Local Coverage Determination (LCD)

LCD - MolDX: Molecular Assays for the Diagnosis of Cutaneous Melanoma (L39375)

Links in PDF documents are not guaranteed to work. To follow a web link, please use the MCD Website.

Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATES
Noridian Healthcare Solutions, LLC	A and B MAC	02101 - MAC A	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02102 - MAC B	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02201 - MAC A	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02202 - MAC B	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02301 - MAC A	J - F	Oregon
Noridian Healthcare Solutions, LLC	A and B MAC	02302 - MAC B	J - F	Oregon
Noridian Healthcare Solutions, LLC	A and B MAC	02401 - MAC A	J - F	Washington
Noridian Healthcare Solutions, LLC	A and B MAC	02402 - MAC B	J - F	Washington
Noridian Healthcare Solutions, LLC	A and B MAC	03101 - MAC A	J - F	Arizona
Noridian Healthcare Solutions, LLC	A and B MAC	03102 - MAC B	J - F	Arizona
Noridian Healthcare Solutions, LLC	A and B MAC	03201 - MAC A	J - F	Montana
Noridian Healthcare Solutions, LLC	A and B MAC	03202 - MAC B	J - F	Montana
Noridian Healthcare Solutions, LLC	A and B MAC	03301 - MAC A	J - F	North Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03302 - MAC B	J - F	North Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03401 - MAC A	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03402 - MAC B	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03501 - MAC A	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03502 - MAC B	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03601 - MAC A	J - F	Wyoming
Noridian Healthcare Solutions, LLC	A and B MAC	03602 - MAC B	J - F	Wyoming

LCD Information

Document Information

LCD ID
L39375

LCD Title
MolDX: Molecular Assays for the Diagnosis of Cutaneous Melanoma

Proposed LCD in Comment Period
N/A

Source Proposed LCD
DL39375

Original Effective Date
For services performed on or after 08/06/2023

Revision Effective Date
N/A

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
06/22/2023

Notice Period End Date
08/05/2023

Issue

Issue Description

This LCD outlines limited coverage for this service with specific details under **Coverage Indications, Limitations and/or Medical Necessity**.

Issue - Explanation of Change Between Proposed LCD and Final LCD

Changes were made to reflect the addition of recently published guidelines. Additional minor edits were made for clarity.

CMS National Coverage Policy

Title XVIII of the Social Security Act, §1862(a)(1)(A) allows coverage and payment for only those services that are considered to be reasonable and necessary

42 CFR §410.32(a) Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions

CMS Internet-Only Manual, Pub. 100-02, Medicare Policy Manual, Chapter 15, §80 Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests, §80.1.1 Certification Changes

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

The purpose of this test is to assist dermatopathologists to arrive at the correct diagnosis of melanoma versus non-melanoma when examining skin biopsies.

This Medicare contractor will provide limited coverage for molecular Deoxyribonucleic acid (DNA)/Ribonucleic acid (RNA) assays that aid in the diagnosis or exclusion of melanoma from a biopsy when ALL of the following clinical conditions are met:

- The test is ordered by a board-certified or board-eligible dermatopathologist
- The specimen is a primary (non-metastatic, non-re-excision specimen) cutaneous melanocytic neoplasm for which the diagnosis is equivocal/uncertain (i.e., clear distinction between benign or malignant cannot be achieved using clinical and/or histopathological features alone) despite the performance of standard-of-care test procedures and relevant ancillary tests (i.e., immunohistochemical stains)
- The specimen includes an area representative of the lesion or portion of the lesion that is suspicious for malignancy
- 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
- The patient has not been tested with the same or similar assay for the same clinical lesion
- The test is validated for use in the intended-use population and is performed according to its stated intended-use
- The test demonstrates Analytical and Clinical Validity (AV and CV) and Clinical Utility (CU) and undergoes a technical assessment (TA) by MolDx® to demonstrate compliance of the service with this policy

Tests that demonstrate similar indicated uses and equivalent or superior performance to covered tests may similarly be covered under this policy.

