

**EFFECTIVE DATE:** 10|01|2018

**POLICY LAST UPDATED:** 06|05|2018

## **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.

## **MEDICAL CRITERIA**

Not applicable

## **PRIOR AUTHORIZATION**

Not applicable

## **POLICY STATEMENT**

### **BlueCHiP for Medicare**

Gene expression testing in the evaluation of patients with suspicious pigmented lesions is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

Gene expression testing in the evaluation of patients with melanocytic lesions with indeterminate histopathologic features is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

Gene expression testing in the evaluation of patients with cutaneous melanoma is not covered for all indications as the evidence is insufficient to determine the effects of the technology on health outcomes.

### **Commercial Products**

Gene expression testing in the evaluation of patients with suspicious pigmented lesions is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

Gene expression testing in the evaluation of patients with melanocytic lesions with indeterminate histopathologic features is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

Gene expression testing in the evaluation of patients with cutaneous melanoma is considered not medically necessary for all indications as the evidence is insufficient to determine the effects of the technology on health outcomes.

## **COVERAGE**

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered 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, more than 90,000 new cases of melanoma are expected to be diagnosed and more than 9000 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 sunexposed 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.

### **Diagnosis**

Primary care physicians evaluate suspicious pigmented lesions to determine who should be referred to dermatology. Factors considered include both a patient's risk for melanoma as well as visual examination of the lesion. The visual examination assesses whether the lesion has features suggestive of melanoma. Criteria for features suggestive of melanoma have been developed. One checklist is the ABCDE checklist:

- Asymmetry;
- Border irregularities;
- Color variegation;
- Diameter  $\geq 6$  mm;
- Evolution.

Another criteria commonly used is the "ugly duckling" sign. An ugly duckling is a nevus that is obviously different from others in a given patient. Primary care physicians generally have a low threshold for referral to dermatology.

Melanoma is difficult to diagnose based on visual examination and the criterion standard for diagnosis is histopathology. There is a low threshold for excisional biopsy of suspicious lesions for histopathologic examination due to the procedure's ease and low risk as well as the high probability of missing melanoma. However, the yield of biopsy is fairly low. The number of biopsies performed to yield one melanoma diagnosis has been estimated to be about 15 for U.S. dermatologists. Therefore a test that could accurately identify those lesions not needing biopsy (ie, a rule-out test for biopsy) could be clinically useful.

### **Treatment and Surveillance**

Many treatment and surveillance decisions are determined by a patient's prognostic stage group based the American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) staging system. The prognostic groups are as follows: stage I, T1a through T2a primary melanomas without evidence of regional or distant metastases; stage II, T2b through T4b primary melanomas without evidence of lymphatic disease or distant metastases; stage III: pathologically documented involvement of regional lymph nodes or in transit or satellite metastases (N1 to N3); stage IV: distant metastases.

Patients may also undergo sentinel lymph node biopsy (SLNB) to gain more definitive information about the status of the regional nodes.

Wide local excision is the definite surgical treatment of melanoma. Following surgery, patients with AJCC stage I or II (node-negative) melanoma do not generally receive adjuvant therapy. Patients with higher risk melanoma receive adjuvant immunotherapy or targeted therapy. Ipilimumab has been shown to prolong recurrence-free survival by approximately 25% compared with placebo at a median of 5.3 years in patients with resected, stage III disease. Nivolumab has been shown to further prolong survival compared with

ipilimumab by approximately 35% at 18 months. For patients who are BRAF V600 variant-positive with stage III melanoma, the combination of dabrafenib plus trametinib has been estimated to prolong relapse-free survival by approximately 50% over 3 years.

Patients with stage I and II disease should undergo an annual routine physical and dermatologic examination. However, follow-up strategies and intervals have not been standardized or tested, and there is no consensus. These patients typically do not receive surveillance imaging. Patients with stage III melanoma may be managed with more frequent follow-up and imaging surveillance following therapy.

## **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. The Pigmented Lesion Assay, myPath Melanoma, and DecisionDx-Melanoma tests are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

For individuals with suspicious pigmented lesions (based on ABCDE and/or ugly duckling criteria) being considered for biopsy who receive gene expression profiling with the DermTech Pigmented Lesion Assay to determine which lesions should proceed to biopsy, the evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have melanocytic lesions with indeterminate histopathologic features who receive gene expression profiling with the myPath Melanoma test added to histopathology to aid in diagnosis of melanoma, the evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with American Joint Committee on Cancer (AJCC) stage I or II cutaneous melanoma who receive gene expression profiling with the DecisionDx-Melanoma test to determine whether to perform sentinel lymph node biopsy (SLNB), the evidence is insufficient to determine the effects of the technology on health outcomes.

## **CODING**

### **BlueCHiP for Medicare and Commercial Products**

There are currently no specific codes for the panel tests which are applicable to this policy. CPT code 81401 represents only 2 of the genes that are included in the DermTech PLA test. 81401 does not include any of the remaining genes in the test, so this code does not represent “DermTech PLA”, “MyPath Melanoma” or “DecisionDx UM Melanoma”. Providers should instead file with one of the following unlisted codes:

- 81479 Unlisted molecular pathology procedure
- 81599 Unlisted multianalyte assay with algorithmic analysis
- 84999 Unlisted chemistry procedure

## **RELATED POLICIES**

Genetic Testing Services

## **PUBLISHED**

Provider Update, August 2018

## **REFERENCES**

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