# Local Coverage Determination (LCD): MolDX: DecisionDx-Melanoma (L37750)

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 | STATE(S) |
|---|---|---|---|---|
| Noridian Healthcare Solutions, LLC | A and B MAC | 01111 - MAC A | J - E | California - Entire State |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01112 - MAC B | J - E | California - Northern |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01182 - MAC B | J - E | California - Southern |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01211 - MAC A | J - E | American Samoa Guam Hawaii Northern Mariana Islands |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01212 - MAC B | J - E | American Samoa Guam Hawaii Northern Mariana Islands |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01311 - MAC A | J - E | Nevada |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01312 - MAC B | J - E | Nevada |
| Noridian Healthcare Solutions, LLC | A and B MAC | 01911 - MAC A | J - E | American Samoa California - Entire State Guam Hawaii Nevada Northern Mariana Islands |

# LCD Information

# Document Information

**LCD ID**
L37750

**LCD Title**
MolDX: DecisionDx-Melanoma

**Proposed LCD in Comment Period**
N/A

**Source Proposed LCD**
DL37750

**AMA CPT / ADA CDT / AHA NUBC Copyright Statement**
CPT codes, descriptions and other data only are copyright 2017 American Medical Association. All Rights Reserved. Applicable FARS/HHSARS apply.

Current Dental Terminology © 2017 American Dental Association. All rights reserved.

**Original Effective Date**
For services performed on or after 02/10/2019

**Revision Effective Date**
N/A

**Revision Ending Date**
N/A

**Retirement Date**
N/A

**Notice Period Start Date**
12/26/2018

**Notice Period End Date**
02/09/2019

# 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.

Title XVIII of the Social Security Act, §1833(e). Prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

42 Code of Federal Regulations (CFR) 410.32(a). Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS On-Line Manual, Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, §§80.0, 80.1.1, 80.2. Clinical Laboratory services.

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Chapter 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes".

# Coverage Guidance

## Coverage Indications, Limitations, and/or Medical Necessity

The DecisionDx-Melanoma test is covered only when the following clinical conditions are met:

- Patients diagnosed with clinical stage, sentinel lymph node biopsy (SLNB) eligible, T1 and T2 cutaneous melanoma tumors (as defined in AJCC Staging Manual v8, 2017) with clinically negative sentinel node basins who are being considered for SLNB to determine eligibility for adjuvant therapy. (Per current NCCN and ASCO guidelines, SLNB eligible patients are defined as:
    - Patients with T1a tumors:
        - in whom there is significant uncertainty about the adequacy of microstaging (positive deep margin), or
        - with Breslow depth <0.8 mm and with other adverse features (e.g. very high mitotic index [≥2/mm2], lymphovascular invasion, or a combination of these factors)
    - Patients with T1b tumors (≥0.8 mm or < 0.8 mm with ulceration)
- Patients with T2 tumors

Claims for DecisionDx-Melanoma testing will be denied when testing does not meet all of the above criteria.

## Summary of Evidence

### Background

Cutaneous melanoma (CM) is increasing in incidence in the U.S., with more than 87,000 cases expected to be diagnosed in 2017 and nearly 10,000 deaths each year [1]. Of these, more than 70,000 patients are diagnosed with Stage I or II disease (localized) as determined by the American Joint Committee on Cancer (AJCC) staging system [1]. Patients with early stage melanoma (i.e. AJCC Stage I-II) are regarded as good-prognosis based on population-based risk estimates. However, due to the greater number of individuals

within these earlier stages, more than twice as many people diagnosed with early stage disease will ultimately die of melanoma compared to those diagnosed with Stage III melanoma [2].

The DecisionDx-Melanoma test is a 31-gene expression profile (GEP) that determines a CM patient's risk for metastatic disease [3-6]. The test classifies patients as having a tumor with low (Class 1) or high (Class 2) risk for developing metastasis within 5 years of diagnosis. Patients with a Class 1 tumor profile also have a low likelihood of being sentinel lymph node (SLN) positive. Thus, the individualized risk profile result of this test can be used to guide use of SLNB in the context of patient-specific management plans.

