MEDICAL POLICY

POLICY TITLE	GENERAL APPROACH TO GENETIC TESTING
POLICY NUMBER	MP 2.326

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**11/1/2024**

I. POLICY

This policy applies only if there is not a specific Medical Policy that outlines criteria for testing. If a specific policy does exist, then the criteria for medical necessity in that policy supersede the guidelines in this policy. If there is a disagreement about the medical necessity for a test under a specific policy, alternative tests must meet criteria of any applicable specific policies as well.

Genetic testing may be considered **medically necessary** for a genetic or heritable disorder when the following are met.

For ALL genetic testing, the condition being tested for must have either:

- Reduced life expectancy; **or**
- At least moderate to severe morbidity

In addition, 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 *Medically Necessary Criteria* section below.

A. Testing affected (symptomatic) individual
    1. Diagnostic
    2. Prognostic
    3. Therapeutic
B. Testing of DNA from cancer cells of an affected individual to benefit the individual
    1. Diagnostic
    2. Prognostic
    3. Therapeutic (testing to predict treatment response)
C. Testing an asymptomatic individual to determine future risk of disease
D. Testing an individual to benefit a family member, no benefit for individual being tested.

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Genetic testing that does not meet the criteria for a specific category is considered **investigational** or **not medically necessary.**

Genetic testing is considered **not medically necessary** when:

- Testing is not considered standard of care, such as when the clinical diagnosis can be made without the use of a genetic test
- Testing is not clinically appropriate for the patient's condition, for example, when it would 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 nonmedical (e.g., social) reasons
    - Testing is not expected to provide a definitive diagnosis that would obviate the need for further testing.
- Testing is performed primarily for the convenience of the patient, physician, or other health care provider.
- Testing would result in outcomes that are equivalent to outcomes using an alternative strategy, and the genetic test is more costly.

Genetic testing is considered **investigational** when there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

"At-home" or "direct-to-consumer" genetic testing is considered **investigational** as there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Medically Necessary Criteria

A. Affected (Symptomatic) Individual

1. Diagnostic Testing for an Affected (Symptomatic) Individual

Diagnostic testing is completed to confirm or exclude genetic or heritable variants in a symptomatic person. This refers to a molecular diagnosis supported by the presence of a known pathologic variant. For the purposes of genetic testing, a symptomatic person is defined as a person with a clinical phenotype that is correlated with a known pathologic variant.

Diagnostic testing of an affected (symptomatic) individual's germline DNA to benefit the individual (excluding reproductive testing) may be considered **medically necessary** when the following are **also** met:

- An association of the marker with the disorder has been established; **and**
- Symptoms of the disease are present; **and**
- A definitive diagnosis cannot be made based on history, physical examination, pedigree analysis, and standard diagnostic studies/tests; **and**
- The clinical utility of identifying the variant has been established as evidenced by the following:
    - Leads to changes in clinical management of the condition that improve outcomes; **or**
    - Eliminates the need for further clinical workup or invasive testing; **or**

- Leads to discontinuation of interventions that are unnecessary and/or ineffective.

2. Prognostic Testing for an Affected (Symptomatic) Individual

Prognostic testing is completed to determine or refine estimates of disease natural history or recurrence in patients already diagnosed with disease in order to predict natural disease course, (e.g., aggressiveness, recurrence, risk of death). This type of testing may use gene expression of affected tissue to predict the course of disease (e.g., testing breast cancer tissue with Oncotype DX).

Prognostic testing of an affected (symptomatic) individual's germline DNA to benefit the individual (excluding reproductive testing) may be considered **medically necessary** when the following are **also** met:

- An association of the marker with the natural history of the disease has been established; **and**
- Clinical utility of identifying the variant has been established as evidence by the following:
  - Provides incremental prognostic information above that of standard testing; **and**
  - Reclassifies patients into clinically relevant prognostic categories for which there are different treatment strategies; **and**
  - Reclassification leads to changes in management that improve outcomes.

