Local Coverage Determination (LCD):
MolDX: Percepta© Bronchial Genomic Classifier (L36886)

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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 **Original Effective Date**

L36886

LCD Title
MolDX: Percepta© Bronchial Genomic Classifier

Proposed LCD in Comment Period
N/A

Source Proposed LCD
DL36886

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

For services performed on or after 05/15/2017

Revision Effective Date
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Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
03/30/2017

Notice Period End Date
05/14/2017

CMS National Coverage Policy

Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for

items or services that "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim lacking the necessary documentation to process the claim. 42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests:
Conditions.

CMS Internet Only Manuals, Publication 10004, Medicare Claims Processing Manual¨ Ch. 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

This Medicare contractor will provide limited coverage for the Percepta Bronchial Genomic Classifier (Veracyte, Inc., South San Francisco, CA) to identify patients with clinical low- or intermediate-risk of malignancy, after a non-diagnostic bronchoscopy, who may be followed with CT surveillance in lieu of further invasive biopsies or surgery. A patient's clinical risk of malignancy may be ascertained by the McWilliams or Gould risk assessment models. Coverage does not include clinical high risk patients or patients with known lung cancer.

Summary of Evidence

Lung cancer is the leading cause of cancer deaths in the United States[1]. New screening programs are expected to save lives through early detection, but are also expected to increase the number of patients who undergo invasive procedures to evaluate suspicious lung nodules and lesions[2].

Traditionally, following the identification of a suspicious lung nodule or lesion, clinical characteristics are utilized to determine risk and to determine whether patients should proceed to an invasive biopsy. Clinical characteristics that have statistically correlated with a higher risk of malignancy in risk assessment models include older age, smoking history, nodule size and speculation[3, 4]. Anatomic location, solid versus part-solid or non-solid characteristics, and time since smoking discontinuation have had less consistent correlation. However, variation in cohort demographics and data availability used in developing these models, including prevalence of malignancy (3.7% to 54%), have challenged consistent utilization of these models when used alone in clinical practice.

The American College of Chest Physicians published clinical guidelines in 2013 to assist clinicians with assigning risk allocation[5].

Table 1: American College of Chest Physicians (ACCP) – Assessment of the probability of malignancy based on clinical factors alone[5].

Probability of Malignancy		
Low (<5%)	**Intermediate (5-65%)**	**High (>65%)**
Young, less smoking, no prior cancer, smaller nodule size, regular margins,	Mixture of low and high probability features	Older, heavy smoking, prior cancer, larger size, irregular/spiculated margins, and/or upper-lobe location

and/or non-upper-lobe location

At the current time, in the absence of definitive guidelines, patients assigned with a physician-assessed low or intermediate risk for malignancy may be considered for serial CT surveillance or invasive biopsy[5], and many of these patients ultimately undergo surgery for benign disease[6].

Newer predictive models, which incorporate a number of radiological and clinical features to predict malignancies, may be more predictive than physician assessment alone in preventing invasive procedures in patients with benign nodules[3, 4]. Even with these risk models, supplementary methods to improve diagnostic accuracy are important to prevent unneeded morbidity, mortality and costs from invasive procedures, without increasing the risk of missing a malignancy.

Bronchoscopy is a non-surgical diagnostic method that enables physicians to visualize and collect cells from the patient's lung airways. An estimated 250,000 patients undergo bronchoscopy each year in the United States to evaluate lung nodules that are suspicious for cancer[7]. Up to 40% of bronchoscopy procedures result in a non-diagnostic outcome, which means the clinician could not reach a clinically actionable benign or malignant diagnosis[4]. Physicians are then faced with the dilemma of whether to monitor these patients with CT surveillance or proceed to a surgical lung biopsy or transthoracic needle biopsy associated with a greater risk of morbidity, such as pneumothorax or hemorrhage, or mortality[8, 9].

Percepta™ Bronchial Genomic Classifier (Percepta BGC) Test Description and Performance

The Percepta BGC is a messenger-RNA assay measuring gene expression of 23 lung cancer associated genes and patient age. The assay is performed on cytology brushings of bronchial epithelial cells collected during a bronchoscopy from the main stem bronchus and stored in an RNA preservative at 4°C immediately after collection. The assay results are reported as a categorical result based on the patient's physician-assessed pretest risk of malignancy as described below.