Per current national guidelines, a SLNB procedure is considered for all patients with melanoma pathologic Stage T1b and above, as well as those patients with T1a tumors in whom there is significant uncertainty about the adequacy of microstaging [7, 8]. Patients with a positive SLN are at substantially increased risk for distant metastatic disease and death [2], however, the procedure only provides prognostic information, and the MSLT-II study showed no survival benefit associated with completion lymphadenectomy in SLN positive patients [9]. Currently, the identification of SLN positive patients helps identify Stage III patients who can potentially benefit from targeted and immunotherapeutic agents in the adjuvant setting [10-13]. The procedure can be associated with complications in a substantial proportion of patients such as pain, seromas, nerve damage and edema, and requires a large team of dedicated personnel, including nuclear medicine physicians, surgeons, and pathologists [14-16]. It has been estimated that the cost of a SLNB can be 10 times that of a wide excision alone, and the cost per life saved in a patient population with low prevalence of positive SLN can approach 1 million dollars [17]. Overall, the likelihood of a positive SLN after the SLNB procedure is 16% [2, 18], but this is variable for specific populations [18-21]. Elderly patients account for a substantial proportion of CM patients, and 60% of melanoma-related deaths occur in patients ≥65 years-old. While older age is associated with a poor prognosis, fewer elderly patients are SLN positive [19-23], which indicates that the prognostic value of SLNB is limited in this population [24, 25].

In general, a 5% likelihood for a positive SLN is recommended as a threshold for performing this procedure in a patient population [18]. Analysis of Castle's retrospective cohort (n=782) identified that DecisionDx-Melanoma Class 1A patients (probability score <0.5) with tumors who had a Breslow thickness (BT) of ≤2.0 mm (AJCC T1-T2) achieved a positive SLNB rate below 5% [26]. To validate this clinical use of the Class 1A cut-point for the DecisionDx-Melanoma test, two contemporary, multi-center, prospective study cohorts were tested: 584 patient cohort from two published prospective studies (overall 14% SLN positive rate) [6, 27] and a 837 patient cohort from prospectively tested patients at 5 large academic institutions (overall 12% SLN positive rate) [26]. The rate of SLN positivity in both prospective study cohorts aligns with the SLN positivity rate in the general population of melanoma patients who have undergone SLNB. The results show that in patients from the Medicare-eligible population (65 years old and over) who had a SLNB performed, those patients who had a DecisionDx-Melanoma Class 1A T1 or T2 tumor, have a 98.4% probability of being SLN negative. Thus, in this patient group, the DecisionDx-Melanoma test achieves a NPV that is comparable to other molecular tests used to guide surgical management decisions [28-31].

Analysis of the two prospective cohorts combined (n=1,421 patients) shows that SLN positivity rates are enriched from 12.8% using current SLNB criteria to 18.6% in those patients who would undergo the SLN biopsy procedure (T1/T2 with a Class 2 DecisionDx-Melanoma test result and T3/T4 patients). The rate of SLN positivity in the 65 years and older population from Castle's prospective cohort (n=629) is 14.6% of Class 1A patients and 11.9% for Class 2B patients. SLNB positivity rates for T3 tumors is 8.7% for Class 1A compared to 18% for Class 1B-2B; for T4 tumors it is 17% and 17% respectively. Importantly, the 5-year melanoma specific survival (MSS) rate for T1/T2 Class 1 patients remains favorable; with 99% MSS, comparable to that observed in T1a tumors and for which current guidelines do not recommend SLNB [7, 32, 33]. Furthermore, T1/T2 Class 1 patients show 5-year overall survival (OS) of 97% and distant metastasis free survival (DMFS) of 93% [33]. The MSLT-II study demonstrated that a delay in lymph node dissection does not adversely affect survival, thus clinical follow up of Class 1 patients and lymphadenectomy for those few who develop clinically detectable nodal disease should achieve similar outcomes to those who currently undergo a planned SLNB [9]. Thus, the test identifies a patient population with <5% likelihood of a positive SLN and high survival rates and therefore has utility in guiding SLNB decisions in patients 65 years-old and over with T1-T2 CM tumors. In this population, the test could potentially reduce the rate of SLNB by up to 78%

while still maintaining a MSS survival rate of 99% in those patients with low-risk tumor biology who can safely avoid the procedure.

