DermTech Pigmented Lesion Assay

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Introduction

DermTech Pigmented Lesion Assay (PLA) is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedures addressed by this guideline	Procedure code
DermTech Pigmented Lesion Assay	0089U

Criteria

Introduction

Requests for DermTech PLA are reviewed using the following criteria.

This test is considered Experimental, Investigational, or Unproven.

- Experimental, Investigational, or Unproven (E/I/U) refers to tests, or uses of tests, that have insufficient data to demonstrate an overall health benefit. This typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity) and significantly improves patient health outcomes (clinical utility). Such tests are also not generally accepted as the standard of care in the evaluation or management of a particular condition.
- In the case of laboratory testing, FDA approval or clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight. In addition, FDA approval or clearance often does not include an assessment of clinical utility.

What is melanoma?

Definition

According to the American Cancer Society (ACS), the incidence of primary cutaneous melanoma varies by age and sex. The incidence of melanoma has been reported to be increasing at a rate of 3% annually among women ages 50 and older.[1]

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Melanoma accounts for the majority of skin cancer related deaths, but treatment is nearly always curative with early detection of disease. Minimal depth (thin) melanomas have a cure rate of nearly 100%, while tumors with a Breslow depth of greater than 4mm have a 10-year survival rate of less than 50%.[2]

Standard of care for the assessment of clinically suspicious pigmented skin lesions is surgical biopsy with pathologic evaluation. However, histopathology is believed to have inherent limitations. Some lesions that are likely to be true melanomas based on clinical behavior do not meet the complete set of histologic criteria to establish a melanoma diagnosis.[2] There is also considerable interrater variability with visual image and pattern recognition of skin lesions.[3] In an effort to improve patient survival, a number of novel noninvasive techniques have been developed to classify pigmented skin lesions at an earlier stage.[4]

Test information

Introduction

The Pigmented Lesion Assay (PLA) is a non-invasive method for the biopsy of clinically atypical pigmented lesions or moles using an adhesive patch to obtain mRNA from the surface of the suspicious lesion.

According to the manufacturer, the PLA assesses gene expression consistent with melanoma and is intended as a decision making aid for the clinician to determine whether or not to biopsy a pigmented skin lesion, clinically suspicious for melanoma.[5] The test is intended for use on pigmented lesions suspicious for melanoma that meet at least one of the A (asymmetry) B (border) C (color) D (diameter) E (evolving) criteria for which the clinician would like additional information prior to surgical biopsy. Uses of the PLA include the following: lesions being followed for change; lesions in cosmetically sensitive areas of the body; lesions on individuals with possible risks for complications during surgical biopsy; or lesions among individuals who refuse biopsy.[5]

The PLA is a non-invasive method for the assessment of clinically atypical pigmented lesions or moles using an adhesive patch to obtain mRNA from the surface of the suspicious lesion. The method of adhesive tape stripping has been used to obtain RNA from the stratum corneum for gene expression of other disorders, such as allergic and irritant skin reactions and psoriasis.[6] The PLA detects the expression of 2 specific genes, PRAME and LINC00518, both of which are believed to play key roles in oncogenesis and both of which have been shown to be elevated in melanoma. If sufficient material is available, a DNA-based TERT Add-On Assay can be performed to detect TERT promoter mutations as well. If one or more of these biomarkers is detected, the test is considered positive. The positive lesions generally undergo surgical biopsy to definitively establish a melanoma diagnosis. The test manufacturer notes that this assay cannot be used on mucous membranes, palms of the hands, or soles of the feet.[3,5]

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Guidelines and evidence

American Academy of Dermatology

The American Academy of Dermatology (AAD) acknowledged that the clinical and prognostic significance of the use of biomarkers and mutational analysis is still unclear and there are gaps regarding their clinical usefulness that have yet to be addressed. The 2019 guideline stated:[4]

