Medical Policy

Malignant Genetic Testing for Familial Melanoma

Policy Number: OCA 3.78
Version Number: 15
Version Effective Date: 02/01/17

Product Applicability

- All Plan\* Products

Well Sense Health Plan
- New Hampshire Medicaid
- NH Health Protection Program

Boston Medical Center HealthNet Plan
- MassHealth
- Qualified Health Plans/ConnectorCare/Employer Choice Direct
- Senior Care Options ◊

Notes:
+ Disclaimer and audit information is located at the end of this document.
◊ The guidelines included in this Plan policy are applicable to members enrolled in Senior Care Options only if there are no criteria established for the specified service in a Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) on the date of the prior authorization request. Review the member’s product-specific benefit documents at www.SeniorsGetMore.org to determine coverage guidelines for Senior Care Options.

Policy Summary

The Plan considers genetic testing for mutations associated with susceptibility to familial malignant melanoma to be experimental and investigational. **Plan prior authorization is required for all molecular and chromosomal genetic testing** except for prenatal genetic screening tests for a member with one of the pregnancy diagnosis codes specified in the Applicable Coding section of the Genetic Testing Guidelines and Pharmacogenetics medical policy (policy number OCA 3.7272), Chromosomal Microarray Analysis for Unexplained Intellectual Disabilities and/or Multiple Congenital Anomalies medical policy (policy number OCA 3.573), or Genetic Testing for Fragile X-Associated Disorders medical policy (policy number OCA 3.571) when applicable Plan criteria are met. Biochemical genetic...
tests used to study the amount or activity level of proteins to indicate changes to the DNA require prior authorization only when the test is included in the Applicable Coding section of a Plan genetic testing medical policy. See the Plan’s Genetic Testing and Pharmacogenetics medical policy (policy number OCA 3.727) rather than this Plan policy for genetic testing to predict the effectiveness of treatment for malignant melanoma or for any other indication.

The Plan supports the National Comprehensive Cancer Network (NCCN) guidelines for genetic counseling for all genetic tests conducted with Plan members; NCCN recommends that adequate pre-test and post-test genetic counseling be provided by a health care professional with expertise in genetics. Genetic counseling provided to a Plan member (and/or guardian if the member is under the age of 18) should be documented in the member’s medical record and conducted by an appropriately trained practitioner with expertise and experience in genetics, including a provider acting within the scope of the practitioner’s license and practice, clinical geneticist, or genetic counselor.

It will be determined during the Plan’s standard prior authorization review process if the service is considered experimental and investigational for the requested use. Review the Plan’s policy, Experimental and Investigational Treatment (policy number OCA 3.12), for the product-specific definitions of experimental or investigational treatment. See the following Plan policies for additional prior authorization guidelines for genetic testing available at www.bmchp.org for BMC HealthNet Plan members (or at www.SeniorsGetMore.org for Senior Care Options members) and www.wellsense.org for Well Sense Health Plan members:

1. Chromosomal Microarray Analysis for Unexplained Intellectual Disabilities and/or Multiple Congenital Anomalies, policy number OCA 3.573
2. Gene Expression Profiling of Tumor Tissue to Predict Cancer Recurrence and Risk Stratification (Including Oncotype DX™ and Other Tests), policy number OCA 3.572
3. Genetic Testing for Fragile X-Associated Disorders, policy number OCA 3.571
4. Genetic Testing Guidelines and Pharmacogenetics, policy number OCA 3.727
5. Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome, policy number OCA 3.57
6. Genetic Testing for Hereditary Colorectal Cancer, policy number OCA 3.64
7. Genetic Testing for Hereditary Thrombophilia, policy number OCA 3.728
8. Preimplantation Genetic Testing (Preimplantation Genetic Diagnosis and Pregenetic Screening), policy number OCA 3.726

Genetic Testing for Familial Malignant Melanoma

*Plan refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.
Familial Malignant Melanoma: Genetic condition in which the risk of melanoma is passed from generation to generation within a family. Familial melanoma usually refers to families in which two (2) or more first-degree relatives (i.e., biological parent, sibling, and/or child) have been diagnosed with melanoma. The condition has also been defined as a family with three (3) melanoma patients (irrespective of the degree of relationship), family with at least three (3) first, second, and/or third degree affected members or two (2) affected family members in which at least one (1) was diagnosed before age 50 years or pancreatic cancer occurred in a first or second degree relative, or one (1) family member who has had multiple primary melanomas.