Clinical validation of DecisionDx-Melanoma as a prognostic test for CM patients was performed in three multicenter, prospectively designed archival tissue studies including 782 patients [3-5]. These studies have shown that the test accurately predicts risk for local/regional recurrence, distant metastasis, melanoma-related mortality, and all-cause mortality independent of clinicopathologic factors used in staging and that the test shows improved sensitivity and negative predictive value (NPV) for recurrence-free (RFS), distant metastasis-free (DMFS), melanoma-specific (MSS) and overall (OS) survival individually or in conjunction with established clinicopathologic factors. Three prospective, independent studies (n= 510) and an interim analysis of two prospective registries (n=322) have confirmed the prognostic accuracy of DecisionDx-Melanoma [6, 34-36].

The DecisionDx-Melanoma test may improve net health outcomes by accurately identifying patients who are at risk of developing metastatic disease and would otherwise go undetected, as well as patients with a low likelihood of having a positive SLN. Net health outcomes are improved for low risk Class 1 patients who can consider avoiding SLNB and associated surgical and anesthesia risk (T1-T2 patients), as well as intensive follow up and exposure to radiation from imaging procedures, and for high risk Class 2 patients by improved guidance to perform SLNB.

## Summary of Analytical and Clinical Performance

### General

| Intended Use | The DecisionDx-Melanoma test is intended for SLNB-eligible T1 and T2 cutaneous melan (as defined in AJCC Staging Manual v8, 2017) with clinically negative sentinel node basi being considered for SLNB to determine eligibility for adjuvant therapy |
| --- | --- |
| Validated Specimen Type(s) | Formalin-fixed, paraffin-embedded (FFPE) specimens of the primary tumor. |

### Analytical Performance [37]

| Description | Results (with 95% Confidence Intervals if applicable)[1] |
| --- | --- |
| Repeatability (within run precision) 21 samples (in triplicate) three PCR cards, 1 instrument, 1 operator, 3 runs 2 days, 1 manufacturing reagent lot. | Binary Classification (Class 1 / Class 2): 100% (94-100%) Subcla (Class 1A/1B; Class 2A/2B): 98% (91-100%) |
| Intermediate precision (between run precision) | |
| **Inter-operator/instrument:** 22 samples, 2 instruments, 2 operators, 2 runs, 2 day, 1 manufacturing reagent lots | Binary Classification (Class 1 / Class 2): 95% (77-100.0%) Subcla (Class 1A/1B; Class 2A/2B): 95% (77-100%) |
| **Inter-assay:** 143 samples, 2 instruments, 2 operators, 15 runs, multiple days (2.5 year interval), multiple manufacturing lots | Binary Classification (Class 1 / Class 2): 99% (96-100.0%) Subcla (Class 1A/1B; Class 2A/2B): 92% (87-96%) |
| Reproducibility (between sites) | Not applicable |
| Minimum input RNA quantity | 5 ng RNA |
| Minimum tumor content (for FFPE specimens) | 40% by histomorphology |
| Limit of blank (LOB) | CT undetermined for blank |
| Limit of detection (LOD) | Not applicable |
| Limits of quantitation (LOQ) | Not applicable |
| Linearity | Not applicable |

