Gene Expression Profiling of Melanomas

Policy Number: PG0119
Last Review: 03/01/2021

PARAMOUNT
ADVANTAGE | ELITE | HMO
INDIVIDUAL MARKETPLACE |
PROMEDICA MEDICARE
PLAN | PPO

GUIDELINES

This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.
Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.
This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.

SCOPE

X Professional
X Facility

DESCRIPTION

Gene expression profiling (GEP) tests differ from germline genetic tests. Germline genetic testing, analyzes an individual's deoxyribonucleic acid (DNA) and can identify genetic mutations to determine inherited risk of disease. An individual's germline DNA is constant and works as a baseline for the body's genetic material. RNA activity is measured by gene expression analysis. It is dynamic and responds to cellular environmental signals. GEP tests are typically performed on tumor tissue but may also be performed on other specimens such as blood (using circulating tumor DNA or circulating tumor cells). These tests often use microarray technology though other methodologies are also possible. GEP tests are used to determine prognosis, refine risk stratification and/or optimize treatment regimens primarily for cancer.

Cutaneous melanoma represents less than 5% of skin malignancies but results in the most skin cancer deaths. Cutaneous melanoma occurs in all parts of the skin, including the soles of feet, on the palms of the hand, in between toes and fingers, and underneath the finger and toenails. The incidence of cutaneous melanoma continues to increase, and it is currently the sixth most common cancer in the United States. In 2020, it is estimated that 100, 000 new cases of melanoma will be diagnosed and 6850 individuals may die of the condition in the United States. Elderly men are at highest risk; however, melanoma is the most common cancer in young adults aged 25 to 29 years. Standard treatment options for stage 1 and 2 melanoma are excision with or without sentinel lymph node examination. Current risk factors to predict localized tumor aggression include Breslow tumor thickness, tumor ulceration, and mitotic rate of the tumor cells. Regional lymph node involvement significantly negatively impacts the rate of survival, and the likelihood of which increases with increasing tumor thickness.

Myriad myPath® Melanoma is a clinically validated test to be used as an adjunct to histopathology when the distinction between a benign nevus and a malignant melanoma cannot be made confidently by histopathology alone. The test measures the expression of 23 genes by qRT-PCR methodology and distinguishes melanoma from nevi with a sensitivity of 90% and a specificity of 91%. 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 classifies a melanocytic lesion as 'likely benign,' 'likely malignant,' or 'indeterminate.'

DecisionDx-Melanoma™ testing is a multigene expression assay designed to predict metastasis in individuals with stage I or stage II cutaneous melanoma who have no sign of disease beyond the original tumor. The multi-analyte test is performed using formalin-fixed, paraffin-embedded primary melanoma tissue, and utilizes genetic amplification technology to examine the mRNA expression of 31 gene targets The laboratory test is a signature of 31 genes, 28 discriminating genes and 3 control genes, that classifies tumors as class 1 (low risk of metastasis) or

class 2 (high risk of metastasis), using reverse transcription polymerase chain reaction (RT-PCR) on formalin-fixed paraffin-embedded (FFPE) primary tumor tissue specimens obtained from either biopsy or excision of the cutaneous melanoma.

Uveal Melanoma (UM), also called ocular melanoma, is the most common form of primary eye cancer. UM affects the iris, ciliary body, and choroid portions of the uveal tract. UM is an aggressive cancer that often forms undetectable micrometastases before diagnosis of the primary tumor. Eye-sparing radiation (brachytherapy or proton beam therapy) is the most common treatment approach, but approximately 10% of patients will undergo enucleation due to large and/or aggressive tumors that cannot be managed with radiation or due to eye pain or vision loss. Local treatment by radiation or enucleation is highly successful at controlling the primary tumor, with only ~5% chance of local recurrence. The main goals of treatment are to reduce the risk of metastasis, prevent local growth and destruction of ocular tissues and preserve as much vision as possible.

DecisionDx-UM™ (Castle Biosciences Inc.) determines the molecular signature of a patient's tumor. The DecisionDx-UM test is also known as the gene expression profile test for uveal melanoma, based on the expression of 15 genes in Uveal Melanoma patients. The DecisionDx-UM test is intended to determine metastatic risk and enable risk-based management. The results of the test provide knowledge regarding the risk of near term metastasis (5 years). Tumors with a Class 1 signature are associated with a good prognosis and a low potential to metastasize, while tumors with a Class 2 signature have a high potential to spread. The DecisionDX tests are available only from Castle Biosciences Inc. [There is not enough research to show that any other gene expression tests can help to guide patient management and improve health outcomes for people with melanoma. Therefore, gene expression assays other than the DecisionDX-UM™ test are considered investigational in patients with melanoma.]

Pigmented Lesion Assay (PLA) (DermTech) test measures expression of 6 genes (PRAME, LINC00518, CMIP, B2M, ACTB, PPIA). The test is performed on skin samples of lesions at least 5 mm in diameter obtained via noninvasive, proprietary adhesive patch biopsies of a stratum corneum specimen. The test does not work on the palms of hands, soles of feet, nails, or mucous membranes, and it should not be used on bleeding or ulcerated lesions.

The staging of melanoma is important to predict risk of recurrence and guide surveillance and treatment. Identifying patients at high risk for metastatic disease might assist in selecting patients for adjuvant treatment and more intensive surveillance for metastatic disease, if such changes lead to improved outcomes.

POLICY

HMO, PPO, Individual Marketplace, Elite/ProMedica Medicare Plan, Advantage
Gene Expression Profiling of Melanomas testing coverage listed below, may not be all-inclusive, for all product lines. Codes: 0089U, 0090U, 81401, 81529, 81552, 81479, 81599

myPath Melanoma testing requires a prior authorization for all product lines.

