DRAFT Medical Coverage Policy | Proteomic Testing for Targeted Therapy in Non-Small-Cell Lung Cancer

EFFECTIVE DATE: 01|01|2024
POLICY LAST UPDATED: 09|06|2023

OVERVIEW

Proteomic testing has been proposed as a way to predict survival outcomes, as well as the response to and selection of targeted therapy for patients with non-small-cell lung cancer (NSCLC). One commercially available test (the VeriStrat assay) has been investigated as a predictive marker for response to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors.

The following test(s) is addressed in this policy:

- VeriStrat® (Biodesix) CPT code 81538

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

The use of proteomic testing in the management of non-small-cell lung cancer may be considered medically necessary for the following test;

- VeriStrat® (Biodesix) CPT code 81538

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.

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 Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable laboratory benefits/coverage.

BACKGROUND

Lung cancer is the leading cause of cancer death in the U.S., with an estimated 228,820 new cases and 135,720 deaths due to the disease in 2020.1, NSCLC accounts for approximately 85% of lung cancer cases and includes nonsquamous carcinoma (adenocarcinoma, large cell carcinoma, other cell types) and squamous cell carcinoma.

The stage at which lung cancer is diagnosed has the greatest impact on prognosis.2, Localized disease confined to the primary site has a 59.8 % relative 5-year survival but accounts for only 18 % of lung cancer cases at diagnosis. Mortality increases sharply with advancing stage. Metastatic lung cancer has a relative 5-year survival of 6.3%. Overall, advanced disease, defined as regional involvement and metastatic, accounts for approximately 80% of cases of lung cancer at diagnosis. These statistics are mirrored for the population of NSCLC, with 85% of cases presenting as advanced disease and up to 40% of patients with metastatic disease.

In addition to tumor stage, age, sex, and performance status are independent prognostic factors for survival particularly in early-stage disease. Wheatley-Price et al (2010) reported on a retrospective pooled analysis of 2349 advanced NSCLC patients from 5 randomized chemotherapy trials.3, Women had a higher response rate to platinum-based chemotherapy than men. Additionally, women with adenocarcinoma histology had greater overall survival than men. A small survival advantage exists for squamous cell carcinoma over non-bronchiolar nonsquamous histology.4,

The oncology clinical care and research community use standard measures of performance status: Eastern Cooperative Oncology Group scale and Karnofsky Performance Scale.

Treatment approaches are multimodal and generally include surgery, radiotherapy, and chemotherapy (either alone or in combination with another treatment, depending on disease stage and tumor characteristics). Per the National Comprehensive Cancer Network (NCCN) guidelines, the clinical management pathway for stage I or II NSCLC is dependent on surgical findings and may involve resection, radiotherapy, chemotherapy, or chemoradiation. First-line chemotherapy regimens for neoadjuvant and adjuvant therapy utilize platinum-based agents (eg, cisplatin, carboplatin) in combination with other chemotherapeutics and/or radiotherapy. Treatment recommendations are based on the overall health or performance status of the patient, presence or absence of metastases, as well as the presence or absence of a treatment-sensitizing genetic variant. These aspects inform the selection of targeted and systemic therapies.1,

For patients who experience disease progression following initial systemic therapy, subsequent treatment regimens are recommended, mainly featuring novel programmed death-ligand 1 (PD-L1) inhibitors. The NCCN also includes recommendations for targeted therapy or immunotherapy in patients with biomarkers, including sensitizing epidermal growth factor receptor (*EGFR*) mutations. For patients with sensitizing *EGFR* mutations, recommendations include first-line therapy with EGFR tyrosine kinase inhibitors (TKIs) afatinib, erlotinib, dacomitinib, gefitinib, erlotinib plus ramucirumab, erlotinib plus bevacizumab (nonsquamous), or osimertinib and subsequent therapy with osimertinib. The NCCN does not make any recommendations for the use of EGFR TKIs in the absence of a confirmed sensitizing *EGFR* mutation. Initial systemic therapy recommendations can be considered for multiple, symptomatic, systemic lesions.1,

CODING

Medicare Advantage Plans and Commercial Products

The following CPT code(s) is covered when filed with an ICD-10 diagnosis code(s)* listed below:

This code can be used for the VeriStrat® (Biodesix)

81538 Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival.

