## Contractor Information

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<th>CONTRACT TYPE</th>
<th>CONTRACT NUMBER</th>
<th>JURISDICTION</th>
<th>STATE(S)</th>
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LCD Information

Document Information

**LCD ID**
L36886

**LCD Title**
MolDX: Percepta© Bronchial Genomic Classifier

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

**Source Proposed LCD**
DL36886

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**Original Effective Date**
For services performed on or after 05/15/2017

**Revision Effective Date**
For services performed on or after 12/01/2019

**Revision Ending Date**
N/A

**Retirement Date**
N/A

**Notice Period Start Date**
03/30/2017

**Notice Period End Date**
05/14/2017
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**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
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\textsuperscript{5}, and many of these patients ultimately undergo surgery for benign disease\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{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>
<thead>
<tr>
<th>Pretest Risk of Malignancy</th>
<th>Percepta Negative Result</th>
<th>Percepta Positive Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt;10%)</td>
<td>Very Low (&lt;1%)</td>
<td>Low (&lt;10%)</td>
</tr>
<tr>
<td>Intermediate (10-65%)</td>
<td>Low (&lt;10%)</td>
<td>Intermediate (10-65%)</td>
</tr>
<tr>
<td>High (&gt;65%)</td>
<td>High (&gt;65%)</td>
<td>Very High (&gt;85%)</td>
</tr>
</tbody>
</table>

**Table 2: Percepta Classifier Results**
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

<table>
<thead>
<tr>
<th>Description</th>
<th>Results (with 95% Confidence Intervals if applicable) (^\text{1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precision, inter-assay total variability</td>
<td>Qualitative (categorical call concordance): 86.7% (26 of 30; 95% CI: 69.3%-96.2%)</td>
</tr>
<tr>
<td>(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)</td>
<td>Quantitative (score): pooled SD = 0.259 (95% CI 0.217 to 0.304) (Represents 4.3% of score range, roughly -3 to +3)</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>Qualitative (categorical call concordance): 93.5% (43 of 46; 95% CI: 82.1%-98.6%)</td>
</tr>
<tr>
<td>(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&amp;D and CLIA labs)</td>
<td>Total RNA: 157 – 243 ng (standard input is 200 ng) RNA Integrity Number ≥4 Ambion WT Expression Kit: 24 months from manufacturing, 1 year from receipt</td>
</tr>
<tr>
<td>Analytical sensitivity: Minimum input</td>
<td>Affymetrix Gene ST Arrays: 24 months from manufacturing, 1 year from receipt</td>
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<tr>
<td>Critical reagent shelf-life stability (when stored per manufacturer’s recommendations)</td>
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</table>

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Clinical Performance

Results (with 95% Confidence Intervals if applicable)*

<table>
<thead>
<tr>
<th>Description</th>
<th>Low pretest risk (n = 62)</th>
<th>Intermediate pretest risk (n = 101)</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>100% (16-100%)</td>
<td>88% (68-97%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>56% (42-69%)</td>
<td>48% (35-62%)</td>
</tr>
<tr>
<td>Negative Predictive Value (NPV)</td>
<td>100% (89-100%)</td>
<td>91% (75-98%)</td>
</tr>
<tr>
<td>Positive Predictive Value (PPV)</td>
<td>7% (1-24%)</td>
<td>40% (27-55%)</td>
</tr>
<tr>
<td>Cancer prevalence</td>
<td>5%</td>
<td>41%</td>
</tr>
</tbody>
</table>

*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\(^1\). 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:

<table>
<thead>
<tr>
<th>Low Risk (&lt;10%)</th>
<th>Intermediate Risk (10-60%)</th>
<th>High Risk (&gt;60%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodules &lt; 10 mm</td>
<td>Nodules 10 - 30 mm 10 to 60 pk/yr smoking history</td>
<td>Nodules &gt;30 mm &gt;60 pk/yr smoking history</td>
</tr>
<tr>
<td>&lt;10 pk/yr smoking history</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Using Clopper-Pearson method
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

<table>
<thead>
<tr>
<th>Pre-Test Risk:</th>
<th>Post-Test Risk:</th>
<th>Post-Test Diagnostic Strategy:</th>
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</thead>
<tbody>
<tr>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Proceed to further work up</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Low Risk</td>
<td>CT surveillance</td>
</tr>
<tr>
<td>Low Risk</td>
<td>Low Risk</td>
<td>CT surveillance</td>
</tr>
<tr>
<td>Low Risk</td>
<td>Very Low Risk</td>
<td>CT surveillance</td>
</tr>
</tbody>
</table>

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
Bibliography


Revision History Information

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<td>• Revisions Due To Code Removal</td>
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### 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 10/29/2019 with effective dates 12/01/2019 - N/A

Updated on 08/15/2017 with effective dates 08/25/2017 - 11/30/2019

Updated on 03/17/2017 with effective dates 05/15/2017 - N/A

### Keywords

- 81479

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**Creation of Uniform LCDs With Other MAC Jurisdiction**

- information has been moved to the companion article, this article is linked to the LCD.

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