



Geisinger Health Plan Policies and Procedure Manual

Policy: MP355

Section: Medical Policy

Subject: Plasma-based Proteomic Testing in the Management of Pulmonary Nodules

Applicable line of business:

Commercial	x	Medicaid	x
Medicare	x	ACA	x
CHIP	x		

I. Policy: Plasma-based Proteomic Testing in the Management of Pulmonary Nodules

II. Purpose/Objective:

To provide a policy of coverage regarding Plasma-based Proteomic Testing in the Management of Pulmonary Nodules

III. Responsibility:

- A. Medical Directors
- B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

Commercial

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicare

Geisinger Gold Medicare Advantage HMO, PPO, and HMO D-SNP plans are offered by Geisinger Health Plan/Geisinger Indemnity Insurance Company, health plans with a Medicare contract. Continued enrollment in Geisinger Gold depends on contract renewal. Geisinger Health Plan/Geisinger Indemnity Insurance Company are part of Geisinger, an integrated health care delivery and coverage organization.

CHIP

Geisinger Health Plan Kids (GHP Kids) is a Children’s Health Insurance Program (CHIP) offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicaid

Geisinger Health Plan Family (GHP Family) is a Medical Assistance (Medicaid) insurance program offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

- a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
- b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
- c. in accordance with current standards of good medical treatment practiced by the general medical community.
- d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
- e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

- (i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
- (ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
- (iii) The service or benefit will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.

DESCRIPTION:

Plasma-based proteomic screening has been investigated as a tool to risk-stratify pulmonary nodules. Nodules identified as likely benign would allow members to undergo serial CT scans of their nodules (active surveillance), instead of undergoing 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.

COMMERCIAL and MEDICARE BUSINESS SEGMENT

CRITERIA FOR COVERAGE:

Xpresys Lung 2 (BDX-XL2) (Nodify XL2) (Nodify CDT) 0080U, 0360U

The BDX – XL2 test will be considered medically necessary when **all of the** following criteria are met:

- Member is at least 40 years of age; **and**
- Lung nodule is between 8mm and 30mm in diameter; **and**
- Member has a pre-test cancer risk of 50% or less, as assessed by the Mayo Clinic Model for Solitary Pulmonary Nodules. <https://www.mdcalc.com/solitary-pulmonary-nodule-spn-malignancy-risk-score-mayo-clinic-model>

Percepta Bronchial Genomic Classifier 84999

The Percepta Bronchial Genomic Classifier will be considered medically necessary when **all of the** following criteria 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; **and**:

Low Risk (<10%)	Intermediate Risk (10-60%)	High Risk (>60%)
Nodules < 10 mm <10 pk/yr smoking history	Nodules 10 - 30 mm 10 to 60 pk/yr smoking history	Nodules >30 mm >60 pk/yr smoking history

and:

- 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,

Pre-Test Risk:	Post-Test Risk:	Post-Test Diagnostic Strategy:
Intermediate	Intermediate	Proceed to further work up
Intermediate	Low Risk	CT surveillance
Low Risk	Low Risk	CT surveillance
Low Risk	Very Low Risk	CT surveillance

and:

- Test is ordered by physician certified in PERCEPTA® Certification and Training Registry (CTR)

Per Medicare Coverage: (See MoIDx L37054: BDX-XL2; MoIDX: Percepta® Bronchial Genomic Classifier L36886)

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.

EXCLUSIONS:

Plasma-based proteomic screening, gene expression of bronchial brushings or nasal swab, and flow cytometry of sputum tests not specifically listed above have not been evaluated and satisfactorily validated to be effective, and are therefore considered **Unproven** and **NOT COVERED**. This includes, but is not limited to: LungLB, LungLife AI, OncobiotaLUNG, CyPath Lung, etc.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

Medicaid Business Segment:

Any requests for services, that do not meet criteria set in the PARP, will be evaluated on a case by case basis.

CODING ASSOCIATED WITH:

The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.