ICD-10 diagnosis code(s)*
C33
C34-C34.92
C38.4
C45.0

RELATED POLICIES
Biomarker Testing Mandate
Genetic Testing Services

PUBLISHED
Provider Update, November 2023

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD) for Biomarkers for Oncology (L35396)
2. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD) for Article - Billing and Coding: Biomarkers for Oncology (A52986)
3. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 5.2022. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 28, 2022.
4. Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Lung and Bronchus Cancer. n.d.; https://seer.cancer.gov/statfacts/html/lungb.html. Accessed November 9, 2021.
5. Wheatley-Price P, Blackhall F, Lee SM, et al. The influence of sex and histology on outcomes in non-small-cell lung cancer: a pooled analysis of five randomized trials. Ann Oncol. Oct 2010; 21(10): 2023-2028. PMID 20332134
6. Chansky K, Sculier JP, Crowley JJ, et al. The International Association for the Study of Lung Cancer Staging Project: prognostic factors and pathologic TNM stage in surgically managed non-small cell lung cancer. J Thorac Oncol. Jul 2009; 4(7): 792-801. PMID 19458556
7. Keedy VL, Temin S, Somerfield MR, et al. American Society of Clinical Oncology provisional clinical opinion: epidermal growth factor receptor (EGFR) Mutation testing for patients with advanced non-small-cell lung cancer considering first-line EGFR tyrosine kinase inhibitor therapy. J Clin Oncol. May 20 2011; 29(15): 2121-7. PMID 21482992
8. Lindeman NI, Cagle PT, Beasley MB, et al. Molecular testing guideline for selection of lung cancer patients for EGFR and ALK tyrosine kinase inhibitors: guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology. J Thorac Oncol. Jul 2013; 8(7): 823-59. PMID 23552377
9. Lee CK, Brown C, Gralla RJ, et al. Impact of EGFR inhibitor in non-small cell lung cancer on progression-free and overall survival: a meta-analysis. J Natl Cancer Inst. May 01 2013; 105(9): 595-605. PMID 23594426
10. Ciuleanu T, Stelmakh L, Cicenas S, et al. Efficacy and safety of erlotinib versus chemotherapy in second-line treatment of patients with advanced, non-small-cell lung cancer with poor prognosis (TITAN): a randomised multicentre, open-label, phase 3 study. Lancet Oncol. Mar 2012; 13(3): 300-8. PMID 22277837
11. Karampeazis A, Voutsina A, Souglakos J, et al. Pemetrexed versus erlotinib in pretreated patients with advanced non-small cell lung cancer: a Hellenic Oncology Research Group (HORG) randomized phase 3 study. Cancer. Aug 01 2013; 119(15): 2754-64. PMID 23661337
12. Garassino MC, Martelli O, Broggini M, et al. Erlotinib versus docetaxel as second-line treatment of patients with advanced non-small-cell lung cancer and wild-type EGFR tumours (TAILOR): a randomised controlled trial. Lancet Oncol. Sep 2013; 14(10): 981-8. PMID 23883922