DecisionDx and DecisionDx-UM requires a prior authorization for all product lines.

COVERAGE CRITERIA
HMO, PPO, Individual Marketplace, Elite/ProMedica Medicare Plan, Advantage

Molecular diagnostic tests used to assist in risk stratification of melanoma patients are covered when:
The patient has a personal history of melanoma AND:

- Either
  - Has Stage T1b and above OR
  - Has T1a with documented concern about adequacy of microstaging
- Is undergoing workup or being evaluated for treatment, AND
- Does not have metastatic disease AND
- Presumed risk for a positive Sentinel Lymph Node Biopsy (SLNB) based on clinical, histological, or other information is >5% AND

- Has a disease stage, grade, and Breslow thickness (or other qualifying conditions) within the intended use of the test

MyPath Melanoma
Paramount considers gene expression profiling/classification of cutaneous melanoma with myPath® Melanoma medically necessary when:

- Ordered by a dermatopathologist as an adjunct to histopathology because the distinction between a benign nevus and a malignant melanoma cannot be made confidently by histopathology alone; **and**
- Results of testing will directly impact clinical decision making. Healthcare providers can use the test results to provide significantly better medical care for the individual; **and**
- The testing method is considered to be scientifically valid and proven to have clinical utility based on prospective evidence
- The patient may be subjected to additional intervention, such as re-excision and/or sentinel lymph node biopsy, as a result of the diagnostic uncertainty.

DecisionDx-Melanoma
The DecisionDx-Melanoma test is covered as per the MolDX: Melanoma Risk Stratification Molecular Testing policy, when the following additional conditions are met:

- Patients diagnosed with cutaneous melanoma ≥ 0.3 mm without distant metastases in Breslow thickness where additional risk stratification information beyond anatomic and pathologic staging will influence management decisions regarding the following:
  - Sentinel Lymph Node Biopsy decision (T1-T2 only)
  - Appropriateness of adjuvant therapy
  - Determining the appropriate level of follow up, imaging, and referrals
- Patients diagnosed with cutaneous melanoma < 0.3 mm in Breslow thickness being considered for sentinel lymph node biopsy:
  - in whom there is significant uncertainty about the adequacy of microstaging (positive deep margin), or
  - with other adverse features (e.g. very high mitotic index [≥2/mm2], lymphovascular invasion, or a combination of these factors)

DecisionDx-UM
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. The test discriminates patients with high risk (class 2) for early distal recurrent disease from those with minimal risk of distal metastasis (class 1A). Identification of high-risk patients allows early referral to a medical oncologist with expertise in the management of uveal melanomas, which includes intensified metastatic surveillance and/or metastasis intervention, and stratification for entry into clinical trials with adjuvant therapy.

CPT CODES		**HMO, PPO, Individual Marketplace**	**Elite/ProMedica Medicare Plan**	**Advantage**
0089U	Oncology (melanoma), gene expression profiling by RTqPCR, PRAME and LINC00518, superficial collection using adhesive patch(es)	**Non-Covered**	**Prior Authorization required**	**Non-Covered**
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	**Prior Authorization required**	**Prior Authorization required**	~~**Non-Covered**~~ **Prior Authorization required as of 4/1/2021**

81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) [when specified as the following, e. g. , DecisionDx-PRAME]: • LINC00518 (long intergenic non-protein coding RNA 518)(eg, melanoma), expression analysis • PRAME (preferentially expressed antigen in melanoma)(eg, melanoma), expression analysis	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
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	**Prior Authorization required as of 4/1/2021**	**Prior Authorization required as of 4/1/2021**	**Prior Authorization required as of 4/1/2021**
81552	Oncology (uveal melanoma), MRNA, gene expression profiling by real-time RT-PRC or 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81479	Unlisted molecular pathology procedure	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81599	Unlisted multianalyte assay with algorithmic analysis	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
Additional Medical Policy Reference: PG0041 Genetic Testing				

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to https://www.paramounthealthcare.com/services/providers/medical-policies/ .

REVISION HISTORY EXPLANATION
ORIGINAL EFFECTIVE DATE: 11/01/2012

Date	Explanation & Changes
03/21/14	• Policy reviewed and updated to reflect most current clinical evidence • Policy approved per The Technology Assessment Working Group (TAWG) committee as revised
03/19/15	• Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
03/25/16	• Added code 81599 to policy • Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
05/27/16	• Changed title from DecisionDX-UM to Gene Expression Profiling of Melanomas • Added DecisionDx-Melanoma for Cutaneous Melanoma as non-covered to policy • Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)

08/25/17	• Added myPath Melanoma for cutaneous melanoma as covered without prior authorization for all product lines • DecisionDX-UM is now covered without prior authorization for Elite only per CMS guidelines • Removed code 84999 and added ICD-10 codes C69.31, C69.32, C69.41, C69.42, C69.91, C69.92 to policy per CMS guidelines • Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
07/26/18	• Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
07/09/19	• Policy research update and review. Coverage criteria determined. MyPath Melanoma testing was covered with no prior authorization and now will require a prior authorization with effective date of 10/1/19. Decision DX-Melanoma and DecisionDX-UM were non-covered and now will be covered with prior authorization
12/14/2020	• Medical policy placed on the new Paramount Medical policy format
03/01/2021	• Noted procedure code 0081U is a deleted procedure code, removed. • Added procedure codes 0089U, 0090U, 81529 • Per ODM 0090U is now covered, requires a prior authorization • Updated DecisionDx-Melanoma criteria

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services

Ohio Department of Medicaid

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets

Hayes, Inc.

Industry Standard Review