterQual criteria is used to determine medical necessity for a majority of genetic testing, and is found in the online authorization tool:

https://www.bcbsri.com/BCBSRIWeb/Login.do?redirectTo=/providers/preauth/preauthProviderOverview.jsp

NOTE REGARDING PANEL TESTING: Please refer to the Policy Statement below for specific information regarding panel testing before utilizing the medical necessity criteria.

The following criteria is used in the online authorization tool when separate criteria is not identified for the test being performed.

Carrier screening (preconception or prenatal testing) for genetic diseases is considered medically necessary when one of the following criteria is met:

- One or both individuals have a first- or second-degree relative (see definitions below) who is affected
- One individual is known to be a carrier
- One or both individuals are members of a population known to have a carrier rate that exceeds a threshold considered appropriate for testing for a particular condition

First-degree relatives include a biological parent, brother, sister, or child.
Second-degree relatives include a biologic grandparent, aunt, uncle, niece, nephew, grandchildren, and half-sibling.

Genetic screening or testing for genetic or hereditary conditions is considered medically necessary when the diagnostic test of the individual's germline will benefit the individual and one of the following criteria is met:

- To confirm a suspected diagnosis in a patient with signs and/or symptoms of the condition

- To identify a causative etiology for a clinical syndrome, for which there are multiple possible underlying conditions
- Testing an asymptomatic individual to determine future risk of disease

Genetic testing for cancer is considered medically necessary when one of the following criteria is met:

- Testing an asymptomatic patient to determine future risk of cancer
- Therapeutic testing of cancer cells from an affected individual to benefit the individual by directing targeted treatment based on specific somatic mutations.

PRIOR AUTHORIZATION

Prior authorization is required for Medicare Advantage Plans and recommended for Commercial Products.

Prior authorization is required for each component of panel testing when it is not a next generation sequencing panel and when the panel is represented by multiple CPT codes. Each individual CPT code must be entered into and processed through the online authorization tool independently.

Requests for genetic testing should be obtained via the BCBSRI online preauthorization tool, which is available only to BCBSRI-participating providers. All other providers need to fax a preauthorization request to Utilization Management at (401) 272-8885.

If a genetic test or family is not found in the online authorization tool, please fax a request to our Utilization Management Dept at (401) 272-8885.

Medicare Advantage Plans

There are limited codes on the attached grid in which diagnosis coding in the Local Coverage Determination (LCD) is used for medical necessity determination. These codes are identified with information in the Comments column. For those designated codes when the request is for a covered diagnosis in the LCD, no prior authorization is needed. For all other indications, InterQual criteria will be used to review the request via the online authorization tool.

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

Genetic testing is considered medically necessary when the criteria in the online authorization tool and/or BCBSRI's Policy has been met.

Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member."

Medicare Advantage Plans

Genetic testing, using panels of genes, including Next Generation Sequencing, is not covered when the focus of the testing is on an individual component of the panel and there is an appropriate test available for the individual component. Individual components of a panel may be submitted for review and may be considered

medically necessary when criteria is met. This testing, using panels of genes is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

Some genetic testing services for the screening or diagnosis of genetic disorders are not covered as the evidence is insufficient to determine the effects of the technology on health outcomes. See Coding Section for details.

Commercial Products
Genetic testing, using panels of genes, including Next Generation Sequencing, is considered not medically necessary when the focus of the testing is on an individual component of the panel and there is an appropriate test available for the individual component. Individual components of a panel may be submitted for review and may be considered medically necessary when criteria is met. This testing, using panels of genes is not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

Some genetic testing services for the screening or diagnosis of genetic disorders are considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes. See Coding Section for details.

COVERAGE

Medicare Advantage Plans and Commercial Products
Benefits may vary between groups/contracts. Please refer to the Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable genetic testing coverage/benefits and not medically necessary/not covered benefits/coverage.

BACKGROUND

Commercially available genetic tests can guide intervention in symptomatic or asymptomatic people, identify people at risk for future disorders, predict the prognosis of diagnosed diseases, and predict treatment response.

Molecular Pathology
Molecular pathology procedures are medical laboratory procedures involving the analyses of nucleic acid (ie, DNA, RNA) to detect variants in genes that may be indicative of germline (eg, constitutional disorders) or somatic (eg, neoplasia) conditions, or to test for histocompatibility antigens (eg, HLA). Code selection is typically based on the specific gene(s) that is being analyzed. Genes are described using Human Genome Organization (HUGO) approved gene names.

Next Generation Sequencing
Genomic sequencing procedures (GSPs) and other molecular multianalyte assays GSPs are DNA and RNA sequence analysis methods that simultaneously assay multiple genes or genetic regions relevant to a clinical situation. They may target specific combinations of genes or genetic material or assay the exome or genome. The technology used for genetic sequencing is commonly referred to as next generation sequencing (NGS) or massively parallel sequencing (MPS). GSPs are performed on nucleic acids from germline or neoplastic samples.