13. Auliac JB, Chouaid C, Greillier L, et al. Randomized open-label non-comparative multicenter phase II trial of sequential erlotinib and docetaxel versus docetaxel alone in patients with non-small-cell lung cancer after failure of first-line chemotherapy: GFPC 10.02 study. Lung Cancer. Sep 2014; 85(3): 415-9. PMID 25082565
14. Cicenas S, Geater SL, Petrov P, et al. Maintenance erlotinib versus erlotinib at disease progression in patients with advanced non-small-cell lung cancer who have not progressed following platinum-based chemotherapy (IUNO study). Lung Cancer. Dec 2016; 102: 30-37. PMID 27987585
15. Biodesix. VeriStrat proteomic test. 2019; https://www.biodesix.com/products/lung-cancer/veristrat. Accessed November 9, 2021.
16. Taguchi F, Solomon B, Gregorc V, et al. Mass spectrometry to classify non-small-cell lung cancer patients for clinical outcome after treatment with epidermal growth factor receptor tyrosine kinase inhibitors: a multicohort cross-institutional study. J Natl Cancer Inst. Jun 06 2007; 99(11): 838-46. PMID 17551144
17. Keshtgarpour M, Tan WS, Zwanziger J, et al. Prognostic Value of Serum Proteomic Test and Comorbidity Index in Diversified Population with Lung Cancer. Anticancer Res. Apr 2016; 36(4): 1759-65. PMID 27069156
18. Wang DX, Liu H, Yan LR, et al. The relationship between serum amyloid A and apolipoprotein A-I in high-density lipoprotein isolated from patients with coronary heart disease. Chin Med J (Engl). 2013; 126(19): 3656-61. PMID 24112159
19. Santoso A, Kaniawati M, Bakri S, et al. Secretory Phospholipase A2 Is Associated with the Odds of Acute Coronary Syndromes through Elevation of Serum Amyloid-A Protein. Int J Angiol. Mar 2013; 22(1): 49-54. PMID 24436584
20. Kotani K, Koibuchi H, Yamada T, et al. The effects of lifestyle modification on a new oxidized low-density lipoprotein marker, serum amyloid A-LDL, in subjects with primary lipid disorder. Clin Chim Acta. Nov 2009; 409(1-2): 67-9. PMID 19723514
21. Bozinovski S, Uddin M, Vlahos R, et al. Serum amyloid A opposes lipoxin A to mediate glucocorticoid refractory lung inflammation in chronic obstructive pulmonary disease. Proc Natl Acad Sci U S A. Jan 17 2012; 109(3): 935-40. PMID 22215599
22. Filippin-Monteiro FB, de Oliveira EM, Sandri S, et al. Serum amyloid A is a growth factor for 3T3-L1 adipocytes, inhibits differentiation and promotes insulin resistance. Int J Obes (Lond). Aug 2012; 36(8): 1032-9. PMID 21986708
23. Diamandis EP. Analysis of serum proteomic patterns for early cancer diagnosis: drawing attention to potential problems. J Natl Cancer Inst. Mar 03 2004; 96(5): 353-6. PMID 14996856
24. Fidler MJ, Fhied CL, Roder J, et al. The serum-based VeriStrat(R) test is associated with proinflammatory reactants and clinical outcome in non-small cell lung cancer patients. BMC Cancer. Mar 20 2018; 18(1): 310. PMID 29558888
25. Jacot W, Lhermitte L, Dossat N, et al. Serum proteomic profiling of lung cancer in high-risk groups and determination of clinical outcomes. J Thorac Oncol. Aug 2008; 3(8): 840-50. PMID 18670301
26. Abbatiello S, Ackermann BL, Borchers C, et al. New Guidelines for Publication of Manuscripts Describing Development and Application of Targeted Mass Spectrometry Measurements of Peptides and Proteins. Mol Cell Proteomics. Mar 2017; 16(3): 327-328. PMID 28183812
27. Amann JM, Lee JW, Roder H, et al. Genetic and proteomic features associated with survival after treatment with erlotinib in first-line therapy of non-small cell lung cancer in Eastern Cooperative Oncology Group 3503. J Thorac Oncol. Feb 2010; 5(2): 169-78. PMID 20035238
28. Kuiper JL, Lind JS, Groen HJ, et al. VeriStrat((R)) has prognostic value in advanced stage NSCLC patients treated with erlotinib and sorafenib. Br J Cancer. Nov 20 2012; 107(11): 1820-5. PMID 23079575
29. Akerley W, Boucher K, Rich N, et al. A phase II study of bevacizumab and erlotinib as initial treatment for metastatic non-squamous, non-small cell lung cancer with serum proteomic evaluation. Lung Cancer. Mar 2013; 79(3): 307-11. PMID 23273522
30. Gautschi O, Dingemans AM, Crowe S, et al. VeriStrat(R) has a prognostic value for patients with advanced non-small cell lung cancer treated with erlotinib and bevacizumab in the first line: pooled analysis of SAKK19/05 and NTR528. Lung Cancer. Jan 2013; 79(1): 59-64. PMID 23122759