| | |
|---|---|
| Interfering substances | Not applicable[2] |
| Specimen stability, primary | FFPE x 4 years at RT per literature and up to 16 years in outcom... analysis from validation cohort |
| Specimen stability, intermediate (extracted RNA) | 96 hours when stored at -80°C per SOP |
| Specimen stability, intermediate (cDNA) | 96 hours when stored at 4°C per SOP 30 days when stored at -20... |
| Critical reagent closed/shelf-life stability (manufacturer's recommendations/lab validated) | Applied Biosystems TaqMan® Low Density Array, -20°C x 24 mont... months (lab) Applied Biosystems TaqMan® Open Array, -20°C x 12... 3 months (lab) Applied Biosystems High-Capacity cDNA Reverse Tr... Kit , -20 °C x 8 months / 3 months (lab) |
| | Applied Biosystems TaqMan® PreAmp Master Mix Kit, 4°C x 9 mon... months (lab) |
| | Applied Biosystems TaqMan® OpenArray Master Mix, -20°C x 12 m... months (lab) |
| | Applied Biosystems RNAse Inhibitor, -20 °C x 42 months / 3 month... Qiagen Deparaffinization Solution, room temperature x 3 months Q... Buffer PKD, room temperature x 3 months |
| | Qiagen Dnase Booster Buffer, room temperature x 3 months Qiage... K, room temperature x 3 months |
| | Qiagen QIAsymphony RNA kit, room temperature x 3 months |
| Critical reagent open/in use stability | Per lab validation or manufacturer's specifications |

[1]Using Clopper-Pearson method

[2]Since the gene expression profile is based on ratios of gene to controls, rather than an absolute value, the effect of an interfering agent is expected to affect all genes equally and result in failed amplification.

**Clinical Performance: Utility**

Data below shows that using the DecisionDx-Melanoma test for SLNB guidance in T1/T2 as defined by AJCC v8 identifies a patient population with <5% likelihood of a positive SLN with high rates of MSS, OS and DMFS, OS and therefore may have utility in guiding SLNB decisions in Medicare patients. In this population, the test will reduce the rate of SLNB by up to 52% while still maintaining a MSS survival rate of 99% in those patients with low-risk tumor biology who can safely avoid the procedure.

**Summary of DecisionDx-Melanoma performance in SLNB guidance in T1/T2 melanoma patients ≥65 years old, eligible for SLNB biopsy**

| Cohort | Overall N | NPV | SLN+ Rate T1/T2 Patients | SLN+ Rate T1/T2 Class 1B-2B Patients | SLN+ Rate All Patients Directed to SLN... |
|---|---|---|---|---|---|
| Castle Prospective Studies[c] | 193 | 0.99 (0.93-1) | 3.33% | 7.32% | 15.79% |
| Independent Validation Cohort[d] | 335 | 0.97 (0.93-0.99) | 5.29% | 10.00% | 12.23% |
| Combined | 528 | 0.98 (0.95-0.99) | 4.61% | 9.09% | 13.58% |

NPV = Negative Predictive Value in for SLN positivity in SLNB eligible T1/T2 patients with Class 1A DecisionDx-Melanoma test result

[a]Patients eligible for SLNB per NCCN guidelines or had a SLNB procedure performed

[b]SLNB positive rate in all patients undergoing SLNB after guidance with test (T1/T2 Class 1B-2B and T3/T4)

[c]Data from two contemporary, prospective, multicenter studies (total n=584) [6, 27]
[d]Data from independent cohort from 5 academic centers (total n=837) [26]

**Expected survival outcomes in T1/T2 patients who avoid or undergo SLNB based on DecisionDx-Melanoma class result**

| Patient Group | MSS | OS | DMFS |
|---|---|---|---|
| T1/T2 Class 1 (No SLNB) | 99.3% | 97.2% | 93.4% |
| T1/T2 Class 2 SLNB Negative | 95.3% | 95.3% | 86.3% |
| T1/T2 Class 2 SLNB Positive | 73.8% | 52.4% | 52.5% |

Data from three retrospective, multicenter cohorts (N=690)
Median follow up time of cohort = 6.5 yr [3-5, 26]
Note: Limited data for Class 1 T1/T2 patients who were found to be SLNB positive under current guidelines showed MSS, OS and DMFS rates of 100%, 90.7 and 75.7%.