MultiAnalyte Assays with Algorithmic Analyses
Multianalyte Assays with Algorithmic Analyses (MAAAs) are procedures that utilize multiple results derived from panels of analyses of various types, including molecular pathology assays, fluorescent in situ hybridization assays, and non-nucleic acid-based assays (eg, proteins, polypeptides, lipids, carbohydrates). Algorithmic analysis using the results of these assays as well as other patient information (if used) is then performed and typically reported as a numeric score(s) or as a probability. MAAAs are typically unique to a single clinical laboratory or manufacturer.

A genetic panel is defined as a test that simultaneously evaluates multiple genes, as opposed to sequential testing of individual genes. This includes panels performed by next-generation sequencing (NGS), massive parallel sequencing, and chromosomal microarray analysis. The definition of a panel will not include panels that report on gene expression profiling, which generally do not directly evaluate genetic variants.

New genetic technology, such as NGS and chromosomal microarray, has led to the ability to examine many genes simultaneously. This in turn has resulted in a proliferation of genetic panels. Panels using next-generation technology are currently widely available, covering a broad range of conditions related to inherited disorders, cancer, and reproductive testing. These panels are intuitively attractive to use in clinical care because they can analyze multiple genes more quickly and may lead to greater efficiency in the workup of genetic disorders. It is also possible that newer technology can be performed more cheaply than direct sequencing, although this may not be true in all cases.

Newer sequencing techniques were initially associated with higher error rates than direct sequencing. While there are limited published data directly comparing the accuracy of NGS with direct sequencing, several publications have reported that the concordance between NGS and Sanger sequencing is greater than 99% for cancer susceptibility testing, inherited disorders, and hereditary hearing loss. Another potential pitfall is the easy availability of a multitude of genetic information, much of which has uncertain clinical consequences. Variants of uncertain significance are found commonly and in greater numbers with NGS than with direct sequencing.

The intended use for these panels is variable, for example, for the diagnosis of hereditary disorders, a clinical diagnosis may be already established, and genetic testing is performed to determine whether this is a hereditary condition, and/or to determine the specific variant present. In other cases, there is a clinical syndrome (phenotype) with a broad number of potential diagnoses, and genetic testing is used to make a specific diagnosis. For cancer panels, there are also different intended uses. Some panels may be intended to determine whether a known cancer is part of a hereditary cancer syndrome. Other panels may include somatic mutations in a tumor biopsy specimen that may help identify a cancer type or subtype and/or help select best treatment.

There is no standardization to the makeup of genetic panels. Panel composition is variable, and different commercial products for the same condition may test a different set of genes. The makeup of the panels is determined by the specific lab that developed the test. In addition, the composition of any individual panel is likely to change over time, as new variants are discovered and added to existing panels.

Definitions

Genetic Testing

Genetic testing involves the analysis of chromosomes, DNA, RNA, genes, or gene products to detect inherited (germline) or noninherited (somatic) genetic variants related to disease or health.

Carrier Testing

A carrier of a genetic disorder has 1 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 person has 1 normal copy of the gene and 1 mutated copy of the gene; such a person may be affected with the disorder, may be unaffected but at high risk of developing the disease later in life, or may remain unaffected because of the sex-limited nature of the disease.

Carrier testing may be offered to people: (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.

Germline Variants

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

Somatic Variants
Somatic variations 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, they will not be passed on to offspring.

Pharmacogenomics
Pharmacogenomics studies how a person's genetic makeup affects his or her body's response to drugs.

Limitations of Genetic Testing
- The testing methods may not detect all variants that may occur in a gene
- Genetic testing may identify variants of uncertain 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 yet be identified
- Genetic testing is subject to laboratory error

There are several tests with a lack of demonstrated clinical utility based on extremely limited published data and/or insufficient evidence demonstrating the clinical validity of the test. In these cases, the evidence is insufficient to determine the effect of the technologies on health outcomes and are therefore considered not medically necessary.

CODING
See the attached grid for Medicare Advantage Plans and Commercial Products coverage of Genetic Testing Codes.

Genetic Testing Codes and Coverage

RELATED POLICIES
Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer
Medicare Advantage Plans National and Local Coverage Determinations
Envisia for Idiopathic Pulmonary Fibrosis
Gene Expression Profiling and Protein Biomarkers for Prostate Cancer Management
Gene Expression Profiling for Cutaneous Melanoma
Genetic and Protein Biomarkers for the Diagnosis and Cancer Risk Assessment of Prostate Cancer
Genetic Testing for Mental Health Conditions
Human Leukocyte Antigen (HLA) Testing Mandate
In Vitro Chemoresistance and Chemosensitivity Assays
Laboratory Tests Post Transplant and for Heart Failure
Molecular Markers in Fine Needle Aspiration of the Thyroid
Molecular Testing in the Management of Pulmonary Nodules
Multimarker Serum Testing Related to Ovarian Cancer
Newborn Metabolic, Endocrine and Hemoglobinopathy, and Newborn Hearing Loss Screening Programs Mandate
PathfinderTG® Molecular Testing
Preventive Services for Medicare Advantage Plans
Preventive Services for Commercial Members
Proprietary Lab Analyses (PLA)
Proteogenomic Testing for Patients with Cancer

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