Summary of Evidence

Melanoma is an aggressive cancer with an estimated 106,110 cases and 7,180 deaths in 2021.[1] The lifetime risk of developing melanoma in the United States is approximately 2.6% (1 in 38) for Caucasians, 0.1% (1 in 1,000) for African Americans, and 0.6% (1 in 167) for Latinos.[1] Melanoma is more common in men overall, but before age 50 the rates are higher in women than in men. The average age of people diagnosed with melanoma is 65. Many melanomas are curable if detected early and diagnosed accurately. The five year survival for localized melanoma is 99%, compared with only 27% among patients with distant metastases.[2]

Melanoma can be difficult to diagnose, particularly in its earliest stages, yet accurate diagnosis of melanocytic neoplasms is vital to optimal patient outcomes. Histopathologic examination has long been the gold standard for melanoma diagnosis, and while it is adequate for most cases, evidence suggests that approximately 15-20% of all biopsied melanocytic neoplasms are difficult to diagnose by histopathology alone.[3-5] Subspecialty training and experience in dermatopathology is associated with improved diagnostic accuracy and subsequent clinical management of patients with challenging melanocytic lesions.[5-8] However, even experienced dermatopathologists disagree in some cases, and, depending on the type of lesions evaluated, diagnostic discordance may be substantial.[6,7,9,10] In equivocal cases, patients may receive diagnoses that are indeterminate or inaccurate, leading to inappropriate treatment. Unnecessary re-excisions, sentinel lymph node biopsies, and protracted clinical follow-up

may result when a diagnostically challenging benign lesion is reported as indeterminate.[11,12] Conversely, a diagnostically challenging melanoma mistakenly classified as a benign nevus may result in undertreatment and subsequent progression to late-stage melanoma.[11,12] Consequently, adjuncts to histopathology have been sought in efforts to improve diagnostic accuracy in equivocal cases.

Gene expression profiles (GEP) can serve as beneficial adjuncts to histopathology in the evaluation of equivocal melanocytic lesions. The myPath® Melanoma assay (Castle Biosciences, Phoenix, AZ) is a 23-gene expression profile (23-GEP) developed to provide an objective, reproducible, and accurate adjunctive method for differentiating malignant melanoma from benign nevi.[13-16] The test is intended for use by dermatopathologists confronting primary cutaneous melanocytic neoplasms for which the diagnosis of malignant melanoma versus benign nevus is equivocal/uncertain (i.e., a clear distinction between benign or malignant cannot be achieved using clinical and/or histopathological features alone). Use of the test in these cases increases definitive diagnoses, and evidence suggests it may reduce unnecessary procedures in benign lesions.[17,18]

The myPath® Melanoma test quantifies the expression of 23 genes by quantitative reverse transcription-polymerase chain reaction (RT-PCR). Fourteen of the 23 genes are known to be over-expressed by malignant melanomas relative to benign nevi. The remaining 9 are stably expressed reference genes which allow correction for sample-to-sample variations in RT-PCR efficiency and errors in sample quantification (normalization). The signature genes represent 3 distinct pathways that contribute to melanoma pathogenesis, including aspects of melanocyte differentiation as well as characteristics of the tumor microenvironment such as cell-cell signaling and tumor-induced host immune responses.[13,14] The test uses 5 to 7 standard-thickness (4-5 µm) sections taken from the routinely processed formalin-fixed paraffin-embedded (FFPE) tissue of the existing biopsy specimen, allowing its integration into routine clinical practice and its use even in small, early-stage lesions. The quantified expression of all 23 genes is combined algorithmically and reported as a single numerical score. That number (the myPath® Melanoma 'score'), is plotted on a scale that depicts the entire range of scores observed in clinical validation studies.[14] Physicians receive a report showing this single numerical score and the corresponding classification: 'likely malignant', 'likely benign', or 'indeterminate'.