- 0080U Oncology (lung), mass spectrometric analysis of galectin-3-binding protein and scavenger receptor cysteine-rich type 1 protein M130, with five clinical risk factors (age, smoking status, nodule diameter, nodule-spiculation status and nodule location), utilizing plasma, algorithm reported as a categorical probability of malignancy {BDX-XL2 (Nodify XL2)}
- 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}
- 0317U Oncology (lung cancer), four-probe FISH (3q29, 3p22.1, 10q22.3, 10cen) assay, whole blood, predictive algorithm-generated evaluation reported as decreased or increased risk for lung cancer (LungLB, LungLife AI)
- 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}
- 0395U Oncology (lung), multi-omics (microbial DNA by shotgun next generation sequencing and carcinoembryonic antigen and osteopontin by immunoassay), plasma, algorithm reported as malignancy risk for lung nodules in early-stage disease (OncobiotaLUNG)
- 0406U Oncology (lung), flow cytometry, sputum, 5 markers (meso-tetra [4-carboxyphenyl] porphyrin [TCPP], CD206, CD66b, CD3, CD19), algorithm reported as likelihood of lung cancer (CyPath Lung)

84999 Unlisted chemistry procedure (*Percepta® Bronchial Genomic Classifier or EarlyCDT Lung*)

Current Procedural Terminology (CPT®) © American Medical Association: Chicago, IL

LINE OF BUSINESS:

Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:

Centers for Medicare & Medicaid Services. MoDx L37054: BDX-XL2

Centers for Medicare & Medicaid Services MoDx: Percepta® Bronchial Genomic Classifier L36886

Swensen SJ, Silverstein MD, et al., The probability of malignancy in solitary pulmonary nodules. Application to small radiologically indeterminate nodules. *Arch Intern Med* 1997;157: 849

Mazzone PJ, Sears CR, Arenberg DA, et al. Evaluating Molecular Biomarkers for the Early Detection of Lung Cancer: When Is a Biomarker Ready for Clinical Use? An Official American Thoracic Society Policy Statement. *Am J Respir Crit Care Med*. Oct 01 2017; 196(7): e15-e29.

Vachani A, Whitney DH, Parsons EC, et al. Clinical Utility of a Bronchial Genomic Classifier in Patients With Suspected Lung Cancer. *Chest*. Jul 2016; 150(1): 210-8.

Ferguson JS, Van Wert R, Choi Y, et al. Impact of a bronchial genomic classifier on clinical decision making in patients undergoing diagnostic evaluation for lung cancer. *BMC Pulm Med*. May 17 2016;16(1): 66

Silvestri GA, Tanner NT, Kearney P, et al. Assessment of Plasma Proteomics Biomarker's Ability to Distinguish Benign From Malignant Lung Nodules: Results of the PANOPTIC (Pulmonary Nodule Plasma Proteomic Classifier) Trial. *Chest*. Sep 2018; 154(3): 491-500.

Trivedi NN, Arjomandi M, Brown JK, et al. Risk assessment for indeterminate pulmonary nodules using a novel, plasma-protein based biomarker assay. *Biomed Res Clin Pract*.2018; 3(4):10.15761/brcp.1000173

Fish A, Vachani A, Massion P et. al. Novel multiplexed plasma biomarkers and clinical factors augment risk assessment for indeterminate pulmonary nodules in former smokers. *American Journal of Respiratory and Critical Care Medicine* 2019;199:A7452

Tanner NT, Springmeyer SC, Porter A, et al. Assessment of Integrated Classifier's Ability to Distinguish Benign From Malignant Lung Nodules: Extended Analyses and 2-Year Follow-Up Results of the PANOPTIC (Pulmonary Nodule Plasma Proteomic Classifier) Trial. *Chest*. Mar 2021; 159(3): 1283-1287.

Sullivan FM, Mair FS, Anderson W, et al. Earlier diagnosis of lung cancer in a randomised trial of an autoantibody blood test followed by imaging. *Eur Respir J*. 2021;57(1).

González Maldonado S, Johnson T, Motsch E, Delorme S, Kaaks R. Can autoantibody tests enhance lung cancer screening? — An evaluation of EarlyCDT® Lung in context of the German lung cancer screening intervention trial (LUSI). *Transl Lung Cancer Res*. 2021;10(1):233-242.

