FEP Medical Policy Manual

FEP 2.04.120 Gene Expression Profiling for Uveal Melanoma

Effective Policy Date: July 1, 2023

Original Policy Date: September 2014

Related Policies:

None

Gene Expression Profiling for Uveal Melanoma

Description

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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, and gene expression profile testing is commercially available.

OBJECTIVE

The objective of this evidence review is to assess whether net health outcomes are improved when gene expression profile testing is used to determine the prognosis of patients with uveal melanoma compared to determining prognosis without gene expression profile testing.

POLICY STATEMENT

Gene expression profiling for uveal melanoma with DecisionDx-UM is **medically necessary** for individuals with primary, localized uveal melanoma.

Gene expression profiling for uveal melanoma that does not meet the above criteria is **investigational.**

POLICY GUIDELINES

None

BENEFIT APPLICATION

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

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.

FDA REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). The DecisionDx-UM test (Castle Biosciences, Phoenix, AZ) is available under the auspices of the CLIA. Laboratories that offer laboratory-developed tests must be licensed by the 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.

RATIONALE

Summary of Evidence

For individuals who have localized uveal melanoma who receive a gene expression profiling (GEP) test for uveal melanoma (DecisionDx-UM), 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. One commercially available test identified (DecisionDx-UM) has published data related to its clinical validity, and is the focus of this review. Six studies of clinical validity identified used the GEP score to predict melanoma metastases and melanoma-specific survival. All 6 reported that GEP classification correlated strongly with metastatic disease and/or melanoma mortality. Four studies compared GEP classification with other prognostic markers, and GEP class had the strongest association among the markers tested. GEP classification appears to be a strong predictor of metastatic disease and melanoma death. There are no studies directly showing clinical utility. Absent of direct evidence, a chain of evidence can be constructed to determine whether using the results of GEP testing for management decisions improves the net health outcome of patients with uveal melanoma. 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 through detection of metastases earlier. However, classification into the low-risk group would support a reduction in the burden of surveillance without apparent harm. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network guidelines (v2.2022) for uveal melanoma state that if biopsy is performed, "molecular/chromosomal testing for prognostication is preferred over cytology alone." The guidelines include DecisionDx-UM classes as 1 of the factors used to risk-stratify patients for systemic imaging and note that risk stratification to determine the frequency of follow-up should be based on the highest risk factor present.[14,]

Melanoma Focus

In 2015, Melanoma Focus, a British medical nonprofit that focuses on melanoma research, published guidelines on uveal melanoma.[15,] These guidelines, which were created using a process accredited by NICE, contained the following statements on prognosis and surveillance.

"3.5.1 Prognostic factors/tool

1. Prognostic factors of uveal melanoma are multi-factorial and include clinical, morphological and genetic features. The following features should be recorded:

- Age
- Gender
- Tumour location
- Tumour height
- Tumour Largest [sic] basal diameter
- Ciliary body involvement
- Extraocular melanoma growth (macroscopic)

The following features should be recorded if tissue is available:

- Cell type (modified Callender system)
- Mitotic count (number/40 high power fields in H&E [hematoxylin and eosin] stained sections)
- Presence of extravascular matrix patterns (particularly closed connective tissue loops; enhanced with Periodic acid Schiff staining). Grade A
- Presence of extraocular melanoma growth (size, presence or absence of encapsulation). [GRADE A]

3.5.2 Prognostic biopsy

1. There should be a fully informed discussion with all patients, explaining the role of biopsy including the benefits and risks. The discussion should include:

- Risks of having the biopsy
- Limitations of the investigation
- Benefits of future treatments (including possible recruitment to trials)
- Impact on quality of life (2022)

2. Use the current (i.e. 7th) Edition of the Tumor Node Metastasis staging system for prognostication is highly recommended. (2022)

3. Use of multifactorial prognostication models incorporating clinical, histological, immunohistochemical and genetic tumour features should be considered. (2022)

3.6 Surveillance

1. Prognostication and surveillance should be led by a specialist multidisciplinary team that incorporates expertise from ophthalmology, radiology, oncology, cancer nursing and hepatic services.

2. Prognostication and risk prediction should be based on the best available evidence, taking into account clinical, morphological and genetic cancer features.

3. All patients, irrespective of risk, should have a holistic assessment to discuss the risk, benefits and consequences of entry into a surveillance programme. The discussion should consider risk of false positives, the emotional impact of screening as well as the frequency and duration of screening. An individual plan should be developed.

4. Patients judged at high-risk of developing metastases should have 6-monthly life-long surveillance incorporating a clinical review, nurse specialist support and liver specific imaging by a non-ionising modality.

5. Liver function tests alone are an inadequate tool for surveillance. "

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
September 2014	New policy	Gene expression profiling for uveal melanoma is considered investigational
September 2015	Replace policy	Policy updated with literature review through April 28, 2015; no references added. Policy statement unchanged.
December 2016	Replace policy	Policy updated with literature review through April 29, 2016; references 2-4, 6-9, 11, 14, and 16-18 added. Policy statement unchanged.
March 2017	Replace policy	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
June 2018	Replace policy	Policy updated with literature review through December 11, 2017; no references added. Policy statement unchanged.
June 2019	Replace policy	Policy updated with literature review through December 4, 2018. Reference to new NCCN guidelines specific to uveal melanoma added. Policy statement unchanged.
June 2020	Replace policy	Policy updated with literature review through December 9, 2019; reference on NCCN guidelines updated. Policy statement unchanged.
June 2021	Replace policy	Policy updated with literature review through November 17, 2020; references added. Policy statements unchanged.
June 2022	Replace policy	Policy updated with literature review through January 7, 2022; no references added. Policy statements unchanged.
June 2023	Replace policy	Policy updated with literature review through December 16, 2022; references added. Minor editorial refinements to policy statements; intent unchanged.