Table 2: Percepta Classifier Results

	Post Test Risk of Malignancy	
Pretest Risk of Malignancy	**Percepta Negative Result**	**Percepta Positive Result**
Low (<10%)	Very Low (<1%)	Low (<10%)
Intermediate (10-65%)	Low (<10%)	Intermediate (10-65%)
High (>65%)	High (>65%)	Very High (>85%)

The clinical performance of Percepta BGC has been demonstrated in two prospective-retrospective, multicenter and blinded trials[8, 10]. The results from these trials showed that the classifier is able to detect cancer with a high sensitivity exceeding the performance of bronchoscopy alone[11]. In the low and intermediate pretest risk groups, negative classifier results identified patients at a low risk of malignancy with a high negative predictive value (NPV) of 100% (95% CI 89-100%) and 91% (95% CI 75-98%), respectively, who may be followed with CT surveillance in lieu of further invasive investigation.

The analytical and clinical performance of the Percepta BGC is summarized below.

General

Intended Use	To assess the risk of primary lung cancer in current or former smokers (>100 cigarettes in lifetime) 21 years of age or older with no concurrent or prior cancer who (1) are assessed by their physician to have a low or intermediate pretest risk of malignancy and (2) have had an inconclusive bronchoscopy
Validated Specimen Type(s)	Bronchial epithelial brushing specimen preserved in RNAProtect at the point of collection

Analytical Performance

Description	**Results (with 95% Confidence Intervals if applicable)** [1]
Precision, inter-assay total variability (2 operators; 3 independent runs; 3 manufacturing reagent lots; 10 unique samples run in triplicate with expected scores ranging from -1.10 to +3.29; all in CLIA lab)	Qualitative (categorical call concordance): 86.7% (26 of 30; 95% CI: 69.3%-96.2%) Quantitative (score): pooled SD = 0.259 (95% CI 0.217 to 0.304) (Represents 4.3% of score range, roughly -3 to +3)
Reproducibility (2 operators; 2 independent runs; 2 manufacturing reagent lots; 46 unique samples run in singlicate with expected scores ranging from -1.77 to +4.21; R&D and CLIA labs)	Qualitative (categorical call concordance): 93.5% (43 of 46; 95% CI: 82.1%-98.6%)
Analytical sensitivity: Minimum input	Total RNA: 157 – 243 ng (standard input is 200 ng) RNA Integrity Number ≥4
Critical reagent shelf-life stability (when stored per manufacturer's recommendations)	Ambion WT Expression Kit: 24 months from manufacturing, 1 year from receipt Affymetrix Gene ST Arrays: 24 months from manufacturing, 1 year from receipt Qiagen RNAprotect: 2 years from manufacturing
Specimen stability	21 days at 2-8 °C

[1]Using Clopper-Pearson method

Clinical Performance

Description	Results (with 95% Confidence Intervals if applicable)*	
	Low pretest risk (n = 62)	Intermediate pretest risk (n = 101)
Sensitivity	100% (16-100%)	88% (68-97%)
Specificity	56% (42-69%)	48% (35-62%)
Negative Predictive Value (NPV)	100% (89-100%)	91% (75-98%)
Positive Predictive Value (PPV)	7% (1-24%)	40% (27-55%)
Cancer prevalence	5%	41%

*Using Clopper-Pearson method

The usefulness of the assay in the low and intermediate pretest risk groups has been evaluated in two additional modeling studies[13]. These studies suggest that use of the classifier may safely reduce invasive surgical procedures among patients with a low or intermediate pretest risk following a non-diagnostic bronchoscopy. This Medicare contractor is aware that Veracyte is also currently running the PERCEPTA Registry Trial to prospectively evaluate the clinical utility of the classifier.

The potential usefulness of this test is that it allows physicians to determine which patients with a low or intermediate physician-assessed pretest risk and a non-diagnostic bronchoscopy may be candidates for CT surveillance in lieu of further invasive biopsies or surgical procedures.

Criteria for Coverage

Percepta BGC is covered only when the following clinical conditions are met:

- Current or former smokers age 21 and greater, **and**
- Physician-assessed low or intermediate pretest risk of malignancy based upon the following clinical characteristic stratification[3, 4], **and:**

Low Risk (<10%)	**Intermediate Risk (10-60%)**	**High Risk (>60%)**
Nodules < 10 mm <10 pk/yr smoking history	Nodules 10 - 30 mm 10 to 60 pk/yr smoking history	Nodules >30 mm >60 pk/yr smoking history

- Bronchoscopy is non-diagnostic (actionable benign or malignant diagnosis cannot be reached), **and**
- Percepta BGC results will be utilized to determine whether CT surveillance is appropriate in lieu of further invasive biopsies or surgical procedures as outlined below, **and**