Genetic Testing for Familial Malignant Melanoma: Genetic testing for mutations of the CDKN2A gene (affecting two separate proteins, p16 and p14ARF) and CDK4 gene are used to predict if an individual has an increased susceptibility for malignant melanoma. Variations in another gene, MC1R, may also impact the risk of melanoma. Other inherited genes may be associated with an increased occurrence of melanoma, such as xeroderma pigmentosum (a rare disorder in which patients have a mutation in a gene needed for repair of ultraviolet radiation induced DNA damage and have a high rate of skin cancer, including melanoma) and the BRCA2 gene (gene associated with hereditary breast and ovarian cancer syndrome and is associated with a slightly increased risk of melanoma). Products that offer genetic testing to predict familial malignant melanoma are commercially available, but the clinical validity and clinical utility of this type of testing have not been consistently established. The results of genetic testing for familial malignant melanoma are unlikely to change screening recommendations or clinical care for individuals with this diagnosis or those who have a strong family history of melanoma. Most families with familial malignant melanoma will not have a genetic mutation identified.

Medical Policy Statement

The Plan considers genetic testing for mutations associated with susceptibility to familial malignant melanoma to be experimental and investigational (including but not limited to CDKN2 known familial mutation analysis, CDK4 known familial mutation analysis, CDKN2A sequencing, CDKN2A deletion/duplication analysis, CDK4 sequencing, and all other types of genetic testing). An example of product used for genetic testing of familial malignant melanoma is Melaris® (Myriad Genetics).

Limitations

The Plan considers genetic testing for mutations associated with susceptibility to familial malignant melanoma to be experimental and investigational. Review Plan policy, Genetic Testing Guidelines and Pharmacogenetics (policy number OCA 3.727), for Plan genetic testing guidelines not outlined in this policy, including but not limited to predicting the effectiveness of treatment, multigene panel testing, whole exome sequencing, and whole genome sequencing.
Definitions

**CDK4:** A specific oncogene on chromosome 12q13, this oncogene is extremely rare and its proposed association with melanoma has not yet been established.

**CDKN2A:** Also known as p16, this is a specific gene on chromosome 9p21 that can alter the tumor suppression function. If this gene is altered the cells can grow into a tumor and has been proposed to be associated with the development of melanoma.

**Dysplastic Nevi:** Large, flat, irregular, asymmetric, and variably pigmented moles. They occur primarily on sun-exposed skin, but they also occur in areas that are not exposed to the sun. The moles must be monitored very carefully for any change in size, shape, and color to watch for signs of cancer. Individuals in melanoma-prone families frequently have dysplastic nevi.

**Genetic Testing:** According to U.S. Library of Medicine, genetic testing is defined as a type of medical test that identifies changes in chromosomes, genes, or proteins. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person’s chance of developing or passing on a genetic disorder. More than 1,000 genetic tests are currently in use, and more are being developed. Several methods can be used for genetic testing:

1. Molecular genetic tests (or gene tests) study single genes or short lengths of DNA to identify variations or mutations that lead to a genetic disorder.

2. Chromosomal genetic tests analyze whole chromosomes to see if there are large genetic changes, such as an extra copy of a chromosome or missing DNA, that cause a genetic condition.

3. Biochemical genetic tests study the amount or activity level of proteins; abnormalities in either can indicate changes to the DNA that result in a genetic disorder.