3. Therapeutic Testing for an Affected (Symptomatic) Individual

Therapeutic testing for an affected (symptomatic) individual is completed to determine that a particular therapeutic intervention is effective (or ineffective) for an individual patient. To determine the probability of favorable or adverse response to medications. To detect genetic variants that alter risk of treatment response, adverse events, drug metabolism, drug effectiveness, etc. (e.g., cytochrome p450 testing). To detect genetic variants that adversely affect response to exposures in the environment that are ordinarily tolerated, such as *G6PD* deficiency, genetic disorders of immune function, and aminoacidopathies.

Therapeutic testing for an affected (symptomatic) individual's germline DNA to benefit the individual (excluding reproductive testing) may be considered **medically necessary** when the following are **also** met:

- Genetic testing identifies variants of a phenotype/metabolic state that relate to different pharmacokinetics, drug efficacy, or adverse drug reactions; **and**
- Clinical utility of identifying the variant has been established as evidenced by the following:
  - Leads to initiation of effective medication(s); **or**
  - Leads to discontinuation of medications that are ineffective or harmful OR
  - Leads to clinical meaningful change in dosing of medication that is likely to improve outcomes.

B. Testing of DNA from Cancer Cells of an Affected Individual to Benefit the Individual

The specified categories of testing listed below for an affected (symptomatic) individual's DNA from cancer cells to benefit the individual may be considered **medically necessary** when the following criteria are **also** met:

1. Diagnostic testing - To determine the origin of a cancer or to determine a clinically relevant subgroup that a cancer falls into:
    - Genetic testing is completed to establish the cell origin of a cancer when the origin is uncertain following standard work-up; **and**
    - Clinical utility of identifying the variant has been established as evidenced by the following:
        - Establishes the necessity to start effective treatment; **or**
        - Establishes the necessity to discontinue ineffective or harmful treatment
2. Prognostic testing - To determine the risk of progression, recurrence, or mortality for a cancer that is already diagnosed.
    - An association of the marker with the natural history of the disease has been established; **and**
    - Clinical utility of identifying the variant has been established as evidenced by the following:
        - Provides incremental prognostic information above that of standard testing; **and**
        - Reclassifies patients into clinically relevant prognostic categories for which there are different treatment strategies; **and**
        - Reclassification leads to changes in management that improve outcomes.
3. Therapeutic (testing to predict treatment response) - To determine the likelihood that a patient will respond to a targeted cancer therapy that is based on the presence or absence of a specific variant.
    - Association between a variant and treatment response to a particular drug has been established; **and**
    - Clinical utility has been established as evidenced by the following:
        - The patient is a candidate for targeted drug therapy associated with a specific variant; **and**
        - There is a clinically meaningful improvement in outcomes when targeted therapy is given for the condition.

C. Testing an Asymptomatic Individual to Determine Future Risk of Disease

This testing is completed to detect genetic variants associated with disorders that appear after birth, usually later in life. The testing is intended for individuals with a family history of a genetic disorder, but who themselves have no features of the disorder at the time of testing, in order to determine their risk for developing the disorder.

Testing an asymptomatic individual to determine future risk of disease may be considered **medically necessary** when the following criteria are **also** met:

- An association of the marker with future disorder has been established; **and**
- Clinical utility has been established as evidenced by the following:
    - There is a presymptomatic phase for this disorder in which interventions/surveillance are available; **and**

- Interventions in the presymptomatic phase are likely to improve outcomes:
  - Prevent/delay onset of disease; **or**
  - Detect disease at an earlier stage for which treatment is more effective; **or**
  - Discontinuation of interventions that are ineffective or unnecessary.

D. Testing an individual to benefit a family member with no benefit for individual being tested.

For the following category in which the benefit of testing is for another individual, the definition of medical necessity may not apply. When an individual is tested to benefit a family member, and there is no benefit for the individual being tested, eligibility for coverage is dependent on individual plan benefit language. Individual plans may differ as to whether benefit structure allows testing of an individual to benefit an unaffected family member.

Because of these concerns, the following criteria are considered to be criteria for clinical utility of testing and not for medical necessity.