Histopathology can accurately classify many melanocytic neoplasms and currently serves as the 'gold' standard for the diagnosis of melanoma. In line with standard practice, therefore, adjunctive molecular tests for melanoma diagnosis have largely been developed and initially evaluated using histopathology as the reference standard. The first 2 validation studies of the myPath® Melanoma test demonstrated greater than 90% diagnostic accuracy by comparison to concordant histopathologic diagnoses (diagnoses arrived at independently by multiple expert dermatopathologists).[14,15] To further assess accuracy using a reference standard independent of histopathologic diagnosis and confirm genuine clinical utility, a third clinical validation study was performed in which the test result was compared to the eventual clinical outcomes of tested patients.[16] In a cohort of 182 melanocytic neoplasms collected from patients with documented outcomes (distant metastases for malignant melanomas and median 6+ year uneventful follow-up for benign nevi), the myPath® Melanoma score differentiated malignant melanoma from benign nevi with a sensitivity of 93.8% and a specificity of 96.2%.[16] Overall, clinical studies have shown sensitivity and specificity ranges of 90-94% and 91-96%, respectively, for the 23-GEP.[14-16,19]

A clinical utility study quantified the influence of the myPath® Melanoma score on both the final diagnoses and the treatment recommendations made by board-certified dermatopathologists for 218 prospectively submitted diagnostically challenging (equivocal or uncertain) melanocytic neoplasms encountered during routine clinical practice. Comparison of pre-test and post-test diagnoses demonstrated a 56% increase in definitive diagnoses with use of the myPath® score (a 30% increase in definitive diagnoses of benign nevus and a 12.4% increase in definitive diagnoses of malignant melanoma).[17] In addition, treatment recommendations provided by dermatopathologists changed for 49% of patients after receiving the myPath® result, with 76.6% of those changes aligned to the test result.[17] A second clinical utility study assessed the relationship between test result and change in treatment as measured by pre-test dermatopathologist recommendation and post-test actual treatment delivered to a patient by

the dermatologist. A cohort of 77 patients with pre-test diagnoses of "indeterminate" (equivocal, uncertain) were followed throughout their clinical course. The myPath® test produced definitive scores for all 77 neoplasms, and after a median 12-month follow-up period, the tested patients' dermatologists disclosed the actual treatment carried out in each case.[18] The treatment differed from the pre-test recommendation in 55 of 77 (71.4%) cases, 44 of which produced a benign myPath® test result. Re-excision was the pre-test treatment recommendation for 41 of these 44 cases, yet re-excision was ultimately performed in just 7, indicating that a benign myPath® test result enabled dermatologists to forego further intervention in 33 of the 41 cases, yielding an 80.5% reduction in re-excisions.[18]

DecisionDx® DiffDx™-Melanoma (DiffDx™-Melanoma), also by Castle Biosciences, is a 35-gene expression profile (35-GEP) performed on FFPE tissue that is intended to discern benign from malignant melanocytic lesions. It is based on the RT-PCR quantified expression of 32 discriminant and 3 reference genes. The quantified expression of all 35 genes is combined algorithmically and results in two signatures denoting one of three possible risk groups: 'benign,' 'intermediate,' or 'malignant.'

The training and validation cohorts included a total of 951 samples diagnosed between January 2013 and August 2020, of which 498 were benign and 453 malignant. Clinical Validation was performed in 273 benign and 230 malignant lesions (inclusive of a variety of subtypes), with six dermatopathologists performing the review of cases for diagnostic concordance.[20] Overall, 96.4% of cases received a definitive benign or malignant test result and 3.6% had intermediate-risk, exceeding performance of currently available ancillary diagnostic tools including the myPath® Melanoma test, which classifies up to 15% of challenging melanocytic lesions as indeterminate.[15,20,21] After exclusion of lesions identified as intermediate-risk, the test demonstrated a sensitivity of 99.1%, specificity of 94.3%, positive predictive value of 93.6% and negative predictive value of 99.2%.[20] A multi-center clinical utility study found that use of the 35-GEP test resulted in a change of diagnosis in 41.7% of cases, including diagnostic downgrades in 20.3% and upgrades in 21.4% of diagnostically challenging melanocytic lesion cases.[22] The study also reported a 76.7% decrease in re-excisions in cases with benign 35-GEP results.[22]

