Policy Name: Gene Expression Profiling for Melanoma  
Effective Date: 7/20/2020

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

Coverage Policy

DecisionDx-UM (uveal melanoma) Assay is COVERED for assessment of patients diagnosed with primary, localized, non-metastatic uveal melanoma that has not been previously treated.

DecisionDx-UM (uveal melanoma) Assay is investigative and unproven and therefore NOT COVERED for all other clinical presentations and conditions. There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

All other gene expression profiles for assessment of cutaneous or uveal melanoma are investigative and unproven and therefore NOT COVERED for all indications, including but not limited to:
1. DecisionDx-Melanoma
2. Pigmented Lesion Assay (PLA)
3. myPath® Melanoma
4. DecisionDx-PRAME

There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

Note: See also related position statement, Genetic Testing and Pharmacogenetic Testing.

Description

Melanoma is an aggressive cancer that can be difficult to diagnose. Improved patient outcomes is attributed to accurate and early diagnosis of melanocytic lesions. The reference standard for diagnosis of melanoma is histopathology. Histopathologic examination is adequate for most cases, however, in cases of indeterminate histopathology, long-term follow-up is needed to determine the final clinical diagnosis. In equivocal cases, members are at risk of receiving indeterminate or inaccurate diagnoses may lead to inappropriate treatment. Gene expression profiling (GEP) is purported to provide additional clarity in these difficult to diagnose cases.

A gene expression profile is a laboratory test that measures degree of expression of multiple genes from tumor tissue samples obtained during surgery. Based on assay results, the melanoma is classified into a risk category based on expression of the gene sets that were analyzed.
Many gene expression profiles assays are purported for prediction of melanoma metastasis and recurrence and to assist in the decisions regarding treatment and surveillance. Examples include, but are not limited to:

1. **DecisionDx-UM** test is an RNA gene expression classifier that is based on the expression levels of 15 mRNA transcripts genes. The DecisionDx-UM test is intended for determination of metastatic risk, and to guide surveillance and referral to medical oncology in patients who have a confirmed diagnosis of uveal melanoma (UM) and no evidence of metastatic disease. DecisionDx-UM is performed on tissue from a fresh-frozen fine needle aspirate biopsy (FNAB). Results are reported as a 5-year risk classification for metastasis: low-risk (Class 1A), intermediate risk (Class 1B), or high risk (Class 2).

2. **DecisionDx-Melanoma** is a 31-gene expression profile (GEP) assay that purportedly determines a cutaneous melanoma (CM) patient’s risk for metastatic disease in individuals with stage I or stage II cutaneous melanoma who have no sign of disease beyond the original tumor. The test classifies patients as having a tumor with low (Class 1) or high (Class 2) risk for developing metastasis within 5 years of diagnosis.

3. **Pigmented Lesion Assay (PLA)** measures expression of six genes (PRAME, LINC00518, CMIP, B2M, ACTB, and PPIA). The test is performed on skin samples of lesions obtained via noninvasive, proprietary adhesive patch biopsies of a stratum corneum specimen. The PLA sample report states that for low-risk lesions, physicians should “consider surveillance,” while for moderate- and high-risk lesions, physicians should “recommend a biopsy.” It does not state whether lesions with negative results should be further evaluated with dermoscopy or other techniques to confirm the lesion should not be biopsied.

4. **myPath Melanoma** is a genetic test that measures expression of 23 genes using quantitative reverse-transcription polymerase chain reaction (qRT-PCR) methodology. The myPath test is meant as an add-on test to standard histopathology. An algorithm is applied that combines the measurements of gene expression, assigns a weight to each gene component, and establishes a threshold value. The result is a single numerical score that purportedly classifies a melanocytic lesion as ‘likely benign,’ ‘likely malignant,’ or ‘indeterminate.’ No recommendations for treatment or surveillance are given on the report.

5. **DecisionDx-PRAME** (preferentially expressed antigen in melanoma) is a cancer testis antigen gene that according to Castle Biosciences, is not expressed at appreciable levels in normal adult tissues but its expression can become aberrantly increased in some types of cancer, including sarcoma, hematological malignancies, breast cancer, and melanoma.

**FDA Approval**
Genetic tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA) Act of 1988. Premarket approval from the FDA is not required as long as the assay is performed in a laboratory facility that observes CLIA regulations and the test is not marketed for general distribution.

The DecisionDx-Melanoma, the DecisionDx®-Uveal Melanoma, and the DecisionDx-PRAME are gene expression profile assays developed by Castle Biosciences Inc. and are currently performed only at Castle Biosciences Laboratory. Therefore, these assays are not currently subject to FDA approval.

Other gene expression profile assays not currently subject to FDA approval include, but are not limited to:
1. The Myriad myPath Melanoma test (Myriad Genetic Laboratories, Inc.)
2. The Pigmented Lesion Assay (PLA) (DermTech)

**Prior Authorization**
Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.
Coding Considerations
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes
- 81529 – Oncology (cutaneous melanoma), mRNA, gene expression profiling by real-time RT-PCR of 31 genes (28 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk, including likelihood of sentinel lymph node metastasis
- 81552 – Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis
- 0089U - Oncology (melanoma), gene expression profiling by RTqPCR, PRAME and LINC00518, superficial collection using adhesive patch(es)
- 0090U - Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 23 genes (14 content and 9 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a categorical result (ie, benign, indeterminate, malignant)

Original Effective Date: 7/20/2020
Re-Review Date(s): 1/1/2021 – administrative update; code update

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