**Clinical Performance: Validity**

**Summary of event rates in DecisionDx-Melanoma clinical validity studies**

| Study | Design | Population | Non-censored recurrence rate (95% CI) Events/Total Class | | Non-censo (95% Class |
|---|---|---|---|---|---|
| | | | Class 1 | Class 2 | Class |
| Gerami et al., 2015 CCRa [3] | Archival, prospective design | Stage I-II, n=78; mf/u: 5.7 years | 5.8% (1.2-16%) 3/52 | 69% (48-86%) 18/26 | 3.8% (0.47 2/52 |
| Gerami et al., 2015 JAADb [4] | Archival, prospective design | SLN-eligible, Stage I-III, n=217; mf/u: 4.2 years | 21% (13-32%) 16/76 | 65% (56-72%) 91/141 | 18% (10- 14/7 |
| Zager et al., 2017 [5] | Archival, prospective design | Stage I-III, n=523; mf/u: 6.1 years | 13% (9.8-18%) 42/314 | 48% (41-55%) 100/209 | 9% (6-1 28/31 |
| Greenhaw et al., 2017 [34] | Consecutively tested, single center | Stage I-II, n=256; mean f/u: 1.9 years | 1.4% (0.3-4%) 3/214 | 24% (12-39%) 10/42 | |
| Hsueh et al., 2017 [35] | Prospective, single center | Stage I-III, n=159; mf/u: 2.1 years | 2.6% (0.53-7.3%) 3/117 | 45% (30-61%) 19/42 | |
| Hsueh et al., 2017 [6] | Prospective registries | Stage I-III, n=322; mf/u: 1.5 years | 2% (0.66-4.6%) 5/248 | 27% (17-38%) 20/74 | 1% (0.1- 2/24 |
| Renzetti et al., 2017 [36] | Consecutively tested, single center | Stage I-III, n=95; mf/u: 0.9 years | 4.9% (0.6-17%) 2/41 | 24.1% (13-38%) 13/54 | 2.4% (0.06- 1/41 |

mf/u = median follow-up
Confidence intervals calculated by the Coppler-Pearson method
[a]Recurrence in Gerami et al., 2015 CCR included sentinel lymph node positivity as an event, while all other studies did not. Therefore, for this study, only Stage I-II patients are included.
[b]Patients in this study were eligible for SLNB so they include Stage I-II patients at a higher risk of metastasis, thus event rates in Class 1 is expected to be higher than in other studies.

**Summary of survival outcomes in DecisionDX-Melanoma clinical validity studies**

| Study | Design | Population | Recurrence-free Survival (RFS) rate (95% CI) | |
|---|---|---|---|---|
| | | | Class 1 | Class 2 |

| | | | | |
|---|---|---|---|---|
| Gerami et al., 2015 CCRa [3] | Archival, prospective design | Stage I-II, n=78; mf/u: 5.7 years | 98% (93-100%)[c] | 37% (21-56%) |
| Gerami et al., 2015 JAADb[4] | Archival, prospective design | SLN-eligible, Stage I-III, n=217; mf/u: 4.2 years | 79% (70-90%)[c] | 33% (26-43%) |
| Zager et al., 2017 [5] | Archival, prospective design | Stage I-III, n=523 mf/u: 6.1 years | 88% (85-92%)[c] | 52% (46-60%) |
| Greenhaw et al., 2017 [34] | Consecutively tested, single center | Stage I-II, n=256; mean f/u: 1.9 years | 98% (95-100%)[d] | 74% (59-93%) |
| Hsueh et al., 2017 [35] | Prospective, single center | Stage I-III, n=159 mf/u: 2.1 years | 97% (95-100%)[e] | 54% (41-72%) |
| Hsueh et al., 2017 [6] | Prospective registries | Stage I-III, n=322 mf/u: 1.5 years | 97% (95-100%)[f] | 77% (67-88%) |

mf/u = median follow-up

Survival rates and confidence intervals calculated by Kaplan-Meier method

[a]Recurrence in Gerami et al., 2015 CCR included sentinel lymph node positivity as an event, while all other studies did not. Therefore, for this study, only Stage I-II patients are included.