Other diagnostic adjuncts for melanocytic neoplasms include immunohistochemistry (IHC) to detect expression of the melanoma-associated antigen PRAME (Preferentially Expressed Antigen in Melanoma) as well as tests that rely upon the detection of chromosomal aberrations within neoplastic melanocytes (tumor cytogenetics), such as fluorescence in situ hybridization (FISH)[23-28] and array comparative genomic hybridization (aCGH)/single nucleotide polymorphism (SNP) array.[23,29-32]

Diffuse immunoreactivity for PRAME is found in most primary cutaneous (and ocular) melanomas, whereas most melanocytic nevi either do not express PRAME or express it only in a subpopulation of cells.[33] As such, it can be a useful and lower-cost adjunct for the diagnosis of challenging melanocytic lesions. However, up to 14% of benign melanocytic nevi show some immunoreactivity for PRAME;[33] additionally, the interpretation of positive staining can be subjective. Moreover, though it is highly concordant with FISH, its reported sensitivity is lower than that of the GEP assays, ranging from 75-85% across studies.[20,33,34] PRAME is also a component of the myPath® Melanoma assay[15,16] and is one of the two genes used in a pre-biopsy assay to help guide clinicians on the need for biopsy of a melanocytic lesion.[35]

FISH queries 4 to 6 chromosomal loci through hybridization of fluorescent probes. Tissue requirements are minimal (25-35 µm),[23] and since FISH involves visualization of the tissue, aberrations may be detected within tumor cell subpopulations. Melanomas lacking aberrations at the 4-6 target loci will be undetected, however, generating false negative results,[24-28] while polyploidy may produce false positives[27,28] (but may be detected by experienced observers). Results are uninterpretable (e.g., insufficient signal) in 5-30% of cases.[24-26] Probe sets, cut-off thresholds, and observer skill and experience vary among laboratories, and inter-observer variability occurs.[27,28,32]

In contrast to FISH, SNP array/aCGH methodologies interrogate the genome more broadly[29-32] and signal quantification does not involve human interpretation. However, tumors must be relatively homogenous (~40%),[31] meaning that aberrations in cell subpopulations may go undetected. The large quantity of tissue required (125-375 µm / 10 mm2)[23] restricts use to thicker tumors, and the significance of some aberrations remains unknown.

By comparison to the cytogenetic techniques, the GEP tests quantify the (RNA) transcripts produced by genes over-expressed in malignant melanoma.[13-16] Human interpretation is not involved, maximizing objectivity and reproducibility.[13] Testing is performed in a single laboratory, reducing variation in methods and reagents, and tissue requirements are minimal.[13,20] However, testing requires an area in which neoplastic melanocytes represent approximately 10% of the specimen,[13-15,20] and a proportion of scores are classified as indeterminate (3.6-15% of tested cases).[20,21] The myPath® Melanoma and DiffDx™-Melanoma assays are only validated for primary cutaneous neoplasms, precluding testing of metastases, non-cutaneous melanomas, and re-excision specimens.[13-16,20]

Analysis of Evidence (Rationale for Determination)

Studies demonstrate that Medicare beneficiaries with diagnostically challenging primary cutaneous melanocytic lesions tested with ancillary diagnostic tests (such as GEPs) will have improved outcomes, as defined by an increase in accurate diagnoses, appropriate clinical management and interventions, and a reduction in burdensome and unnecessary treatments.[17,18,20,22]