For testing of an affected individual's germline DNA to a benefit family member(s) the following criteria must be met:

- An association of the genetic variant with clinical disease has been established; **and**
- Family members are available who may be at risk for the disorder; **and**
- The individual tested has a clinical diagnosis of the condition (or represents the family member who is most likely to harbor the pathogenic variant), but genetic testing has not been performed; **and**
- There is a presymptomatic phase for the disorder in which interventions are available; and
- Interventions in the presymptomatic phase are likely to improve outcomes in one of the following ways:
  - Prevent/delay onset of disease
  - Detect disease at an earlier stage for which treatment is more effective
  - Discontinuation of interventions that are ineffective or unneeded

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat, and manage patients with cancer. Guidelines evolve continuously as new treatments and diagnostics emerge and may be used by Capital Blue Cross when determining medical necessity according to this policy.

POLICY GUIDELINES

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

This policy does not address reproductive genetic testing. See separate policies.

Testing should be cleared or approved by the U.S. Food and Drug Administration as an in vitro diagnostic test (LDT) or performed in a Clinical Laboratory Improvement Amendment compliant or approved laboratory and validated as a laboratory developed test.

Frequency of Testing

In the absence of specific information regarding advances in the knowledge of variant characteristics for a particular disorder, the current literature indicates that genetic tests for inherited disease need only be performed **once per lifetime** of the patient.

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the HUman Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology— "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Diseased-Assoc.Variant	Disease-associated change in the DNA sequence.
	Variant	Change in DNA sequence
	Familial Variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives.

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely Pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

ACMG: American College of Medical Genetics and Genomics; AMP: Association of Molecular Pathology.

Genetic Counseling

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's 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.

Cross-reference:

See related policies at the end of this document

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO: Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

III. DESCRIPTION/BACKGROUND

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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. This concept 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.

IV. RATIONALE

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SUMMARY OF EVIDENCE

This conceptual framework addresses genetic testing in nonreproductive settings. Genetic testing in reproductive settings is addressed separately. For categories of genetic testing for which the benefit of testing is the individual, criteria for medical necessity apply. When the benefit of testing is not for the individual, but for a family member, medical necessity criteria may not apply, and the criteria are developed for clinical utility.

V. DEFINITIONS

TOP

ANALYTIC VALIDITY of a genetic test defines its ability to accurately and reliably measure the genotype of interest.

ARRAY COMPARATIVE GENOMIC HYBRIDIZATION (chromosomal microarray analysis [CMA], microarray-based comparative genomic hybridization, array CGH, a-CGH, aCGH, or virtual karyotype) is a technique to detect genomic copy number variations at a higher resolution level than chromosome-based comparative genomic hybridization (CGH).

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.

CHROMOSOME is one of the threadlike “packages” of genes and other DNA in the nucleus of a cell.

COPY-NUMBER VARIATIONS are alterations of the DNA of a genome that results in the cell having an abnormal number of copies of one or more sections of the DNA. CNVs correspond to relatively large regions of the genome that have been deleted (fewer than the normal number) or amplified (more than the normal number) on certain chromosomes. For example, the chromosome that normally has sections in order as A-B-C-D might instead have sections A-B-C-C-D (a duplication of "C") or A-B-D (a deletion of "C").

CLINICAL VALIDITY of a genetic test defines its ability to detect or predict the associated disorder (phenotype).

DIRECT-TO-CONSUMER GENETIC TESTING refers to genetic tests that are marketed directly to consumers via television, print advertisements, or the Internet. This form of testing, which is also known as at-home genetic testing, provides access to a person’s genetic information without necessarily involving a doctor or insurance company in the process.

DNA a large nucleic acid molecule, found principally in the chromosomes of the nucleus of a cell, that is the carrier of genetic information.

FIRST-DEGREE RELATIVE refers to a parent, sibling, or child.

GENE is the basic unit of heredity, made of DNA, the code for a specific protein.

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

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.

GENOTYPE is the specific genetic makeup of an individual, usually in the form of DNA.

IN VITRO DIAGNOSTICS tests on samples such as blood or tissue that can detect diseases or other conditions and can be used to monitor a person's overall health to help cure, treat, or prevent diseases.