[b]Patients in this study were eligible for SLNB so they include Stage I-II patients at a higher risk of metastasis, thus event rates in Class 1 is expected to be higher than in other studies

[c]5-year survival outcomes

[d]3-year survival outcomes

[e]2-year survival outcomes

[f]1.5-year survival outcomes

**Analysis of Evidence
(Rationale for Determination)**

Level of Evidence

Quality of evidence – Moderate
Strength of evidence – Low
Weight of evidence - Low

This contractor will cover the DecisionDx-Melanoma test for patients diagnosed with SLNB eligible T1b and T2 tumor who are being considered for SLNB. The DecisionDx-Melanoma assay should not be ordered if a patient and his/her physician do not intend to act upon the test result. Continued coverage is dependent on the publication and/or presentation of additional clinical utility data demonstrating the impact of the test's use on patient management decisions with (1) 95% or greater DMFS and MSS at 3 years in patients directed to no SLNB by the test compared to standard of care, and (2) evidence of higher SLNB positivity in patients selected for this procedure by the test compared to standard of care.

# Coding Information

**Bill Type Codes:**

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type.Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

N/A

**Revenue Codes:**

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

N/A

**CPT/HCPCS Codes**

**Group 1 Paragraph:**

N/A

**Group 1 Codes:**

| CODE | DESCRIPTION |
|------|-------------|
| 81599 | UNLISTED MULTIANALYTE ASSAY WITH ALGORITHMIC ANALYSIS |

**ICD-10 Codes that Support Medical Necessity**

**Group 1 Paragraph:**

N/A

**Group 1 Codes:**

| ICD-10 CODE | DESCRIPTION |
|-------------|-------------|
| C43.0 | Malignant melanoma of lip |
| C43.10 | Malignant melanoma of unspecified eyelid, including canthus |
| C43.111 | Malignant melanoma of right upper eyelid, including canthus |
| C43.112 | Malignant melanoma of right lower eyelid, including canthus |
| C43.121 | Malignant melanoma of left upper eyelid, including canthus |
| C43.122 | Malignant melanoma of left lower eyelid, including canthus |

| ICD-10 CODE | DESCRIPTION |
|---|---|
| C43.20 | Malignant melanoma of unspecified ear and external auricular canal |
| C43.21 | Malignant melanoma of right ear and external auricular canal |
| C43.22 | Malignant melanoma of left ear and external auricular canal |
| C43.30 | Malignant melanoma of unspecified part of face |
| C43.31 | Malignant melanoma of nose |
| C43.39 | Malignant melanoma of other parts of face |
| C43.4 | Malignant melanoma of scalp and neck |
| C43.51 | Malignant melanoma of anal skin |
| C43.52 | Malignant melanoma of skin of breast |
| C43.59 | Malignant melanoma of other part of trunk |
| C43.60 | Malignant melanoma of unspecified upper limb, including shoulder |
| C43.61 | Malignant melanoma of right upper limb, including shoulder |
| C43.62 | Malignant melanoma of left upper limb, including shoulder |
| C43.70 | Malignant melanoma of unspecified lower limb, including hip |
| C43.71 | Malignant melanoma of right lower limb, including hip |
| C43.72 | Malignant melanoma of left lower limb, including hip |
| C43.8 | Malignant melanoma of overlapping sites of skin |
| C43.9 | Malignant melanoma of skin, unspecified |
| D03.111 | Melanoma in situ of right upper eyelid, including canthus |
| D03.112 | Melanoma in situ of right lower eyelid, including canthus |
| D03.121 | Melanoma in situ of left upper eyelid, including canthus |
| D03.122 | Melanoma in situ of left lower eyelid, including canthus |