**Multigene Panel Tests:** Tests that evaluate more than one (1) gene simultaneously to detect changes in gene expression most commonly associated with certain diseases and other genes that may have limited evidence of an association to the disorder. Multigene panel tests may involve traditional exon-by-exon sequencing of targeted genes to identify genetic variants or use next-generation sequencing. Each laboratory establishes its own set of criteria for selecting the genes represented in a panel, even when panels are used for the same or similar clinical indications. The lack of regulatory oversight of genetic testing means that laboratories can change the components of a panel at any time, making it difficult to evaluate the clinical utility of multigene panel tests. See the *Genetic Testing Guidelines and Pharmacogenetics* medical policy (policy number OCA 3.727) rather than this policy for Plan guidelines related to multigene panel testing.
Next-Generation Sequencing (NGS or Massively Parallel Sequencing): Genetic testing that involves sequencing of millions of DNA fragments using the following three (3) levels of molecular analysis: (1) Disease-targeted gene panels to sequence genes with an established role in the targeted disease, (2) exome sequencing of coding regions of the genome to include less common variants associated with the disease (i.e., a coding region is the segment of a gene that contains a protein-coding sequence called an exon in all 22,000 genes of the human genome); and (3) genome sequencing of both the coding and non-coding regions of the genome (i.e., the non-coding regions in between exons are called introns). Multiple sequencing platforms and different processes result in variability in test results among laboratories.

Whole Exome Sequencing (WES)/ Whole Genome Sequencing (WGS): Sequencing the protein coding regions (called exons) of all of an individual’s genes (known as the exome). While exons represent only 1% of the genome, they account for approximately 85% of disease-causing variants. Through identification of variants across the exome, WES avoids the need to run multiple single-gene tests, which require prior information about variants affecting the disease. WES has been performed in a number of cancers, whereby comparison between tumor DNA and normal DNA from the same individual allows identification of variants specific to the tumor, which may provide information used for diagnosis and treatment. WES is targeted sequencing of the subset of the human genome that contains functionally important sequences of protein-coding DNA, while whole genome sequencing (WGS) uses next-generation sequencing techniques to sequence both coding and non-coding regions of the genome. See the Genetic Testing Guidelines and Pharmacogenetics medical policy (policy number OCA 3.727) rather than this policy for Plan guidelines related to WES and WGS.

Applicable Coding

The Plan uses and adopts up-to-date Current Procedural Terminology (CPT) codes from the American Medical Association (AMA), International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) diagnosis codes developed by the World Health Organization and adapted in the United Stated by the National Center for Health Statistics (NCHS) of the Centers for Disease Control under the U.S. Department of Health and Human Services, and the Health Care Common Procedure Coding System (HCPCS) established and maintained by the Centers for Medicare & Medicaid Services (CMS). Because the AMA, NCHS, and CMS may update codes more frequently or at different intervals than Plan policy updates, the list of applicable codes included in this Plan policy is for informational purposes only, may not be all inclusive, and is subject to change without prior notification. Whether a code is listed in the Applicable Coding section of this Plan policy does not constitute or imply member coverage or provider reimbursement. Providers are responsible for reporting all services using the most up-to-date industry-standard procedure and diagnosis codes as published by the AMA, NCHS, and CMS at the time of the service.

Providers are responsible for obtaining prior authorization for the services specified in the Medical Policy Statement section and Limitation section of this Plan policy, even if an applicable code appropriately describing the service that is the subject of this Plan policy is not included in the Applicable Coding section of this Plan policy. Coverage for services is subject to benefit eligibility under Genetic Testing for Familial Malignant Melanoma

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the member’s benefit plan. Please refer to the member’s benefits document in effect at the time of the service to determine coverage or non-coverage as it applies to an individual member. See Plan reimbursement policies for Plan billing guidelines. Review the Plan’s policy, Genetic Testing Guidelines and Pharmacogenetics, policy number OCA 3.727, for additional guidelines regarding genetic testing.

