

## Medical Coverage Policy | Molecular Testing in the Management of Pulmonary Nodules



**EFFECTIVE DATE:** 11|01|2025

**POLICY LAST REVIEWED:** 07|02|2025

### OVERVIEW

Plasma-based proteomic screening and gene expression profiling of bronchial brushing are molecular tests available in the diagnostic workup of pulmonary nodules. To rule out malignancy, invasive diagnostic procedures such as computed tomography (CT) guided biopsies, bronchoscopies, or video assisted thoracoscopic are often required, but each carry procedure-related complications ranging from post procedure pain to pneumothorax. Molecular diagnostic tests have been proposed to aid in risk stratifying patients to eliminate or necessitate the need for subsequent invasive diagnostic procedures.

The following tests are addressed in this policy:

- Nodify CDT® (Biodesix®, Inc) (CPT code 0360U)
- REVEAL Lung Nodule Characterization (MagArray) (CPT code 0092U)

### MEDICAL CRITERIA

#### Medicare Advantage Plans and Commercial Products

Effective 11/1/2025, the following test(s) are considered medically necessary when the medical criteria in the online authorization tool for participating providers is met:

- Nodify XL2 (BDX-XL2) (Biodesix®, Inc) - CPT code 0080U
- Percepta® Bronchial Genomic Classifier (Veracyte) - CPT code 81479

### PRIOR AUTHORIZATION

#### Medicare Advantage Plans and Commercial Products

Prior Authorization is required for the Percepta® Bronchial Genomic Classifier (Veracyte) test and Nodify XL2 (BDX-XL2) test for Medicare Advantage Plans and is recommended for Commercial Products.

There is no specific CPT coding for some of the services referenced in this policy. Therefore, an Unlisted CPT code should be used (see Coding Section for details). All Unlisted genetic testing CPT codes require prior authorization to determine what service is being rendered and if the service is covered or not medically necessary. See the Related Policies section.

**Note:** Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

## **POLICY STATEMENT**

### **Medicare Advantage Plans and Commercial Products**

The following test(s) are covered:

- Nodify CDT® is covered.

Effective 11/1/2025, the following test(s) may be considered medically necessary when the medical criteria in the online authorization tool for participating providers is met:

- Nodify XL2 (BDX-XL2) (Biodesix®, Inc)
- Percepta® Bronchial Genomic Classifier (Veracyte)

The following test(s) are not covered for Medicare Advantage Plans and not medically necessary for Commercial Products as evidence is insufficient to determine that the technology results in an improvement in the net health outcome:

- REVEAL Lung Nodule Characterization (MagArray)

### **Commercial Products**

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. §27-19-81 described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

## **COVERAGE**

Benefits may vary between groups and contracts. Please refer to the appropriate section of the Benefit Booklet, Evidence of Coverage or Subscriber Agreement for services not covered/medically necessary.

## **BACKGROUND**

### **Pulmonary Nodules**

Pulmonary nodules are a common clinical problem that may be found incidentally on a chest x-ray or computed tomography (CT) scan or during lung cancer screening studies of smokers. The primary question after the detection of a pulmonary nodule is the probability of malignancy, with subsequent management of the nodule based on various factors such as the radiographic characteristics of the nodules (e.g., size, shape, density) and patient factors (e.g., age, smoking history, previous cancer history, family history, environmental/occupational exposures). The key challenge in the diagnostic workup for pulmonary nodules is appropriately ruling in patients for invasive diagnostic procedures and ruling out patients who should forgo invasive diagnostic procedures. However, due to the low positive predictive value of pulmonary nodules detected radiographically, many unnecessary invasive diagnostic procedures and/or surgeries are performed to confirm or eliminate the diagnosis of lung cancer.

### **Proteomics**

Proteomics is the study of the structure and function of proteins. The study of the concentration, structure, and other characteristics of proteins in various bodily tissues, fluids, and other materials has been proposed as a method to identify and manage various diseases, including cancer. In proteomics, multiple test methods are used to study proteins. Immunoassays use antibodies to detect the concentration and/or structure of proteins. Mass spectrometry is an analytic technique that ionizes proteins into smaller fragments and determines mass and composition to identify and characterize them.

### **Plasma-Based Proteomic Screening for Pulmonary Nodules**

Plasma-based proteomic screening has been investigated to risk-stratify pulmonary nodules as likely benign to increase the number of patients who undergo serial CT scans of their nodules (active surveillance), instead of invasive procedures such as CT-guided biopsy or surgery. Additionally, proteomic testing may also determine

a likely malignancy in clinically low-risk or intermediate-risk pulmonary nodules, thereby permitting earlier detection in a subset of patients.