**ICD-10 Codes that DO NOT Support Medical Necessity**

N/A

**Additional ICD-10 Information**

N/A

# General Information

**Associated Information**

N/A

## Sources of Information

N/A

## Bibliography

1. Siegel, R.L., K.D. Miller, and A. Jemal, *Cancer Statistics, 2017.* CA Cancer J Clin, 2017. **67**(1): p. 7-30.
2. Morton, D.L., et al., *Final trial report of sentinel-node biopsy versus nodal observation in melanoma.* N Engl J Med, 2014. **370**(7): p. 599-609.
3. Gerami, P., et al., *Development of a prognostic genetic signature to predict the metastatic risk associated with cutaneous melanoma.* Clin Cancer Res, 2015. **21**(1): p. 175-83.
4. Gerami, P., et al., *Gene expression profiling for molecular staging of cutaneous melanoma in patients undergoing sentinel lymph node biopsy.* J Am Acad Dermatol, 2015. **72**(5): p. 780-5 e3.
5. Zager, J.S., et al., *Performance of a prognostic 31-gene expression profile in an independent cohort of 523 cutaneous melanoma patients.* BMC Cancer, 2018. **18**(1): p. 130.
6. Hsueh, E.C., et al., *Interim analysis of survival in a prospective, multi-center registry cohort of cutaneous melanoma tested with a prognostic 31-gene expression profile test.* J Hematol Oncol, 2017. **10**(1): p. 152.
7. Coit, D.G., et al., *Melanoma, Version 2.2018.* NCCN Clinical Practice Guidelines in Oncology 2018.
8. Wong, S.L., et al., *Sentinel Lymph Node Biopsy and Management of Regional Lymph Nodes in Melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Clinical Practice Guideline Update.* J Clin Oncol, 2017: p. JCO2017757724.
9. Faries, M.B., et al., *Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma.* N Engl J Med, 2017. **376**(23): p. 2211-2222.
10. Eggermont, A.M., et al., *Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): a randomised, double-blind, phase 3 trial.* Lancet Oncol, 2015. **16**(5): p. 522-30.
11. Eggermont, A.M., et al., *Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy.* N Engl J Med, 2016. **375**(19): p. 1845-55.
12. Long, G.V., et al., *Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-Mutated Melanoma.* New England Journal of Medicine, 2017. **0**(0): p. null.
13. Weber, J., et al., *Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma.* New England Journal of Medicine, 2017. **0**(0): p. null.
14. Moody, J.A., et al., *Complications of sentinel lymph node biopsy for melanoma - A systematic review of the literature.* Eur J Surg Oncol, 2017. **43**(2): p. 270-277.
15. Ascha, M., M.S. Ascha, and B. Gastman, *Identification of Risk Factors in Lymphatic Surgeries for Melanoma: A National Surgical Quality Improvement Program Review.* Ann Plast Surg, 2017.
16. Bagaria, S.P., M.B. Faries, and D.L. Morton, *Sentinel node biopsy in melanoma: technical considerations of the procedure as performed at the John Wayne Cancer Institute.* J Surg Oncol, 2010. **101**(8): p. 669-76.
17. Agnese, D.M., et al., *Cost-effectiveness of sentinel lymph node biopsy in thin melanomas.* Surgery, 2003. **134**(4): p. 542-7; discussion 547-8.
18. Han, D., et al., *Clinicopathologic predictors of sentinel lymph node metastasis in thin melanoma.* J Clin Oncol, 2013. **31**(35): p. 4387-93.
19. Cavanaugh-Hussey, M.W., et al., *Older Age is Associated with a Higher Incidence of Melanoma Death but a Lower Incidence of Sentinel Lymph Node Metastasis in the SEER Databases (2003-2011).* Ann Surg Oncol, 2015. **22**(7): p. 2120-6.
20. Sinnamon, A.J., et al., *Association Between Patient Age and Lymph Node Positivity in Thin Melanoma.* JAMA Dermatol, 2017.
21. Sondak, V.K., et al., *Mitotic rate and younger age are predictors of sentinel lymph node positivity: lessons learned from the generation of a probabilistic model.* Ann Surg Oncol, 2004. **11**(3): p. 247-58.
22. Balch, C.M., et al., *Age as a prognostic factor in patients with localized melanoma and regional metastases.* Ann Surg Oncol, 2013. **20**(12): p. 3961-8.
23. Balch, C.M., et al., *Age as a predictor of sentinel node metastasis among patients with localized melanoma: an inverse correlation of melanoma mortality and incidence of sentinel node metastasis among young and old patients.* Ann Surg Oncol, 2014. **21**(4): p. 1075-81.