KARYOTYPE is the chromosomal complement of an individual, including the number of chromosomes and any abnormalities

A LABORATORY DEVELOPED TEST (LDT) is a type of in vitro diagnostic test that is designed, manufactured, and used within a single laboratory.

MICROARRAY is a tool for analyzing gene expression that consists of a small membrane or glass slide containing samples of many genes arranged in a regular pattern. Each spot on an array is associated with a particular gene. Each color in an array represents either healthy (control) or diseased (sample) tissue. Depending on the type of array used, the location and intensity of a color will indicate whether the gene, or variant, is present in either the control and/or sample DNA. It will also provide an estimate of the expression level of the gene(s) in the sample and control DNA.

MITOCHONDRIA are intracellular organelles that are responsible for energy production and cellular respiration.

MITOCHONDRIAL DISEASE refers to one of hundreds of congenital illnesses that result from variants in mitochondrial DNA. As a result, the mitochondria are unable to completely burn food and oxygen in order to generate energy.

VARIANT is a permanent structural alteration in DNA.

PHARMACOGENOMICS The study of how an individual's genetic makeup affects the body's response to drugs.

PHENOTYPE is the physical characteristics of an organism or the presence of a disease that may or may not be genetic.

RNA is a molecule similar to DNA. Unlike DNA, RNA is single-stranded. RNA delivers DNA's genetic message to the cytoplasm of a cell where proteins are made.

SECOND-DEGREE RELATIVE refers to an aunt, uncle, niece, nephew, or grandparent.

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

THIRD-DEGREE RELATIVE refers to a great aunt/uncle, first cousin, or great grandmother/grandfather.

VARIABLE EXPRESSION refers to variation in the manner in which a trait is manifested. When there is variable expressivity, the trait may vary in clinical expression from mild to severe.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross' medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Procedure Codes that may be associated with this policy:

Proprietary Laboratory Analyses (PLA) Codes*:

0019U, 0029U, 0035U, 0084U, 0154U, 0155U, 0172U, 0173U, 0177U, 0180U, 0181U, 0182U, 0183U, 0184U, 0185U, 0186U, 0187U, 0188U, 0189U, 0190U, 0191U, 0192U, 0193U, 0194U, 0195U, 0196U, 0197U, 0199U, 0200U, 0201U, 0216U, 0217U, 0230U, 0231U, 0232U, 0233U, 0234U, 0236U, 0258U, 0266U, 0268U, 0269U, 0270U, 0271U, 0272U, 0273U, 0274U, 0276U, 0277U, 0278U, 0282U, 0342U, 0481U

Tier 1 Molecular Pathology Procedure Codes*:

81105, 81106, 81107, 81108, 81109, 81110, 81111, 81112, 81120, 81121, 81168, 81171, 81172, 81173, 81174, 81175, 81176, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81185, 81186, 81187, 81188, 81189, 81190, 81200, 81204, 81205, 81209, 81220, 81221, 81222, 81223, 81224, 81233, 81234, 81236, 81237, 81238, 81239, 81247, 81248, 81249, 81250, 81251, 81255, 81260, 81261, 81262, 81263, 81264, 81265, 81266, 81267, 81268, 81271, 81272, 81273, 81274, 81278, 81283, 81284, 81285, 81286, 81288, 81289, 81290, 81302, 81303, 81304, 81305, 81306, 81309, 81312, 81314, 81315, 81316, 81320, 81329, 81330, 81331, 81333, 81334, 81336, 81337, 81340, 81341, 81342, 81343, 81344, 81347, 81348, 81350, 81357, 81360, 81361, 81362, 81363, 81364

Tier 2 Molecular Pathology Procedure Codes*:

81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479

Genomic Sequencing Procedures and Other Molecular Multianalyte Assays*

81434, 81441, 81442

*If the specific analyte is listed in a specific code, the specific CPT code would be reported; however, if the specific analyte is not listed in the more specific CPT code, the unlisted code (81479) would be reported.

ICD-10-CM Diagnosis Codes:

Diagnosis would depend on the condition for which the testing is being performed, if the test is being performed as screening or carrier testing, and any family history of the condition.

