FEP 2.04.120 Gene Expression Profiling for Uveal Melanoma

Description
Uveal melanoma is associated with a high rate of metastatic disease, and survival after the development of metastatic disease is poor. Prognosis following treatment of local disease can be assessed using various factors, including clinical and demographic markers, tumor stage, tumor characteristics, and tumor cytogenetics. Gene expression profiling (GEP) can be used to determine prognosis. This evidence review addresses whether outcomes are improved when GEP testing is used to determine prognosis of patients with uveal melanoma compared to determining prognosis without GEP testing.

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 Amendments (CLIA). Exome or genome sequencing tests as a clinical service are 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
Gene expression profiling for uveal melanoma with DecisionDX-UM is medically necessary for patients with primary, localized uveal melanoma. Gene expression profiling for uveal melanoma that do not meet the above criteria are investigational.

BENEFIT APPLICATION
Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient’s existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

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

Summary of Evidence
For individuals who have localized uveal melanoma who receive a gene expression profiling (GEP) test for uveal melanoma, the evidence includes cross-sectional studies of assay validation and clinical validity. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, other test performance measures, functional outcomes, health status measures, and quality of life. There is limited published data on the analytic validity of GEP testing. Three studies of clinical validity identified used the GEP score to predict melanoma metastases and melanoma-specific survival. All 3 reported that GEP class correlated strongly with metastatic disease and melanoma mortality. Two studies compared GEP class to other prognostic markers, and GEP class had the strongest association among the markers tested. GEP class appears a strong predictor of metastatic disease and melanoma death. There are no studies directly showing clinical utility. In the absence of direct evidence, an indirect chain of evidence to determine whether using the results of GEP testing for management decisions improves the net health outcome of patients with uveal melanoma. GEP classification appears be a strong predictor metastatic disease and melanoma death. There are no studies directly showing clinical utility. In the absence of direct evidence, an indirect chain of evidence to determine whether using the results of GEP testing for management decisions improves the net health outcome of patients with uveal melanoma. GEP classification appears be a strong predictor metastatic disease and melanoma death. Aaberg et al (2014) have shown an association between GEP classification and treatment, reporting that patients classified as low risk were managed with less frequent and intensive surveillance and were not referred for adjuvant therapy. It is uncertain whether stratification of patients into higher risk categories has the potential to improve outcomes by allowing patients to receive adjuvant therapies or through the detection of metastases earlier. However, classification into the low-risk group would allow reduction in the burden of surveillance without apparent harm. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements
National Comprehensive Cancer Network In its guidelines on melanoma (Version 1.2017), the National Comprehensive Cancer Network (NCCN) states, “Mucosal and uveal melanomas differ significantly from cutaneous melanoma in presentation, genetic profile, staging, response to treatment, and patterns of progression. Ideally, mucosal and uveal melanoma should be treated as diseases distinct from cutaneous melanoma, with care tailored to the individual.”

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


The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.

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POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>September 2014</td>
<td>New Policy</td>
<td>Policy updated with literature review; no references added.</td>
</tr>
<tr>
<td>September 2015</td>
<td>Update Policy</td>
<td>Policy statement unchanged.</td>
</tr>
<tr>
<td>December 2016</td>
<td>Update policy</td>
<td>Policy updated with literature review through April 29, 2016; references 2-4, 6-9, 11, 14, and 16-18 added. Policy statement unchanged.</td>
</tr>
<tr>
<td>March 2017</td>
<td>Update policy</td>
<td>Policy updated with literature review through February 2, 2017; references 5-7, 22, and 24 added. Policy statement changed to medically necessary for patients with localized uveal melanoma</td>
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