24. Fleming, N.H., et al., *Impact of age on the management of primary melanoma patients.* Oncology, 2013. **85** (3): p. 173-81.

25. Macdonald, J.B., et al., *Malignant melanoma in the elderly: different regional disease and poorer prognosis.* J Cancer, 2011. **2**: p. 538-43.

26. Cook RW, Johnson C, Monzon FA. Determination of sentinel lymph node biopsy eligibility using a 31-gene expression profile test in melanoma patients. Presented at in *American College of Mohs Surgery Meeting* 2018. Chicago, IL. (http://castlebiosciences.com/wp-content/uploads/2018/05/Cook-ACMS-2018-SLNB-poster.pdf)

27. Dillon, L.D., et al., *Prospective, Multicenter Clinical Impact Evaluation of a 31-Gene Expression Profile Test for Management of Melanoma Patients.* SKIN J Cutaneous Med, 2018. **2**(2): p. 111-121.

28. *Local Coverage Determination (LCD): MolDX-CDD: ConfirmMDx Epigenetic Molecular Assay (L35632).* 2017, Palmetto GBA.

29. Labourier, E., et al., *Multi-categorical testing for miRNA, mRNA and DNA on fine needle aspiration improves the preoperative diagnosis of thyroid nodules with indeterminate cytology*, in *ENDO 2015: 97th Meeting and Expo of the Endocrine Society* 2015.

30. Silvestri, G.A., et al., *A Bronchial Genomic Classifier for the Diagnostic Evaluation of Lung Cancer.* New England Journal of Medicine, 2015. **373**(3): p. 243-251.

31. *Local Coverage Determination (LCD): MolDX: Percepta© Bronchial Genomic Classifier (L36854).* 2017, Palmetto GBA.

32. Gershenwald, J.E., et al., *Melanoma staging: Evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual.* CA Cancer J Clin, 2017. **67**(6): p. 472-492.

33. Cook, R.W., K.R. Covington, and F.A. Monzon, *Continued evaluation of a 31-gene expression profile to predict metastasis in an expanded cohort of 782 cutaneous melanoma patients*, in *23rd International Pigment Cell Conference (IPCC)* 2017: Denver, CO.

34. Greenhaw, B., D. Brodland, and J. Zitelli, *Estimation of Prognosis in Invasive Cutaneous Melanoma: An Independent Study of the Accuracy of a Gene Expression Profile Test.* Dermatol Surg, 2018. **In Press**.

35. Hsueh, E., et al., *Prospective validation of gene expression profiling in primary cutaneous melanoma.* J Clin Oncol, 2016. **34**(suppl; abstr 9565).

36. Renzetti, M., et al., *Combined experience of two tertiary referral centers with DecisionDx-Melanoma GEP testing*, in *Society of Surgical Oncology* 2017: Seattle, WA.37. Cook, R.W., et al., *Analytic validity of DecisionDx-Melanoma, a gene expression profile test for determining metastatic risk in melanoma patients.* Diagn Pathol, 2018. **13**(1): p. 13.

37. Cook, R.W., et al., *Analytic validity of DecisionDx-Melanoma, a gene expression profile test for determining metastatic risk in melanoma patients.* Diagn Pathol, 2018. **13**(1): p. 13.

# Revision History Information

N/A

# Associated Documents

**Attachments**

N/A

**Related Local Coverage Documents**

Article(s)

A56230 - Response to Comments: MolDX: DecisionDx-Melanoma

LCD(s)

DL37750 - MolDX: DecisionDx-Melanoma

**Related National Coverage Documents**

N/A

**Public Version(s)**

Updated on 12/14/2018 with effective dates 02/10/2019 - N/A

---

# Keywords

- MolDX
- decisiondx
- melanoma
- lymph
- node
- tumor
- cutaneous
- SLN