- “Ancillary diagnostic molecular techniques (eg, CGH, FISH, GEP) may be used for equivocal melanocytic neoplasms.”
- "Routine molecular testing, including GEP [gene expression profiling], for prognostication is discouraged until better use criteria are defined. The application of molecular information for clinical management (eg, sentinel lymph node eligibility, follow-up, and/or therapeutic choice) is not recommended outside of a clinical study or trial."
- “Once a lesion has been identified as clinically concerning, dermoscopy can improve diagnostic accuracy and/or help direct optimal and adequate tissue sampling in the case of very large lesions or those in cosmetically or functionally sensitive areas. Newer noninvasive techniques (eg, reflectance confocal microscopy [RCM], as well as electrical impedance spectroscopy, gene expression analysis, optical coherence tomography, and others can also be considered as these become more readily available.”
- “Lingering questions remain regarding the degree to which the selected gene sets represent genes associated with tumor progression, how they compare with current well-characterized prognostic factors and AJCC eighth edition survival data, and whether they improve prognostic models enough to affect patient management and outcomes. As such, the WG discourages routine baseline GEP for prognostication.”
- “There is insufficient evidence to recommend routine molecular profiling assessment for baseline prognostication. Evidence is lacking that molecular classification should be used to alter patient management outside of current guidelines (eg, NCCN and AAD). The criteria for and the utility of prognostic molecular testing, including GEP, in aiding clinical decision making (eg, SLNB eligibility, surveillance intensity, and/or therapeutic choice) needs to be evaluated in the context of clinical study or trial.”
- “Noninvasive genomic methods (eg, adhesive patch ‘‘biopsy’’) are being investigated to further classify melanocytic lesions as either benign or malignant to guide the need for further biopsy. The uptake of 1 or more of these technologies will eventually depend on cumulative evidence regarding their effectiveness, clinical utility, cost versus benefit, and competing strategies.”

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2024) made no recommendation to use the DermTech PLA test in the evaluation of skin lesions

suspicious for melanoma. With regard to the evaluation of melanocytic lesions for the possibility of melanoma, the NCCN offered the following guidance relevant to the DermTech PLA test:[7]

- "Melanocytic neoplasms of uncertain biological potential present a unique challenge to pathologists and treating clinicians. Ancillary tests to differentiate benign from malignant melanocytic neoplasms include immunohistochemistry (IHC), and molecular testing via comparative genomic hybridization (CGH), fluorescence in situ hybridization (FISH), gene expression profiling (GEP), single nucleotide polymorphism (SNP) array, and next-generation sequencing (NGS). These tests may facilitate a more definitive diagnosis and guide therapy in cases that are diagnostically uncertain or controversial by histopathology. Ancillary tests should be used as adjuncts to clinical and expert dermatopathologic examination and therefore be interpreted within the context of these findings."

In the discussion of follow-up recommendations following a melanoma diagnosis, the NCCN stated the following:

- “Prediagnostic clinical modalities (ie, dermoscopy, total-body photography, sequential digital dermoscopy), noninvasive imaging and other technologies (eg, reflectance confocal microscopy, electrical impedance spectroscopy) may aid in surveillance for new primary melanoma, particularly in patients with high mole count and/or presence of clinically atypical nevi. For melanocytic neoplasms that are clinically/dermoscopically suspicious for melanoma, pre-diagnostic noninvasive patch testing may also be helpful to guide biopsy decisions.”

Selected Relevant Publications

There is insufficient evidence to support the use of DermTech PLA to accurately discriminate between early melanoma and non-melanoma in individuals with clinically suspicious lesions.[2,3,8-21] A recurring limitation within the evidence base is the assumption that non-biopsied PLA negative results are true negatives without follow up assessment for confirmation. Additional limitations include retrospective study designs, small individual study populations, overlapping patient populations, varying follow up times, and a lack of reported health outcomes.

Based on the current evidence, PLA testing may have a high negative predictive value and influence clinical management decisions regarding biopsy but it remains unclear if these PLA-based decisions result in meaningful clinical outcomes. Well-designed studies that report the impact of PLA testing on clinical management decisions together with the health outcomes that result from those decisions are needed to confirm the utility of the DermTech PLA test.

Note This benefit/harm statement only applies to those jurisdictions that do not have Medicare guidance. Based upon the guidelines and evidence provided in the clinical policy, following EviCore's criteria for DermTech will ensure that members will not receive testing for which there is not a body of evidence demonstrating clinical utility and is therefore considered experimental, investigational, or unproven. Use of a test

that does not have evidence to support clinical utility can lead to negative consequences. These include but are not limited to physical implications, psychological implications, treatment burden, social implications, and dissatisfaction with healthcare.[21] However, it is possible that there will be a delay in care while providers search for an appropriate test with sufficient evidence (analytical validity, clinical validity, and clinical utility).

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