Borg M, Wen SWC, Nederby L, et al. Performance of the EarlyCDT® lung test in detection of lung cancer and pulmonary metastases in a high-risk cohort. *Lung Cancer*. 2021;158:85-90

Lee HJ, Mazzone P, Feller-Kopman D, et al. Impact of the Percepta Genomic Classifier on Clinical Management Decisions in a Multicenter Prospective Study. *Chest*. Jan 2021; 159(1): 401-412

Fahrman, J. F., Marsh, T., Irajizad, E., Patel, N., et al Blood-Based Biomarker Panel for Personalized Lung Cancer Risk Assessment. *J Clin Oncol*, 2022;40(8), 876-883

Mazzone, P., Dotson, T., Wahidi, M. M., Bernstein, M., Lee, H. J., et al Clinical validation and utility of Percepta GSC for the evaluation of lung cancer. *PLoS One*, 2022;17(7), e0268567

Tanner NT, Aggarwal J, et al Management of Pulmonary Nodules by Community Pulmonologists: A Multicenter Observational Study. CHEST 2015; 148(6): 1405 – 1414

Garrison GW, Cho JL, et al. ATS Core Curriculum 2021 Adult Pulmonary Medicine: Thoracic Oncology ATS-scholar.2021-0032RE

Pritchett, M et al. "Clinical Utility of the Nodify XL2 Blood-Based Risk Classifier for Management of Benign Pulmonary Nodules in a Real-World Observational Study," CHEST Annual Meeting Abstract and Poster, Oct. 2021.

Paez R, Kammer MN, Massion P. Risk stratification of indeterminate pulmonary nodules. Current Opin Pulm Med. 2021;27:240-48.

Kammer MN, Lakhani DA, Balar AB, et al. Integrated Biomarkers For The Management of Indeterminate Pulmonary Nodules. Am J Respir Crit Care Med. 2021;204(11):1306-1316.

Tanner NT, et al. Assessment of integrated classifier's ability to distinguish benign from malignant lung nodules: Extended analyses and 2-year follow-up results of the PANOPTIC (pulmonary nodule plasma proteomic classifier) trial. Chest 2021 Mar;159(3):1283-1287.

Mazzone P, Dotson T, Wahidi MM, et al. Clinical validation and utility of Percepta GSC for the evaluation of lung cancer. PLoS One. 2022; 17(7): e0268567

Lemieux ME, et al. Detection of early-stage lung cancer in sputum using automated flow cytometry and machine learning. Respir Res 2023 Jan 21;24(1):23

Marmor HN, et al. Biomarkers in lung cancer screening: a narrative review. Curr Chall Thorac Surg 2023 Feb 25;5:5

Tahvilian S, et al. The presence of circulating genetically abnormal cells in blood predicts risk of lung cancer in individuals with indeterminate pulmonary nodules. BMC Pulm Med 2023 Jun 5;23(1):193.

Pritchett MA, Sigal B, Bowling MR, Kurman JS, Pitcher T, Springmeyer SC. Assessing a biomarker's ability to reduce invasive procedures in patients with benign lung nodules: Results from the ORACLE study. PLoS One. 2023;18(7):e0287409

This policy will be revised as necessary and reviewed no less than annually.

Devised: 3/22

Revised: 3/23 (Add Exclusion for Nodify CDT, Early CDT); 9/23 (expand coverage to commercial); 9/24 (add exclusions)

Reviewed:

CMS UM Oversight Committee Approval: 12/23; 11/8/24

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Coverage for experimental or investigational treatments, services and procedures is specifically excluded under the member's certificate with Geisinger Health Plan. Unproven services outside of an approved clinical trial are also specifically excluded under the member's certificate with Geisinger Health Plan. This policy does not expand coverage to services or items specifically excluded from coverage in the member's certificate with Geisinger Health Plan. Additional information can be found in MP015 Experimental, Investigational or Unproven Services.

Prior authorization and/or pre-certification requirements for services or items may apply. Pre-certification lists may be found in the member's contract specific benefit document. Prior authorization requirements can be found at <https://www.geisinger.org/health-plan/providers/ghp-clinical-policies>

Please be advised that the use of the logos, service marks or names of Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company on a marketing, press releases or any communication piece regarding the contents of this medical policy is strictly prohibited without the prior written consent of Geisinger Health Plan. Additionally, the above medical policy does not confer any endorsement by Geisinger Health Plan, Geisinger Quality Options, Inc. and Geisinger Indemnity Insurance Company regarding the medical service, medical device or medical lab test described under this medical policy.