IX. REFERENCES

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1. *ACMG Board of Directors. Clinical utility of genetic and genomic services: a position statement of the American College of Medical Genetics and Genomics. Genet Med. Jun 2015; 17(6):505-507. PMID 25764213*
2. *Teutsch SM, Bradley LA, Palomaki GE, et al. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Initiative: methods of the EGAPP Working Group. Genet Med. Jan 2009; 11(1):3-14. PMID 18813139*
3. *Beltran-Sanchez H, Razak F, Subramanian SV. Going beyond the disability-based morbidity definition in the compression of morbidity framework. Glob Health Action. 2014; 7:24766. PMID 25261699*
4. *Goldfeder RL, Priest JR, Zook JM, et al. Medical implications of technical accuracy in genome sequencing. Genome Med. 2016;8(1):24. Published 2016 Mar 2. doi:10.1186/s13073-016-0269-0*
5. *National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Myelodysplastic syndromes. Version 1.2023. Fort Washington, PA: NCCN; 2023.*

6. *National Institutes of Health (NIH), Genetic and Rare Diseases Information Center (GARD). Unverricht-Lundborg disease. Gaithersburg, MD: NIH/GARD; updated February 2023.*
7. *Kohlmann W, Slavotinek A. Genetic Testing. In: UpToDate Online Journal [serial online]. Waltham, MA: UpToDate; updated October 7, 2022. Literature review current through February 2024.*
8. *National Society of Genetic Counselors Position Statement. Genetic testing of minors for adult-onset conditions. Adopted 2012. Updated April 2018.*
9. *Blue Cross Blue Shield Association Medical Policy Reference Manual. 2.04.91, Genetic Approach to Genetic Testing. December 2017.*

X. POLICY HISTORY

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MP 2.326	**01/01/2019 Administrative Update.** CPT® PLA Codes: Expanded range to include 0080U- 0083U, effective 1/1/19.
	05/15/2019 Consensus Review. Appendices removed. No change to policy statement. CPT® PLA Codes updated to include codes issued 7/1/19: 0001U to 0104U*
	01/01/2020 Administrative Update. Updated PLA codes listed.
	03/11/2020 Administrative Update. Added new code 0169U. Effective 4/1/20.
	05/11/2020 Administrative Update. New PLA codes added to policy, effective 07/01/2020.
	05/11/2020 Consensus Review. No change to policy statements. References added and summary of evidence reviewed.
	11/24/2020 Administrative Update. Added new 2021 codes to policy. 0233U-0224U, 81168, 81278, 81347 and 81348.
	03/25/2021 Consensus Review. No change to policy statement. Revised listed PLA codes in coding section. Added NCCN statement, updated references.
	08/31/2021 Administrative Update. Added new codes to policy: 0258U, 0266U, 0268U-0274U, 0276U-0278U, 0282U
	11/16/2021 Administrative Update. Removed all references to appendix section.
	01/27/2022 Administrative Update. Removed 0024U due to management by Avalon. Effective date 4/1/22.
	02/18/2022 Minor Review. Moved INV statement re: at-home testing from policy guidelines into policy statement. Removed 0007U, 0010U, 0223U, 0224U. Added 0055U, 0059U, 0079U, 0087U, 0120U, 0136U, 0216U-0218U, 0228U-0229U, 0287U, 0297U-0300U.
	03/11/2022 Administrative Update. Added code 0315U, effective date 4/1/2022.
	08/08/2022 Administrative Update. Formatting of coding tables. Effective date 9/1/2022
	09/12/2022 Administrative Update. Added codes, deleted code 0012U, 0013U, 0014U & 0056U Effective date 10/1/22.
	10/28/2022 Administrative Update. Added 0172U. Effective date 12/1/2022.