Nodify CDT® is a proteomic test that uses multi-analyte immunoassay technology to measure autoantibodies associated with tumor antigens. The test helps physicians identify lung nodules that are likely malignant or at higher risk of cancer. Patients with a "high level" Nodify CDT test result have a higher risk of malignancy than predicted by clinical factors alone; invasive diagnostic procedures would be indicated in these cases.

REVEAL Lung Nodule Characterization (MagArray) is a plasma-protein biomarker test that may aid clinicians in characterizing indeterminate pulmonary nodules (4 to 30 mm) in current smokers 25 years of age and older. The test is based on a multianalyte assay with a proprietary algorithmic analysis using immunoassay, microarray, and magnetic nanoparticle detection techniques to obtain laboratory data for calculation of the risk score for lung cancer. The REVEAL Lung Nodule Characterization is presented on a scale from 0 to 100 with a single cut point at 50. The score is based on the measurement of 3 clinical factors (age, sex, and nodule diameter) and 3 proteins (epidermal growth factor receptor, prosurfactant protein B, and tissue inhibitor of metalloproteinases 1) associated with the presence of lung cancer. It may aid a clinician in the decision to perform a biopsy or to consider routine monitoring. It is not intended as a screening or stand-alone diagnostic assay.

### **Gene Expression Profiling**

Gene expression profiling (GEP) is the measurement of the activity of genes within cells. Messenger RNA serves as the bridge between DNA and functional proteins. Multiple molecular techniques such as Northern blots, ribonuclease protection assay, in situ hybridization, spotted complementary DNA arrays, oligonucleotide arrays, reverse transcriptase polymerase chain reaction, and transcriptome sequencing are used in GEP. An important role of GEP in molecular diagnostics is to detect cancer-associated gene expression of clinical samples to assess for the risk for malignancy.

### **Regulatory Status**

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Nodify CDT (Biodesix); and REVEAL Lung Nodule Characterization (MagArray); are available under the auspices of the CLIA. Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration (FDA) has chosen not to require any regulatory review of this test.

For individuals with undiagnosed pulmonary nodules detected by computed tomography who receive plasma-based proteomic screening, the evidence includes prospective cohorts, retrospective studies, and prospective-retrospective studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, morbid events, hospitalizations, and resource utilization. The REVEAL validation study was a retrospective study that demonstrated use as a rule-out test in conjunction with the Veteran's Affairs (VA) Clinical Factors Model when the samples were considered inconclusive or intermediate risk by the VA model. The REVEAL model subsequently correctly identified 65% of intermediate-risk samples as either low or high risk. The negative predictive value and sensitivity were both 94%. Limitations included a small sample size and use in conjunction with just 1 type of testing model. Validation in an independent sample in the intended use population with additional probability models is needed. Indirect evidence suggests that a proteomic classifier with a high negative predictive value has the potential to reduce the number of unnecessary invasive procedures to definitively diagnose benign disease versus malignancy. However, long-term follow-up data would be required to determine the survival outcomes inpatients with a missed diagnosis of lung cancer at earlier, more treatable stages. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

### **CODING**

The following code(s) are covered for Medicare Advantage Plans and Commercial Products:

## **Nodify CDT®**

**0360U** Oncology (lung), enzyme-linked immunosorbent assay (ELISA) of 7 autoantibodies (p53, NY-ESO-1, CAGE, GBU4-5, SOX2, MAGE A4, and HuD), plasma, algorithm reported as a categorical result for risk of malignancy (Nodify CDT® Biodesix, Inc.)

Effective 11/1/2025, the following CPT code(s) may be considered medically necessary for Medicare Advantage Plans and Commercial Products when the medical criteria in the online authorization tool for participating providers is met:

- Nodify XL2 (BDX-XL2) – CPT Code 0080U
- Percepta® Bronchial Genomic Classifier – CPT Code 81479

The following code(s) are not covered for Medicare Advantage Plans and are not medically necessary for Commercial Products:

## **REVEAL Lung Nodule Characterization**

**0092U** Oncology (lung), three protein biomarkers, immunoassay using magnetic nanosensor technology, plasma, algorithm reported as risk score for likelihood of malignancy (**REVEAL Lung Nodule Characterization**)

## **RELATED POLICIES**

Biomarker Testing Mandate

Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations

Genetic Testing Services

Proprietary Laboratory Analysis (PLA)

Unlisted Procedures

## **PUBLISHED**

Provider Update, January/September 2025

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Provider Update, November 2023

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Provider Update, October 2021, February 2021

## **REFERENCES:**

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2. Centers for Medicare and Medicaid Services (CMS) Local Coverage Determination (LCD) article, A59641, Article - Billing and Coding: MoIDX: Proteomics Testing
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