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<tr>
<th>CPT Code</th>
<th>Description: Code Covered When Medically Necessary (Based on Testing Indication)</th>
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<tr>
<td>81404</td>
<td>Molecular pathology procedure, Level 5 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis) CDKN2A (cyclin-dependent kinase inhibitor 2A) (e.g., CDKN2A-related cutaneous malignant melanoma, familial atypical mole-malignant melanoma syndrome), full gene sequence (Plan note: CDKN2A gene sequence testing is considered experimental and investigational to determine susceptibility to familial malignant melanoma. This CPT code includes numerous types of tests. See Plan policy, Genetic Testing Guidelines and Pharmacogenetics, policy number OCA 3.727, for prior authorization guidelines for the additional tests included in this CPT code.)</td>
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</table>

**Clinical Background Information**

Melanoma is a malignant tumor of the skin and causes the majority of skin cancer related deaths. It is most frequently associated with male Caucasians and in individuals who live in sunny climates. The development of melanoma is thought to be linked to genetic mutations in the CDKN2A or p16 gene and is passed on in families as an autosomal dominant trait; the mutations are not linked to the sex chromosomes/gender. If a parent has a mutation, each child has a 1 in 2 or 50% chance of inheriting the chromosome with the mutation on it and may be at risk for developing cancer.

Mutations in the CDKN2A gene are thought to be associated with susceptibility to melanoma. However, there is insufficient evidence to assess the efficacy of testing for this gene at this time. The National Cancer Institute recommends that individuals who have a family history of melanoma and are at risk must be screened appropriately and counseled to avoid sun exposure, wear sun-protective clothing, and use sun screen. Additional recommendations include careful monitoring of all skin changes, specifically in the size, color, and shape of moles, and continued follow up by a qualified dermatologist.

At the time of the Plan’s most recent policy review, the Centers for Medicare & Medicaid Services (CMS) has implemented the following national coverage determinations (NCDs) related to genetic tests: NCD for Colorectal Cancer Screening Tests (210.3) for coverage of immunoassay and guaiac fecal occult blood tests and the Cologuard™ - Multitarget Stool DNA (sDNA) test when CMS applicable.

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criteria are met, NCD for Pharmacogenomic Testing for Warfarin Response (90.1) for medically necessary indications for testing as determined by CMS, and NCD for Cytogenetic Studies (190.3) for coverage based on CMS guidelines. Medicare uses a combination of national and local coverage determinations for making coverage decisions for genetic tests. Medicare administrative contractors (MAC) may implement local coverage determinations (LCDs) that apply only within their own jurisdictions. Verify if applicable CMS criteria are in effect (through an NCD, LCD, or other CMS guidelines) for the specified genetic test, product name, site-specific gene analysis, and the indication for testing on the date of the prior authorization request for a Senior Care Options member.

References


Genetic Testing for Familial Malignant Melanoma

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## Genetic Testing for Familial Malignant Melanoma

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### Regulatory Approval: N/A

<table>
<thead>
<tr>
<th>Original Approval Date</th>
<th>Original Effective Date* and Version Number</th>
<th>Policy Owner</th>
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<tbody>
<tr>
<td>12/12/07: MPCTAC</td>
<td>04/01/08 Version 1</td>
<td>Medical Policy Manager as Chair of Medical Policy, Criteria, and Technology Assessment Committee (MPCTAC) and member of Quality Improvement Committee (QIC)</td>
<td>MPCTAC, QIC, and Utilization Management Committee (UMC)</td>
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<td>12/18/07: UMC</td>
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<td>01/10/08: QIC</td>
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*Effective Date for the BMC HealthNet Plan Commercial Product(s): 01/01/12
*Effective Date for the Well Sense Heath Plan New Hampshire Medicaid Product(s): 01/01/13
*Effective Date for the Senior Care Options Product(s): 01/01/13