The National Comprehensive Cancer Network (NCCN) Guidelines also support ancillary diagnostic testing (including with GEPs) to better classify melanocytic neoplasms of uncertain diagnostic potential. As noted in the guidelines, "Ancillary tests to differentiate benign from malignant melanocytic neoplasms include immunohistochemistry (IHC) and molecular testing via comprehensive 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."[36] The guidelines further recommend that ancillary tests should be used as adjuncts to clinical and expert dermatopathologic examination and consultation and therefore need to be interpreted within the context of these findings.[36]

Each test has benefits and limitations, as noted in the Summary of Evidence. As such, dermatopathologists can choose the test that best suits the patient's needs, according to the criteria outlined in this policy.

The reference to specific tests in this document does not imply coverage by MolDX®. Further, this policy is restricted in scope to molecular (DNA)/RNA tests only; therefore, non-molecular tests for the same intended use, though not covered by this policy, may meet coverage criteria of other local coverage determinations.

This contractor will continue to monitor the evidence and coverage may be re-evaluated following any substantial new evidentiary developments or guideline changes.

General Information

Associated Information

N/A

Sources of Information

N/A

Bibliography

1. American Cancer Society. Key statistics for melanoma skin cancer. https://www.Cancer.Org/cancer/melanoma-skin-cancer/about/key-statistics.Html. Accessed 04/28/2023.
2. American Cancer Society. Survival rates for melanoma skin cancer. https://www.Cancer.Org/cancer/melanoma-skin-cancer/detection-diagnosis-staging/survival-rates-for-melanoma-skin-cancer-by-stage.Html. Accessed 04/28/2023.
3. Shoo BA, Sagebiel RW, Kashani-Sabet M. Discordance in the histopathologic diagnosis of melanoma at a melanoma referral center. *J Am Acad Dermatol.* 2010;62(5):751-756. doi:10.1016/j.jaad.2009.09.043
4. Veenhuizen KC, De Wit PE, Mooi WJ, Scheffer E, Verbeek AL, Ruiter DJ. Quality assessment by expert opinion in melanoma pathology: Experience of the pathology panel of the dutch melanoma working party. *J Path.* 1997;182(3):266-272. doi:10.1002/(SICI)1096-9896(199707)182:3<266::AID-PATH812>3.0.CO;2-#
5. Ronen S, Al-Rohil RN, Keiser E, et al. Discordance in diagnosis of melanocytic lesions and its impact on clinical management. *Arch Pathol Lab Med.* 2021;145(12):1505-1515. doi:10.5858/arpa.2020-0620-OA
6. Piepkorn MW, Longton GM, Reisch LM, et al. Assessment of second-opinion strategies for diagnoses of cutaneous melanocytic lesions. *JAMA Netw Open.* 2019;2(10):e1912597. doi:10.1001/jamanetworkopen.2019.12597
7. Tosteson ANA, Tapp S, Titus LJ, et al. Association of second-opinion strategies in the histopathologic diagnosis of cutaneous melanocytic lesions with diagnostic accuracy and population-level costs. *JAMA Dermatol.* 2021;157(9):1102-1106. doi:10.1001/jamadermatol.2021.1779
8. Elder DE, Piepkorn MW, Barnhill RL, et al. Pathologist characteristics associated with accuracy and reproducibility of melanocytic skin lesion interpretation. *J Am Acad Dermatol.* 2018;79(1):52-59.e55. doi:10.1016/j.jaad.2018.02.070
9. Farmer ER, Gonin R, Hanna MP. Discordance in the histopathologic diagnosis of melanoma and melanocytic nevi between expert pathologists. *Hum Path.* 1996;27(6):528-531. doi:10.1016/s0046-8177(96)90157-4
10. Cerroni L, Barnhill R, Elder D, et al. Melanocytic tumors of uncertain malignant potential: Results of a tutorial held at the XXIX symposium of the International Society of Dermatopathology in Graz, October 2008. *Am J Surg Path.* 2010;34(3):314-326. doi:10.1097/PAS.0b013e3181cf7fa0
11. Hawryluk EB, Sober AJ, Piris A, et al. Histologically challenging melanocytic tumors referred to a tertiary care pigmented lesion clinic. *J Am Acad Dermatol.* 2012;67(4):727-735. doi:10.1016/j.jaad.2012.02.036
12. McGinnis KS, Lessin SR, Elder DE, et al. Pathology review of cases presenting to a multidisciplinary pigmented lesion clinic. *Arch Dermatol.* 2002;138(5):617-621. doi:10.1001/archderm.138.5.617
13. Warf MB, Flake DD II, Adams D, et al. Analytical validation of a melanoma diagnostic gene signature using formalin-fixed paraffin-embedded melanocytic lesions. *Biomark Med.* 2015;9(5):407-416. doi:10.2217/bmm.15.11
14. Clarke LE, Warf MB, Flake DD II, et al. Clinical validation of a gene expression signature that differentiates benign nevi from malignant melanoma. *J Cutan Pathol.* 2015;42(4):244-252. doi:10.1111/cup.12475
15. Clarke LE, Flake DD II, Busam K, et al. An independent validation of a gene expression signature to differentiate malignant melanoma from benign melanocytic nevi. *Cancer.* 2017;123(4):617-628. doi:10.1002/cncr.30385
16. Ko JS, Matharoo-Ball B, Billings SD, et al. Diagnostic distinction of malignant melanoma and benign nevi by a

