

Corporate Medical Policy

Genetic Testing for Cutaneous Malignant Melanoma

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| File Name: | genetic_testing_for_cutaneous_malignant_melanoma |
| Origination: | 8/2011 |
| Last CAP Review: | 1/2012 |
| Next CAP Review: | 1/2013 |
| Last Review: | 1/2012 |

Description of Procedure or Service

A genetic predisposition to cutaneous malignant melanoma is suspected in specific clinical situations: 1) melanoma has been diagnosed in multiple family members; 2) multiple primary melanomas are identified in a single patient; and 3) when there is an early age of onset. A positive family history of melanoma is the most significant risk factor; it is estimated that approximately 10% of melanoma cases report a first- or second-degree relative with melanoma. While some of the familial risk may be related to shared environmental factors, 3 main genes involved in cutaneous malignant melanoma susceptibility have now been identified. CDKN2A, located on chromosome 9p21 encodes proteins that act as tumor suppressors. Mutations at this site can alter the tumor suppressor function. The second gene, CDK4, is an oncogene located on chromosome 12q13, and has been identified in about 6 families worldwide. A third gene, not fully characterized, maps to chromosome 1p22.

The incidence of CDKN2A mutations in the general population is very low. For example, it is estimated that in Queensland, Australia, an area with a high incidence of melanoma, only 0.2% of all patients with melanoma will harbor a CDKN2A mutation. Mutations are also infrequent in those with an early age of onset or those with multiple primary melanomas. However, the incidence of CDKN2A mutations increases with a positive family history; CDKN2A mutations will be found in 5% of families with first-degree relatives, rising to 20%–40% in kindred with 3 or more affected first-degree relatives. Mutation detection rates in the CDK2NA gene is generally estimated as 20%–25% in hereditary CMM, but can vary between 2% and 50% depending on the family history and population studied.

Hereditary cutaneous malignant melanoma (CMM) has been described as a family in which either 2 first-degree relatives are diagnosed with melanoma or a family with 3 melanoma patients irrespective of the degree of relationship. Others have defined hereditary CMM as having at least 3 (first-, second- or third-degree) affected members, or 2 affected family members in which at least 1 was diagnosed before age 50 years or pancreatic cancer occurred in a first- or second-degree relative, or 1 member had multiple primary melanomas.

Other malignancies associated with hereditary CMM, specifically those associated with CDKN2A mutations, have been described. The most pronounced associated malignancy is pancreatic cancer, followed by other gastrointestinal malignancies, breast cancer, brain cancer, lymphoproliferative malignancies, and lung cancer. It is also important to recognize that other cancer susceptibility genes may be involved in these families. In particular, germline BRCA2 gene mutations have been described in families with melanoma and breast cancer, gastrointestinal cancer, pancreatic cancer, or prostate cancer.

Hereditary forms of CMM can occur either with or without a family history of multiple dysplastic nevi. Families with both CMM and multiple dysplastic nevi have been referred to as having familial

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atypical multiple mole and melanoma syndrome (FAMMM). This syndrome is difficult to define since there is no agreement on a standard phenotype, and dysplastic nevi occur in up to 50% of the general population. Atypical or dysplastic nevi are associated with an increased risk for CMM. Initially, the phenotypes of atypical nevi and CMM were thought to cosegregate in FAMMM families, leading to the assumption that a single genetic factor was responsible. However, it was subsequently shown that in families with CDKN2A mutations, there were family members with multiple atypical nevi who were non-carriers of the CDKN2A familial mutation. Thus, the nevus phenotype cannot be used to distinguish carriers from non-carriers of CMM susceptibility in these families.

Some common allele(s) are associated with increased susceptibility to CMM but have low penetrance. One such gene is the Melanocortin 1 receptor gene (MC1R). Variants in this gene are relatively common and have low penetrance for CMM. This gene is associated with fair complexion, freckles and red hair; all risk factors for CMM. Variants in MC1R also modify the CMM risk in families with CDKN2A mutations.

Melaris® is a commercially available genetic test of the CDKN2A gene

*****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 for cutaneous malignant melanoma is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

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 for Cutaneous Malignant Melanoma is covered

Not applicable

When Genetic Testing for Cutaneous Malignant Melanoma is not covered

Genetic testing for mutations associated with hereditary cutaneous malignant melanoma or associated with susceptibility to cutaneous malignant melanoma is considered investigational.

Policy Guidelines

While genetic testing for CDKN2A mutations is recognized as an important research tool, its clinical use will depend on how the results of the genetic analysis can be used to improve patient management. Currently, management of patients considered at high risk for malignant melanoma focuses on reduction of sun exposure, use of sun screens, vigilant cutaneous surveillance of pigmented lesions, and prompt biopsy of suspicious lesions. At present, it is unclear how genetic testing for CDKN2A would alter these management recommendations

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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 service codes: There are no specific CPT codes for genetic testing specifically for susceptibility to malignant melanoma. A series of CPT codes describing the individual steps in the genetic analysis would be used.

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

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.44, 9/16/11

Kanetsky PA, Panossian S, Elder DE et al. Does MC1R genotype convey information about melanoma risk beyond risk phenotypes? *Cancer* 2010; 116(10):2416-28. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2864335/?tool=pubmed>

Specialty Matched Consultant Advisory Panel review 1/2012

Policy Implementation/Update Information

8/16/11 New policy implemented. Genetic testing for mutations associated with hereditary cutaneous malignant melanoma or associated with susceptibility to cutaneous malignant melanoma is considered investigational. Medical Director review 8/2011. Notice given 8/16/11 for effective date 11/22/11. (mco)

2/7/12 Specialty Matched Consultant Advisory Panel review 1/2012. No changes to Policy Statements. (mco)

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.