### Policy Revisions History

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Summary of Revisions</th>
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<tr>
<td>12/01/10</td>
<td>Updated references.</td>
<td>Version 4</td>
<td>12/28/10: MPCTAC 01/26/11: QIC</td>
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<td>12/01/11</td>
<td>Updated labs that currently offer the testing, updated references.</td>
<td>Version 5</td>
<td>12/12/11: MPCTAC 12/20/11: QIC</td>
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<tr>
<td>07/01/12</td>
<td>Off cycle review for Well Sense Health Plan, revised Summary statement, revised Medical Policy Statement, deleted reference to labs offering the testing.</td>
<td>Version 6</td>
<td>08/03/12: MPCTAC 09/0512: QIC</td>
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<td>09/01/12</td>
<td>Review for effective date 01/01/13. Updated language and code list in Applicable Coding section, revised Summary section, removed list of laboratories from the Description of Item or Service, updated references. Referenced Plan’s policy, Experimental and Investigational Treatment.</td>
<td>01/01/13 Version 7</td>
<td>09/19/12: MPCTAC 10/24/12: QIC</td>
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<td>10/01/13</td>
<td>Review for effective date 02/01/14. Updated Summary section and References section. Revised applicable code list and added Plan note to applicable code description.</td>
<td>02/01/14 Version 8</td>
<td>10/16/13: MPCTAC 11/21/13: QIC</td>
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<tr>
<td>07/01/14</td>
<td>Review for effective date 08/01/14. Updated the Summary section.</td>
<td>08/01/14 Version 9</td>
<td>07/21/14: MPCTAC (electronic vote)</td>
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<td>10/01/14</td>
<td>Review for effective date 12/01/14. Updated References, Summary, and Definitions sections. No change to criteria or to the applicable code list.</td>
<td>12/01/14 Version 10</td>
<td>10/15/14: MPCTAC</td>
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<td>12/01/14</td>
<td>Review for effective date 01/01/15. Changed annual review schedule. Updated Summary section.</td>
<td>01/01/15 Version 11</td>
<td>12/02/14: MPCTAC</td>
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<td>11/25/15</td>
<td>Review for effective date 01/01/16. Updated template with list of applicable products and notes. Revised language in the Applicable Coding section.</td>
<td>01/01/16 Version 12</td>
<td>11/18/15: MPCTAC (electronic vote)</td>
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<tr>
<td>01/01/16</td>
<td>Review for effective date 03/01/16. Updated Summary, Definitions, and References sections. Administrative changes made to the Limitations section.</td>
<td>03/01/16 Version 13</td>
<td>01/20/16: MPCTAC</td>
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<td>09/28/16</td>
<td>Review for effective date 11/01/16. Administrative changes made to clarify language related to gender.</td>
<td>11/01/16 Version 14</td>
<td>09/30/16: MPCTAC (electronic vote)</td>
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<td>12/01/16</td>
<td>Review for effective date 02/01/17. Administrative changes made to Summary, Description of Item or Service, Medical Policy Statement, Limitations, Definitions, Clinical Background Information, References, and References to Applicable Laws and Regulations sections.</td>
<td>02/01/17 Version 15</td>
<td>12/21/16: MPCTAC</td>
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**Last Review Date**

12/01/16

**Next Review Date**

12/01/17

**Authorizing Entity**

QIC
Other Applicable Policies

Medical Policy - Chromosomal Microarray Analysis for Unexplained Intellectual Disabilities and/or Multiple Congenital Anomalies, policy number OCA 3.573
Medical Policy - Experimental and Investigational Treatment, policy number OCA 3.12
Medical Policy - Gene Expression Profiling of Tumor Tissue to Predict Cancer Recurrence and Risk Stratification (Including Oncotype DX™ and Other Tests), policy number OCA 3.572
Medical Policy - Genetic Testing for Fragile X-Associated Disorders, policy number OCA 3.571
Medical Policy - Genetic Testing Guidelines and Pharmacogenetics, policy number OCA 3.727
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Medical Policy - Genetic Testing for Hereditary Thrombophilia, policy number OCA 3.728
Medical Policy - Preimplantation Genetic Testing (Preimplantation Genetic Diagnosis and Pregenetic Screening), policy number OCA 3.726

Reference to Applicable Laws and Regulations


Massachusetts General Law. Chapter 111. Section 70G. (M.G.L. c. 111 sec. 70G.) Genetic information and reports protected as private information; prior written consent for genetic testing. Accessed at: https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXVI/Chapter111/Section70G

Disclaimer Information: +

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.

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