gene expression signature and correlation to clinical outcomes. *Cancer Epidemiol Biomarkers Prev.* 2017;26(7):1107-1113. doi:10.1158/1055-9965.EPI-16-0958
17. Cockerell CJ, Tschen J, Evans B, et al. The influence of a gene expression signature on the diagnosis and recommended treatment of melanocytic tumors by dermatopathologists. *Medicine.* 2016;95(40):e4887. doi:10.1097/MD.0000000000004887
18. Cockerell C, Tschen J, Billings SD, et al. The influence of a gene-expression signature on the treatment of diagnostically challenging melanocytic lesions. *Per Med.* 2017;14(2):123-130. doi:10.2217/pme-2016-0097
19. Clarke LE, Mabey B, Flake DD II, et al. Clinical validity of a gene expression signature in diagnostically uncertain neoplasms. *Pers Med.* 2020;17(5):361-371. doi:10.2217/pme-2020-0048
20. Estrada SI, Cleaver NJ, Depcik-Smith N, et al. Development and validation of a diagnostic 35-gene expression profile test for ambiguous or difficult-to-diagnose suspicious pigmented skin lesions. *SKIN J Cutaneous Med.* 2020;4(6):506-522.
21. Minca EC, Al-Rohil RN, Wang M, et al. Comparison between melanoma gene expression score and fluorescence in situ hybridization for the classification of melanocytic lesions. *Mod Pathol.* 2016;29(8):832-843. doi:10.1038/modpathol.2016.84
22. Farberg AS, Ahmed Kl, Bailey CN, et al. A 35-gene expression profile test for use in suspicious pigmented lesions impacts clinical management decisions of dermatopathologists and dermatologists. *SKIN J Cutaneous Med.* 2020;4(6):523-533.
23. North JP, Vemula SS, Bastian BC. Chromosomal Copy Number Analysis in Melanoma Diagnostics. In: Thurin M, Marincola F, eds. *Molecular Diagnostics for Melanoma. Methods in Molecular Biology*. Vol. 1102. Humana Press;2014:199-226.
24. Díaz A, Valera A, Carrera C, et al. Pigmented spindle cell nevus: clues for differentiating it from spindle cell malignant melanoma. A comprehensive survey including clinicopathologic, immunohistochemical, and fish studies. *Am J Surg Pathol.* 2011;35(11):1733-1742. doi:10.1097/PAS.0b013e318229cf66
25. Abásolo A, Vargas MT, Ríos-Martín JJ, Trigo I, Arjona A, González-Cámpora R. Application of fluorescence in situ hybridization as a diagnostic tool in melanocytic lesions, using paraffin wax-embedded tissues and imprint-cytology specimens. *Clin Ex Dermatol.* 2012;37(8):838-843. doi:10.1111/j.1365-2230.2012.04416.x
26. Clemente C, Bettio D, Venci A, et al. A fluorescence in situ hybridization (fish) procedure to assist in differentiating benign from malignant melanocytic lesions. *Pathologica.* 2009;101(5):169-174.
