Submitted by: DermTech, Inc
Name: Burkhard Jansen, MD, Chief Medical Officer
Company/Organization: DermTech, Inc.
Address: 11099 N Torrey Pines Road, Suite 100, La Jolla, CA 92037
Phone: (858)249-9413
Email: bjansen@dermtech.com
Date of request: June 16, 2020
NCCN Guidelines Panel: Melanoma

Sent via email to: submissions@nccn.org

On behalf of DermTech, Inc., I respectfully request the NCCN Melanoma Panel review the enclosed data on DermTech's pre-biopsy and biopsy guiding non-invasive melanoma rule-out test, the Pigmented Lesion Assay (PLA).

The PLA is now supported by 19 peer reviewed publications, covered by Medicare which does not support tests or treatments it deems experimental or investigational, and has benefitted over 50,000 US patients to date by reducing avoidable biopsies by over 90% while missing fewer melanomas based on the test's high negative predictive value. The test inserts a simple non-invasive objective step into the current diagnostic pigmented lesion paradigm (visual inspection – surgical biopsy) in cases in which clinicians require more information to guide their biopsy decisions. We greatly appreciate consideration of all the available peer reviewed evidence including a large real-world utility study (n=3,418) that demonstrates that the PLA reduces avoidable biopsies by over 90% with clinicians following the guidance of the test in over 98% of cases (PLA positive lesions are biopsied, PLA negative lesions are clinically followed and not biopsied) as well as clarification on how the "noninvasive genomic patch test" fits into the diagnostic continuum of pigmented lesion management.

Specific Changes: Recommend the Pigmented Lesion Assay ("PLA") as a useful pre-diagnostic tool that supports a clinician's decision of whether or not to biopsy in the assessment of pigmented skin lesions suspicious of melanoma (changed from "requires further investigation) " *(see v2.2020, ME-11, Common Follow-up Recommendations for All Patients)*.

MolDx Coverage: On February 10, 2020 Medicare Administrative Contractor Palmetto GBA MolDx published an effective Local Coverage Determination (LCD): Pigmented Lesion Assay (L38051), harmonized with other Medicare Administrators' coverage determinations across the MolDx regions.

Rationale: In support of the proposed change, v2.2019 Guidelines for Cutaneous Melanoma correctly characterized the "noninvasive genomic adhesive patch test…" as a "Pre-diagnostic technolog[y] to inform decision about whether to biopsy" and affirmatively stated that the "noninvasive genomic adhesive patch testing" to be outside the guidelines' purview; however, while reference to the noninvasive genomic patch testing was removed appropriately from the Principles of Molecular Testing section in subsequent versions of the guidelines, the designation of requiring "more investigation" *(see v2.2020, ME-11, Common Follow-up Recommendations for All Patients)* ignores the overwhelming evidence that the PLA effectively informs clinical decision making on whether or not to biopsy a pigmented lesion suspicious of melanoma. It is important to highlight further that the pre-diagnostic biopsy guiding PLA is distinct from an also discussed prognostic post-biopsy gene expression test some readers of previous guideline documents confuse it with.

A portfolio of now 19 peer reviewed PLA publications and Medicare coverage based on full MolDx reviews support the proposed change. For ease of use, we include a hyperlinked document of these peer reviewed publications to facilitate their review by this panel while highlighting key evidence not previously considered below.

1. Brouha et al., "Real-world utility of a non-invasive gene expression test to rule out primary cutaneous melanoma – a large US registry study", Journal of Drugs in Dermatology, 2020; 19(3): 257-262. This study evaluated 3,418 cases of pigmented lesions clinically suspicious of melanoma and affirmed real-world utility of the PLA where clinicians followed the guidance offered by PLA positive tests in 99.94% of cases. Unnecessary surgical procedures were avoided in over 3,000 cases. Overall, clinicians followed the guidance of the test in over 98% of cases.

2. Ferris et al., "Impact on Clinical Practice of a Noninvasive Gene Expression Melanoma Rule-Out Test: 12-Month Follow-Up of Negative Test Results and Utility Data from a Large US Registry Study." Dermatol Online J, (2019), 25(5):2-8. This paper evaluated 734 long-term follow-up cases and provided evidence that the PLA missed no (0%) melanomas in a 12-month follow-up period.

3. Palmetto GBA MolDx Local Coverage Determination (LCD): Pigmented Lesion Assay (L38051). This policy clearly defines how the PLA fits into the diagnostic paradigm as a pre-diagnostic and biopsy guiding tool capable of reducing the biopsy rate of non-malignant lesions. Importantly, it also discusses the limitations to the current care standard where clinicians rely on visual inspection plus surgical biopsy.

4. In a study by Berman and colleagues, a consensus panel of nine expert dermatologists/dermatologic surgeons/dermatopathologists convened, almost two years ago, in August 2018 to determine the individual level of evidence for selected publications of gene expression tests used in pigmented lesion management (Berman et al., Appropriate Use Criteria for the Integration of Diagnostic and Prognostic Gene Expression Profile Assays into the Management of Cutaneous Malignant Melanoma: An Expert Panel Consensus-Based Modified Delphi Process Assessment. SKIN. 2019; 3(5):291-298). The panel assigned the highest evidence level (Level 1) to the PLA's 2 clinical validation studies (References 4 and 14 within the provided hyperlinked document; 14 was available online in 2018), but was unable to consider the two large real-world utility studies also highlighted above because these studies relevant to patient-oriented evidence were not available at the time the consensus panel convened. Given these limitations, the panel arrived at the still high "B" Strength of Recommendation Taxonomy (SORT) assessment based on a fraction of the key evidence (B = inconsistent but limited-quality patient-oriented evidence in "patients with atypical lesions requiring assessment beyond visual inspection to help in selection for biopsy" that clinical validation studies do not address). Potential PLA niche uses such as in patients who refuse surgical biopsies or in patients with increased infection risk that were not separately studied received lower SORT scores. A new consensus assessment that considers all evidence available is warranted.

Thank you for your review and consideration. Please let me know if I can answer any questions.

Sincerely,

Burkhard Jansen, MD
Chief Medical Officer, DermTech