	12/01/2022 Administrative Update. Added new codes 0362U, & 81441. Effective 1/1/2023
	04/19/2023 Minor Review. Added statement to introduction box regarding disagreement in medical necessity. Moved two statements from the background section into the policy guidelines. Many codes removed from the coding table as they are on more specific policies. 0232U added. 0061U not a genetic test so moving to MP 4.002. References and related policies updated.
	10/25/2023 Administrative Update. Added 81434 and 81442. Effective 12/1/2023.
	01/05/2024 Administrative Update. Removed codes 0002U, 0032U, 0045U, 0058U, 0059U, 0087U, 0120U, 0174U, 0294U, 0297U-0300U, 0315U, 0332U, and 0333U as they are being moved to MP 2.277. Eff date 6/1/2024.
	04/10/2024 Consensus Review. References and related policies updated. Coding table updated
	09/18/2024 Administrative Update. New code 0481U added, 0078U deleted effective 10/1/2024.

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Policies Related to Genetic Testing

Please note: Due to the rapid changes taking place in the genetic testing field this may not be a complete list of all Capital Blue Cross genetic testing policies. Please review the Capital Blue Cross policy website for additional policies which may have been added since the effective date of this policy.

G2022	Biomarker Testing for Autoimmune Rheumatic Disease
G2055	Prenatal Testing for Fetal Aneuploidy
G2100	In Vitro Chemoresistance and Chemosensitivity Assays
G2113	Oral Cancer Screening and Testing
G2123	Biomarker Testing for Multiple Sclerosis and Related Neurologic Diseases
G2125	Urinary Tumor Markers for Bladder Cancer
G2150	Biomarkers for Myocardial Infarction and Chronic Heart Failure
MP 2.050	Diagnostic Testing and Risk Assessment for Alzheimer's Disease (Biochemical and Genetic)
MP 2.211	Germline Genetic Testing for Hereditary Breast-Ovarian Cancer Syndrome and other High-Risk Cancers

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MP 2.218	Pharmacogenomic and Metabolite Markers for Patients with Inflammatory Bowel Disease Treated with Thiopurines
MP 2.233	Genetic Testing for Cardiac Ion Channelopathies
MP 2.234	Cytochrome p450 Genotype Guided Treatment Strategy
MP 2.241	Molecular Analysis for Targeted Therapy for Non-Small Cell Lung Cancer
MP 2.242	Genetic Testing for Developmental Delay/Intellectual Disability, Autism Spectrum Disorder, and Congenital Anomalies
MP 2.245	Gene Expression-Based Assays for Cancers of Unknown Primary
MP 2.246	Genetic Testing for Familial Cutaneous Malignant Melanoma
MP 2.247	Genetic Testing of CADASIL Syndrome
MP 2.248	Genetic Testing for Predisposition to Inherited Hypertrophic Cardiomyopathy
MP 2.249	Use of Common Genetic Variants (Single Nucleotide Polymorphisms) to Predict Risk of Non-Familial Breast Cancer
MP 2.251	Genetic Testing for Alpha-1 Antitrypsin Deficiency
MP 2.253	Genetic Testing for Inherited Thrombophilia
MP 2.255	Genetic Testing for PTEN Hamartoma Tumor Syndrome
MP 2.257	Genetic Testing for Duchenne and Becker Muscular Dystrophy
MP 2.258	Carrier Screening for Genetic Diseases
MP 2.259	Expanded Molecular Panel Testing of Cancers to Determine Targeted Therapies
MP 2.260	Genetic Testing for Macular Degeneration
MP 2.261	Noninvasive Fetal RHD Genotyping Using Cell-Free Fetal DNA
MP 2.262	Genetic Testing for Epilepsy
MP 2.264	Genetic Testing for Diagnosis and Management of Mental Health Conditions
MP 2.266	Molecular Testing for The Management of Pancreatic Cysts, Barrett Esophagus, And Solid Pancreaticobiliary Lesions
MP 2.267	Circulating Tumor DNA and Circulating Tumor Cells for Cancer Management (Liquid Biopsy)
MP 2.269	Serum Biomarkers for Human Epididymis Protein 4 (HE4)
MP 2.270	Multimarker Serum Testing Related to Ovarian Cancer
MP 2.273	Genetic Testing for Mitochondrial Disorders
MP 2.274	Genetic Testing for Li-Fraumeni Syndrome
MP 2.275	Molecular Markers in Fine Needle Aspirates of the Thyroid
MP 2.276	Genetic Testing for Pathogenic FMR1 Mutations (Including Fragile X Syndrome)
MP 2.277	Investigational Miscellaneous Genetic and Molecular Diagnostic Tests
MP 2.278	Invasive Prenatal (Fetal) Diagnostic Testing
MP 2.280	Genetic and Protein Biomarkers for the Management, Diagnosis, and Risk Assessment of Prostate Cancer
MP 2.281	JAK2, MPL, and CLR Mutation Analysis in Myeloproliferative Neoplasms
MP 2.306	Genotype-Guided Warfarin Dosing
MP 2.307	Genotype-Guided Tamoxifen Treatment
MP 2.308	Genetic Testing for Helicobacter Pylori Treatment

