## Evidence-Based Lung Cancer Risk Assessment Algorithmic Tests

I. Lung cancer risk assessment algorithmic tests with sufficient evidence of clinical validity and utility are considered **medically necessary** when:

   A. The member is age 40 years or older, **AND**

   B. The member has a single lung nodule between 8 and 30 mm in diameter, **AND**

   C. The member has a risk of cancer of 50% or less according to the Mayo risk prediction algorithm, **AND**

   D. The member does NOT have a diagnosis of cancer (except for nonmelanoma skin cancer) within 5 years of the lung nodule detection.

II. Lung cancer risk assessment algorithmic tests with sufficient evidence of clinical validity and utility are considered **investigational** for all other indications where clinical validity and utility have not been demonstrated.

# RATIONALE AND REFERENCES

## Evidence-Based Lung Cancer Risk Assessment Algorithmic Tests

*Centers for Medicare and Medicaid Services (CMS)*

The CMS local coverage determination (LCD) entitled BDX-XL2 (L37031) includes the following coverage criteria for the NodifyXL2 test for the management of a lung nodule:

- Nodule must be between 8 and 30mm in diameter
- Patients must be 40 years or older
- Patients must have a pre-test cancer risk (as assessed by the Mayo Clinic Model for Solitary Pulmonary Nodules) of 50% or less.

“The intended use of the test is to assist physicians in the management of lung nodules by identifying those lung nodules with a high probability of being benign. These lung

nodules would then be candidates for non-invasive computed tomography (CT) surveillance instead of invasive procedures."

Centers for Medicare & Medicaid Services. Medicare Coverage Database: Local Coverage Local Coverage Determination. MolDX: BDX-XL2 (L37031). Effective Date 04/28/2022. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37031

*Pritchett, et al.*

A 2023 study titled: "Assessing a biomarker's ability to reduce invasive procedures in patients with benign lung nodules: Results from the ORACLE study" aimed to assess the clinical impact of proteomic integrated classifier (IC) tests (specifically, NodifyXL2), following confirmation of clinical validity (PANOPTIC trial) in 2018. The study included a matched cohort and ultimately found that "[p]atients with a benign nodule in the IC group underwent fewer invasive procedures (n = 8, 5%) compared to patients in the untested control group (n = 30, 19%), yielding…[a] relative reduction of 74%" (p. 6).

Pritchett MA, Sigal B, Bowling MR, Kurman JS, Pitcher T, Springmeyer SC; ORACLE Study Investigators. Assessing a biomarker's ability to reduce invasive procedures in patients with benign lung nodules: Results from the ORACLE study. PLoS One. 2023 Jul 11;18(7):e0287409. PMID: 37432960; PMCID: PMC10335667 doi:10.1371/journal.pone.0287409.

*Kheir, et al.*

A 2023 retrospective study titled: "Impact of an integrated classifier using biomarkers, clinical and imaging factors on clinical decisions making for lung nodules" compared individuals with lung nodules who were evaluated with the integrated classifier (IC) test (NodifyXL2) versus individuals receiving standard of care. The findings showed that invasive procedures were decreased by 57.5% in individuals with indeterminate lung nodules "without missing a malignant diagnosis at 1-year follow-up)", when compared to the control arm (p. 3563).

Kheir F, Uribe JP, Cedeno J, et al. Impact of an integrated classifier using biomarkers, clinical and imaging factors on clinical decisions making for lung nodules. J Thorac Dis. 2023;15(7):3557-3567. doi:10.21037/jtd-23-42