

Medical Coverage Policy | Gene Expression Profiling for Cutaneous Melanoma



EFFECTIVE DATE: 11|01|2025

POLICY LAST REVIEWED: 07|02/2025

OVERVIEW

Laboratory tests have been developed that detect the expression of different genes in pigmented lesions or melanoma tumor tissue. Test results may help providers and patients decide whether to biopsy suspicious pigmented lesions, aid in diagnosis of lesions with indeterminate histopathologic findings or determine whether to perform sentinel lymph node biopsy in patients diagnosed with stage I or II cutaneous melanoma.

The following tests are addressed in this policy:

- DecisionDx-Melanoma (Castle Biosciences) CPT code 81529
- myPath Melanoma (Castle Biosciences) CPT code 0090U

MEDICAL CRITERIA

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DecisionDx Melanoma - 81529

DecisionDx Melanoma may be considered medically necessary when ALL of the following criteria is ~~are~~ met:

1. The member has either of the following:
 - a. Stage I melanoma (staging based on AJCC American Joint Committee on Cancer), OR
 - b. Stage II melanoma (staging based on AJCC American Joint Committee on Cancer), AND
2. The member does NOT have metastatic disease, AND
3. The results of testing will inform subsequent biopsy decisions, use of adjuvant therapy(ies), or follow-up screening protocols.

myPath Melanoma – 0090U

myPath Melanoma may be considered medically necessary when the following criteria is ~~are~~ met:

- The member has a melanocytic neoplasm that is diagnostically uncertain or equivocal after histopathology.

PRIOR AUTHORIZATION

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Prior authorization is required for the following tests:

- DecisionDx-Melanoma
- myPath Melanoma

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI

provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

POLICY STATEMENT

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The following tests may be considered medically necessary when the medical criteria above are met:

- DecisionDx-Melanoma
- myPath Melanoma

Commercial Products

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. §27-19-81 described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable laboratory benefits/coverage.

BACKGROUND

Cutaneous Melanoma

Cutaneous melanoma accounts for more than 90% of cases of melanoma. For many decades, melanoma incidence was rapidly increasing in the United States. However, recent estimates have suggested the rise may be slowing. In 2018, close to 105,000 new cases of melanoma are expected to be diagnosed and more than 8400 people are expected to die of melanoma.

Risk Factors

Exposure to solar ultraviolet radiation is a major risk factor for melanoma. Most melanomas occur on sun-exposed skin, particularly those areas most susceptible to sunburn. Likewise, features that are associated with an individual's sensitivity to sunlight, such as light skin pigmentation, red or blond hair, blue or green eyes, freckling tendency, and poor tanning ability are well-known risk factors for melanoma. There is also a strong association between high total body nevus counts and melanoma.

Several genes appear to contribute to melanoma predisposition such as tumor suppressor gene CDKN2A, melanocortin-1 receptor (MC1R) gene, and BAP1 variants. Individuals with either familial or sporadic melanoma have a 2 to 3 times increased risk of developing a subsequent primary melanoma. Several occupational exposures and lifestyle factors, such as body mass index and smoking, have been evaluated as possible risk factors for melanoma.

Gene Expression Profiling (GEP)

GEP measures the activity of thousands of genes simultaneously and creates a snapshot of cellular function. Data for GEP are generated by several molecular technologies including DNA microarrays that measure activity relative to previously identified genes and RNA-Seq that directly sequences and quantifies RNA molecules. Clinical applications of GEP include disease diagnosis, disease classification, prediction of drug response and prognosis.

DecisionDx-Melanoma

The DecisionDx test measures expression of 31 genes using quantitative reverse-transcription polymerase chain reaction. The test includes 28 prognostic gene targets and 3 endogenous control genes. The test is performed on standard tissue sections from an existing formalin-fixed, paraffin-embedded biopsy or wide local excision specimen. Clinically negative sentinel node basins (clinically node negative is defined as no signs

of lymph node metastases, consisting of a negative physical examination and preoperative ultrasound). The DecisionDx test report provides a 'class' which stratifies tumors as class 1 or class 2. According to the sample report available on the manufacturer website: "The DecisionDx-Melanoma algorithm generates a value between 0 and 1 with a crossover point of 0.5. Subclassification (A or B) is based on proximity of this value to the crossover point."

Following on a systematic review of available peer-reviewed evidence, cutaneous melanoma prognostic test, DecisionDx-Melanoma, has sufficient evidence for clinical validity to effectively identify patients with a poorer prognosis and for clinical utility in direct more aggressive treatment to promote increased patient survival.

myPath Melanoma

The myPath test measures expression of 23 genes using quantitative reverse-transcription polymerase chain reaction. Fourteen genes are involved in melanoma pathogenesis and are grouped into 3 components related to cell differentiation, cell signaling, and the immune response, and 9 housekeeper genes are also included. The test is performed on 5 standard tissue sections from an existing formalin-fixed, paraffin-embedded biopsy specimen.

The myPath test report includes an algorithmic myPath score ranging from -16.7 to 11.1, with higher, positive scores indicating higher suspicion of malignant disease. The myPath report also classifies these scores: -16.7 to -2.1 are "benign"; -2.0 to -0.1 are "indeterminate"; and 0.0 to +11.1 are "malignant". The myPath test is meant as an add-on test to standard histopathology.

The American Academy of Dermatopathology (AUC Committee Members, 2022) published conditions where a 23 gene qRT-PCR test (MyPath Melanoma) was determined by a review of published evidence to be "majority usually appropriate." These include the differential diagnosis of nevus versus melanoma in fully sampled histopathologically ambiguous tumors, partially sampled nevus versus melanoma in adults, nevus versus nevoid melanoma, and nevus versus melanoma in cosmetically sensitive sites and special sites in pediatric patients. These recommendations specifically exclude scenarios where pathology is definitive for melanoma or for distinction between incompletely sampled sclerosing (desmoplastic) nevus versus desmoplastic melanoma.

CODING

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The following CPT code(s) are covered when medical criteria above are met:

This code can be used for DecisionDx-Melanoma:

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

This code can be used for myPath Melanoma:

0090U Oncology (cutaneous melanoma), mRNA gene expression profiling by RT-PCR of 23 genes (14 content and 9 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical result (ie, benign, intermediate, malignant)

RELATED POLICIES

Biomarker Testing Mandate

Genetic Testing Services

Proprietary Laboratory Analyses (PLA)

PUBLISHED

Provider Update, September 2025

Provider Update, June/September 2024

Provider Update, February/July/November 2023

Provider Update, October 2021

Provider Update, November 2020

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2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Cutaneous Melanoma. Version 2.2024. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf
3. Swetter, SS, Tsao, HH, Bichakjian, CC, et al. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2019;80(1):208-250. doi:10.1016/j.jaad.2018.08.055.
4. ECRI. DecisionDx-Melanoma (Castle Biosciences, Inc.) for Evaluating Prognosis and Guiding Management of Cutaneous Melanoma. Genetic Test Assessment. 2023 Oct.
5. Concert. Evidence Review for Coverage Determination for Cutaneous Melanoma Prognostic Algorithmic Tests. Published 12/22/2023; Re-issued 7/1/2024.
6. Swetter, S and Geller, A. Melanoma: Clinical features and diagnosis. In: UpToDate, Connor RF (Ed), Wolters Kluwer. <https://www.uptodate.com/contents/melanoma-clinical-features-and-diagnosis>

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