POLICY TITLE	GENERAL APPROACH TO GENETIC TESTING
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MP 2.309	KIF6 Genotyping for Predicting Cardiovascular Risk and/or Effectiveness of Statin Therapy
MP 2.310	Genetic Testing for Lipoprotein (a) Variant(s) as a Decision Aid for Aspirin Treatment
MP 2.311	Genotyping for 9p21 Single Nucleotide Polymorphisms to Predict Risk of Cardiovascular Disease and Aneurysm
MP 2.312	Genetic Testing for Hereditary Hemochromatosis
MP 2.315	Multigene Expression Assay for Predicting Recurrence in Colon Cancer
MP 2.316	Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment of Metastatic Colorectal Cancer (KRAS, NRAS, BRAF, and HER2)
MP 2.317	BCR-ABL1 Testing in Chronic Myelogenous Leukemia and Acute Lymphoblastic Leukemia
MP 2.318	Genetic Testing for Hereditary Pancreatitis
MP 2.319	Genetic Testing for Hereditary Hearing Loss
MP 2.320	Genetic Testing for Alpha Thalassemia
MP 2.321	Genetic Testing for Facioscpulohumeral Muscular Dystrophy
MP 2.322	Genetic Testing for CHARGE Syndrome
MP 2.323	General Approach to Evaluating the Utility of Genetic Panels
MP 2.324	Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders
MP 2.325	Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
MP 2.328	Genetic Testing for Idiopathic Dilated Cardiomyopathy
MP 2.331	Genetic Testing for Thoracic Aortic Aneurysms and Dissections, and Related Disorders
MP 2.332	Genetic Testing for Limb Girdle Muscular Dystrophies
MP 2.337	Proteomic Testing for Targeted Therapy in Non-Small-Cell Lung Cancer
MP 2.343	Proteogenomic Testing for Patients with Cancer
MP 2.354	Laboratory and Genetic Testing for Use of 5-Flourouracil in Patients with Cancer
MP 2.355	Genetic Testing for the Diagnosis of Inherited Peripheral Neuropathies
MP 2.357	Genetic Testing for FLT3, NPM1, and CEBPA Variants in Cytogenetically Normal Acute Myeloid Leukemia
MP 2.358	Genetic Testing for Neurofibromatosis
MP 2.360	Gene Expression Profiling for Melanoma
MP 2.361	Genetic Testing for Statin-Induced Myopathy
MP 2.362	Genetic Testing for Fanconi Anemia
MP 2.363	Genetic Testing for Heterozygous Familial Hypercholesterolemia
MP 2.364	Somatic Genetic Testing to Select Individuals with Melanoma or Glioma for Targeted Therapy or Immunotherapy
MP 2.375	Molecular Testing in the Management of Pulmonary Nodules
MP 2.377	Molecular Testing for Germline Variants Associated with Ovarian Cancer (BRIP1, RAD51C, RAD51D, NBN)

MP 2.379	Next-Generation Sequencing For The Assessment of Measurable Residual Disease
MP 2.388	Somatic Biomarker Testing for Immune Checkpoint Inhibitor Therapy (MSI/MMR, PD-L1, TMB)
MP 5.013	Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes
MP 7.009	Preimplantation Genetic Testing
MP 7.028	Chromosomal Microarray Testing for the Evaluation of Pregnancy Loss

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