Nodify BDX-XL2 Test Description

The BDX-XL2 (CPT 0080U) test is a blood-based diagnostic test that utilizes proteomics to facilitate the stratification of patients diagnosed with an incidental pulmonary nodule. The BDX-XL2 test is able to help select those patients whose nodules have a high likelihood of being benign, and those who may be better candidates for non-invasive computed tomography (CT) surveillance versus surgical resection. Per the Medicare Local Coverage Determination (LCD) L37062 *Molecular Diagnostic Services (MolDX): BDX-XL2*, the BDX-XL2 test is covered for patients who are diagnosed with an incidental lung nodule between 8 and 30mm in size and are assessed to have a pre-test cancer risk of 50% or less. The test results rendering a high posttest probability suggests the INCIDENTAL NODULE is likely benign.[1] This allows the patient to forego the unnecessary cost, both physical and financial, of invasive survival procedures in favor of CT surveillance.

BDX-XL2 provides independent information from routine clinical risk factors of lung cancer. Requiring only a routine blood draw, BDX-XL2 bypasses the need for tumor tissue, which is essential for most types of diagnostic testing for pulmonary nodules. BDX-XL2 is performed as a Laboratory Developed Test (LDT) in the Biodesix® laboratory in Seattle, Washington, which is licensed as an accredited Medical Test Site (MTS) by the Washington State Department of Health. Using mass spectrometry (MS) combined with five clinical factors, BDX-XL2 produces a post-test probability that the patient's nodule is benign. In rare instances (less than 3%), a malignant nodule is classified as benign.[2]

BDX-XL2 is a 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 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 and validated lung nodule risk models, and physicians' 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. 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 for both the patient and the insurance plan. Studies to further prove utility of BDX-XL2 in the clinical setting are currently underway.

With increased identification of pulmonary nodules within the United States,[3] the effective management of incidental lung nodules, both in terms of clinical and financial outcomes, will be of increasing importance for patients and insurance plans alike. In another study published in the peer-reviewed journal *Chest* in 2015, which examined the management of pulmonary 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 $pCA<0.05$ underwent either biopsy or surgical resection. Furthermore, 98% of patients with a $pCA<0.15$ were found to have benign nodules.[4] This suggests that many patients are unnecessarily exposed to morbidity and costly procedures. BDX-XL2, solely provided by Biodesix, Inc is, therefore, instrumental in stratifying patients based on their risk of malignancy and ensuring efficient management of pulmonary nodules. It has been proven in peer-reviewed studies that, when integrated with other clinical risk factors, BDX-XL2 effectively identifies nodules that are likely benign.[5] This could limit a patients' exposure to the morbidities and costs associated with invasive testing. BDX-XL2 provides information to clinicians and their patients with pulmonary nodules to help direct treatment options.

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[1] Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD): MolDX: BDX-XL2 (L37031). Washington, DC, 2018. https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37062&ver=5&DocID=L37062&bc=gAAAABAAAAAA&

[2] 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.

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

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

[5] 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.