FEP 2.04.44 Genetic Testing for Familial Cutaneous Malignant Melanoma

Effective Date: July 15, 2017
Related Policies: None

Genetic Testing for Familial Cutaneous Malignant Melanoma

Description
Cutaneous melanoma is the third most common type of skin cancer, but the most lethal. Some cases of cutaneous malignant melanoma are familial. Potential genetic markers for this disease are being evaluated in affected individuals with a family history of disease and in unaffected individuals in a high-risk family.

FDA REGULATORY STATUS
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). Melaris® (Myriad Genetics, Salt Lake City, UT) and other CDKN2A tests are laboratory-developed tests (LDTs) and available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

POLICY STATEMENT
Genetic testing for genes associated with familial cutaneous malignant melanoma or associated with susceptibility to cutaneous malignant melanoma is considered investigational.

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’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.
**BENEFIT APPLICATION**

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

**RATIONALE**

**Summary of Evidence**

For individuals who have cutaneous malignant melanoma and a family history of this disease who receive genetic testing for genes associated with familial cutaneous malignant melanoma, the evidence includes genetic association studies between variants in certain genes and the risk of developing cutaneous melanoma. Relevant outcomes are overall survival, disease-specific survival, test accuracy, and test validity. Data on the analytic validity of testing are lacking. Limitations with clinical validity include difficulties with variant interpretations, variable penetrance of a given variant, and residual risk with a benign variant. Currently, management of melanoma patients do not change based on genetic variants identified in genes associated with familial cutaneous malignant melanoma, therefore, clinical utility is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are asymptomatic and in a family at high risk of developing cutaneous malignant melanoma who receive genetic testing for genes associated with familial cutaneous malignant melanoma, the evidence includes genetic association studies between variants in certain genes and the risk of developing cutaneous malignant melanoma. Relevant outcomes are overall survival, disease-specific survival, test accuracy, and test validity. Data on the analytic validity of testing are lacking. Limitations with clinical validity include difficulties with variant interpretations, variable penetrance of a given variant, and residual risk with a benign variant. Currently, management of patients considered high risk for cutaneous malignant melanoma focuses on reduction of sun exposure, use of sunscreens, vigilant cutaneous surveillance of pigmented lesions, and prompt biopsy of suspicious lesions. It is unclear how genetic testing for variants associated with increased risk of cutaneous malignant melanoma would alter these management recommendations; therefore, clinical utility is lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**Practice Guidelines and Position Statements**

**Melanoma Genetics Consortium**

In 2002, the Melanoma Genetics Consortium, comprising familial melanoma researchers from North America, Europe, and Australia, indicated that genetic testing for melanoma susceptibility should not be offered outside of a research setting.

**American Society of Clinical Oncology**

In a 2002 American Society of Clinical Oncology (ASCO) publication, Kefford et al noted that the sensitivity and specificity of tests for CDKN2A variants are not fully known. Because interpreting genetic tests is difficult and because test results do not alter patient management, ASCO indicated that CDKN2A genetic testing should be performed only in clinical trials for several reasons, including: a low likelihood of finding disease-associated variants in known melanoma susceptibility genes, uncertainty about the functionality and phenotypic expression of the trait among disease-associated variant carriers, and lack of proven melanoma prevention and surveillance strategies. Additionally, it was noted that all individuals with risk factors for cutaneous melanoma should follow programs of sun protection and skin surveillance, not just those considered high risk due to family history.
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In 2010, ASCO updated its policy statement on genetic and genomic testing for cancer susceptibility. ASCO recommended that "genetic tests with uncertain clinical utility, including genomic risk assessment, be administered in the context of clinical trials."

National Comprehensive Cancer Network

Current National Comprehensive Cancer Network guidelines for melanoma (v.1.2017) have added a new bullet to "consider referral to a genetics counselor for p16/CDKN2A mutation [variant] testing in the presence of 3 or more invasive melanomas or a mix of invasive melanoma and pancreatic cancer diagnoses in an individual or family."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

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**POLICY HISTORY**

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>December 2011</td>
<td>New</td>
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<tr>
<td>June 2012</td>
<td>Update Policy</td>
<td>Policy statement changed to not medically necessary.</td>
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<tr>
<td>December 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review, References added and updated.</td>
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