Pre-Test Risk:	Post-Test Risk:	Post-Test Diagnostic Strategy:
Intermediate	Intermediate	Proceed to further work up
Intermediate	Low Risk	CT surveillance
Low Risk	Low Risk	CT surveillance

Low Risk	Very Low Risk	CT surveillance

- Test is ordered by physician certified in Percepta Certification and Training Registry (CTR), **and**
- Patient is monitored for malignancy (suggested monitoring includes serial CT scans at 3 to 6, 9 to 12, and 18 to 24 months, using thin sections and non-contrast, low-dose techniques), **and**
- Physician will report outcomes in all risk groups including those monitored initially and those who undergo immediate intervention, **and**
- Clinical management is consistent with the post-test diagnostic strategy described above in ≥80% of tested patients.

Note: The Percepta BGC test should not be ordered if a physician does not intend to act upon the test result.

Certification and Training Registry Program

The Percepta® Bronchial Genomic Classifier will be made available only to Medicare patients through physicians who participate in a MolDx approved Percepta Certification and Training Registry (CTR) program. This CTR serves to assure the appropriate selection of patients and follow-up to ensure the benefits of the test outweigh its risks. As part of this requirement Veracyte will provide to this Medicare contractor reports every 6 months in a mutually agreed upon format. The CTR will continue for 36 months from the issuance of the final LCD or the presentation of prospective data demonstrating the clinical utility and safety of the assay.

The goals of the Percepta CTR program are as follows:

- To inform physicians and patients on the safe use of Percepta BGC, and
- To ensure that physicians understand the limitations of the test based on its validation studies, and
- Make a good faith effort to identify any safety concerns from the use of the test, and
- To identify the clinical utility of the Percepta BGC test in the intended use patient population.

This Medicare contractor expects Veracyte to:

- Establish and maintain the Percepta Certification and Training Registry (CTR);
- Ensure that healthcare providers who order the Percepta BGC assay are registered and certified in the Percepta CTR program and that the Percepta BGC assay is available only through these providers for Medicare patients;
- Report utilization data by final Percepta risk group;
- Report clinical outcomes in each Percepta risk group;
- Report all patients receiving a "Low or "Very Low" Percepta BGC assay result who are diagnosed with cancer during the CTR program;
- Share all required data and reports in a HIPAA complaint fashion;
- Publish final results in a peer-reviewed scientific journal with an impact factor of ≥4.5.

Analysis of Evidence

(Rationale for Determination)

Level of Evidence:

Quality – Moderate

Strength – Limited

Weight - Limited

This contractor recognizes that evidence for clinical utility for Percepta Bronchial Genomic Classifier to identify patients with clinical low- or intermediate-risk of malignancy after a non-diagnostic bronchoscopy is promising at the current time. This contractor is aware that Veracyte is currently running the PERCEPTA Registry Trial to prospectively evaluate the clinical safety and utility of the classifier. Veracyte will continue to accrue patients in the PERCEPTA Registry Trial and, at interim analyses, demonstrate that in intended-use patients whose post-test risk is very low- or low that there is a statistically significant decrease in the rate of nodule progression as compared to current screening standards. There is no coverage for pretest 'High Risk' patients or 'never smokers'. Continued coverage for the Percepta assay will be dependent on semi-annual review of interim data and/or peer-reviewed publications of clinical utility data demonstrates decreased nodule progression and that patients can be followed with CT surveillance in lieu of further invasive biopsies or surgery.

General Information

Associated Information

Noridian did not receive any comments for the draft LCD, comment period ending 12/15/16.

Sources of Information

N/A

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Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
12/01/2019	R3	The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD. At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Other (The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.)
12/01/2019	R2	As required by CR 10901, all billing and coding information has been moved to the companion article, this article is linked to the LCD.	• Revisions Due To Code Removal
08/25/2017	R1	LCD is revised to remove CDD from title and to add	• Creation of Uniform

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
		newly required fields for Summary of Evidence, Analysis of Evidence and Bibliography.	LCDs With Other MAC Jurisdiction

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)
A57502 - Billing and Coding: MolDX: Percepta© Bronchial Genomic Classifier
LCD(s)
DL36886
- (MCD Archive Site)

Related National Coverage Documents

N/A

Public Version(s)

Updated on 01/29/2020 with effective dates 12/01/2019 - N/A
Updated on 10/29/2019 with effective dates 12/01/2019 - N/A
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Updated on 03/17/2017 with effective dates 05/15/2017 - N/A

Keywords

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