

BDX-XL2 (Nodify XL2®) Test Executive Summary

It is estimated that more than 800,000 lung nodules between 8-30mm in diameter are detected annually in the US – a number that is increasing with more imaging and low-dose computed tomography (LDCT) screening programs. With a growing identification of pulmonary nodules within the United States,¹ the effective management of incidental lung nodules will be of increasing importance for patients, physicians, and insurance plans. In a study published in the peer-reviewed journal *Chest* in 2015 which examined the management of incidental nodules, it was found that, despite advances in imaging and nonsurgical biopsy techniques, invasive sampling of low-risk nodules and surgical resection of benign nodules remain common amongst community pulmonologists. Forty-five percent of patients classified as pretest probability of malignancy (pCA)<0.05 underwent either biopsy or surgical resection. Furthermore, 98% of patients with a pCA<0.15 were found to have benign nodules.² This suggests that many patients are unnecessarily exposed to the morbidities and costs associated with these procedures. Use of the BDX-XL2 (branded by Biodesix, Inc. as Nodify XL2®) blood-based test to guide management of the incidental lung nodules can eliminate unnecessary invasive procedures, potentially resulting in improved quality of life for the patient by avoiding invasive surgery as well as reduced financial expense for both the patient and the insurance plan.³

The BDX-XL2 test is a blood-based proteomic test that analyzes (1) two plasma proteins, LG3BP and C163A, which are independently linked to the inflammatory response to cancer, and (2) five clinical factors. In the prospective, multicenter PANOPTIC trial, published in the peer-reviewed journal *Chest* in 2018, the test demonstrated a sensitivity of 97% (CI, 82-100), a specificity of 44% (CI, 36-52) and a median negative predictive value of 98% (CI, 92-100) in distinguishing benign from malignant nodules. In the study, when compared to traditional cancer risk assessments, BDX-XL2 performed better than PET, commonly used validated lung nodule risk models, and physician's cancer probability estimates (P<.001). The PANOPTIC study concluded that if the test results were used to direct care, 40% fewer invasive procedures would be performed on benign nodules.⁴ As such, BDX-XL2 may have significant clinical utility in guiding incidental nodule management decisions, potentially eliminating unnecessary surgical procedures, resulting in improved quality of life for patients as well as reduced financial expense. Studies to further prove utility of BDX-XL2 in the clinical setting are currently underway.

Key Points:

- 1. BDX-XL2 testing provides independent identification of likely benign nodules to help guide management of the nodule and avoid unnecessary invasive procedures.**
 - BDX-XL2 results of “Likely Benign” or “Reduced Risk”: Lung nodule is likely benign and CT surveillance of the nodule may be the advisable course of management.
 - BDX-XL2 result of “Indeterminate”: Lung nodule may not be benign and further testing (standard of care pathway) may be the advisable course of management.
- 2. BDX-XL2 is a blood-based proteomic test that does not require tissue or additional surgical biopsy.**
 - Provides actionable information to make a more informed nodule management decision for patients based on the probability that the nodule is benign.
- 3. BDX-XL2 is covered by Medicare.**
 - Local Coverage Determination (LCD) L37062 *Molecular Diagnostic Services (MolDX): BDX-XL2* ⁵ reviews the BDX-XL2 test and determined that it is medically necessary for patients diagnosed with a lung nodule between 8 and 30mm and who

have a pre-test cancer risk of 50% or less assessed by the Mayo Clinic Model. The LCD for BDX-XL2 is effective for dates of service performed on or after 7/10/2017.

¹ Tanner, N.T., Aggarwal, J., Gould, M.K., et al. Management of Pulmonary Nodules by Community Pulmonologists. *Chest*, 2015; 148(6): 1405 – 1414.

² Tanner, N.T., Aggarwal, J., Gould, M.K., et al. Management of Pulmonary Nodules by Community Pulmonologists. *Chest*, 2015; 148(6): 1405 – 1414.

³ Huo J, Xu Y, Sheu T, Volk RJ, Shih Y. Complication Rates and Downstream Medical Costs Associated with Invasive Diagnostic Procedures for Lung Abnormalities in the Community Setting. *JAMA Intern Med*. 2019; January 14, 2019. Online.

⁴ Silvestri, G.A., Tanner, N.T., Kearney, P., et al. Assessment of Plasma Proteomics Biomarker's Ability to Distinguish Benign from Malignant Lung Nodules. *Chest*, 2018; 154(3):491-500.

⁵ Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD): MoIDX: BDX-XL2 (L37062). Washington, DC, 2019.

<https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37062&ver=10&DocID=L37062&bc=gAAAABABAAA&>