27. Gerami P, Jewell SS, Morrison LE, et al. Fluorescence in situ hybridization (fish) as an ancillary diagnostic tool in the diagnosis of melanoma. *Am J Surg Pathol.* 2009;33(8):1146-1156. doi:10.1097/PAS.0b013e3181a1ef36
28. Gerami P, Li G, Pouryazdanparast P, et al. A highly specific and discriminatory fish assay for distinguishing between benign and malignant melanocytic neoplasms. *Am J Surg Pathol.* 2012;36(6):808-817. doi:10.1097/PAS.0b013e31824b1efd
29. Bastian BC, LeBoit PE, Hamm H, Bröcker EB, Pinkel D. Chromosomal gains and losses in primary cutaneous melanomas detected by comparative genomic hybridization. *Cancer Res.* 1998;58(10):2170-2175.
30. Bastian BC, Olshen AB, LeBoit PE, Pinkel D. Classifying melanocytic tumors based on DNA copy number changes. *Am J Pathol.* 2003;163(5):1765-1770. doi:10.1016/S0002-9440(10)63536-5
31. Wang L, Rao M, Fang Y, et al. A genome-wide high-resolution array-cgh analysis of cutaneous melanoma and comparison of array-cgh to fish in diagnostic evaluation. *J Mol Diagn.* 2013;15(5):581-591. doi:10.1016/j.jmoldx.2013.04.001
32. Gaiser T, Kutzner H, Palmedo G, et al. Classifying ambiguous melanocytic lesions with fish and correlation with clinical long-term follow up. *Mod Pathol.* 2010;23(3):413-419. doi:10.1038/modpathol.2009.177
33. Lezcano C, Jungbluth AA, Nehal KS, Hollmann TJ, Busam KJ. Prame expression in melanocytic tumors. *Am J Surg Pathol.* 2018;42(11):1456-1465. doi:10.1097/PAS.0000000000001134
34. Lezcano C, Jungbluth AA, Busam KJ. Comparison of immunohistochemistry for prame with cytogenetic test results in the evaluation of challenging melanocytic tumors. *Am J Surg Pathol.* 2020;44(7):893-900. doi:10.1097/PAS.0000000000001492
35. Ferris LK, Jansen B, Ho J, et al. Utility of a noninvasive 2-gene molecular assay for cutaneous melanoma and effect on the decision to biopsy. *JAMA Dermatol.* 2017;153(7):675-680. doi:10.1001/jamadermatol.2017.0473
36. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Melanoma: Cutaneous. Version 1.2023.

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASONS FOR CHANGE

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Articles

A59181 - Billing and Coding: MolDX: Molecular Assays for the Diagnosis of Cutaneous Melanoma

A59441 - Response to Comments: MolDX: Molecular Assays for the Diagnosis of Cutaneous Melanoma

LCDs

DL39375 - MolDX: Molecular Assays for the Diagnosis of Cutaneous Melanoma (MCD Archive Site)

Related National Coverage Documents

N/A

Public Versions

UPDATED ON	EFFECTIVE DATES	STATUS
06/15/2023	08/06/2023 - N/A	Currently in Effect (This Version)

Keywords

N/A