31. Stinchcombe TE, Roder J, Peterman AH, et al. A retrospective analysis of VeriStrat status on outcome of a randomized phase II trial of first-line therapy with gemcitabine, erlotinib, or the combination in elderly patients (age 70 years or older) with stage IIIB/IV non-small-cell lung cancer. J Thorac Oncol. Apr 2013; 8(4): 443-51. PMID 23370367
32. Grossi F, Rijavec E, Genova C, et al. Serum proteomic test in advanced non-squamous non-small cell lung cancer treated in first line with standard chemotherapy. Br J Cancer. Jan 03 2017; 116(1): 36-43. PMID 27898657
33. Spigel DR, Burris HA, Greco FA, et al. Erlotinib plus either pazopanib or placebo in patients with previously treated advanced non-small cell lung cancer: A randomized, placebo-controlled phase 2 trial with correlated serum proteomic signatures. Cancer. Jun 01 2018; 124(11): 2355-2364. PMID 29645086
34. Hanna N, Johnson D, Temin S, et al. Systemic Therapy for Stage IV Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. Oct 20 2017; 35(30): 3484-3515. PMID 28806116
35. Carbone DP, Salmon JS, Billheimer D, et al. VeriStrat classifier for survival and time to progression in non-small cell lung cancer (NSCLC) patients treated with erlotinib and bevacizumab. Lung Cancer. Sep 2010; 69(3): 337-40. PMID 20036440
36. Grossi F, Genova C, Rijavec E, et al. Prognostic role of the VeriStrat test in first line patients with non-small cell lung cancer treated with platinum-based chemotherapy. Lung Cancer. Mar 2018; 117: 64-69. PMID 29395121
37. Herbst RS, Johnson DH, Mininberg E, et al. Phase I/II trial evaluating the anti-vascular endothelial growth factor monoclonal antibody bevacizumab in combination with the HER-1/epidermal growth factor receptor tyrosine kinase inhibitor erlotinib for patients with recurrent non-small-cell lung cancer. J Clin Oncol. Apr 10 2005; 23(11): 2544-55. PMID 15753462
38. Salmon S, Chen H, Chen S, et al. Classification by mass spectrometry can accurately and reliably predict outcome in patients with non-small cell lung cancer treated with erlotinib-containing regimen. J Thorac Oncol. Jun 2009; 4(6): 689-96. PMID 19404214
39. Wu X, Liang W, Hou X, et al. Serum proteomic study on EGFR-TKIs target treatment for patients with NSCLC. Onco Targets Ther. 2013; 6: 1481-91. PMID 24204163
40. Yang L, Tang C, Xu B, et al. Classification of Epidermal Growth Factor Receptor Gene Mutation Status Using Serum Proteomic Profiling Predicts Tumor Response in Patients with Stage IIIB or IV Non-Small-Cell Lung Cancer. PLoS One. 2015; 10(6): e0128970. PMID 26047516
41. Gregorc V, Novello S, Lazzari C, et al. Predictive value of a proteomic signature in patients with non-small-cell lung cancer treated with second-line erlotinib or chemotherapy (PROSE): a biomarker-stratified, randomised phase 3 trial. Lancet Oncol. Jun 2014; 15(7): 713-21. PMID 24831979
42. Peters S, Stahel RA, Dafni U, et al. Randomized Phase III Trial of Erlotinib versus Docetaxel in Patients with Advanced Squamous Cell Non-Small Cell Lung Cancer Failing First-Line Platinum-Based Doublet Chemotherapy Stratified by VeriStrat Good versus VeriStrat Poor. The European Thoracic Oncology Platform (ETOP) EMPHASIS-lung Trial. J Thorac Oncol. Apr 2017; 12(4): 752-762. PMID 28017787
43. Carbone DP, Ding K, Roder H, et al. Prognostic and predictive role of the VeriStrat plasma test in patients with advanced non-small-cell lung cancer treated with erlotinib or placebo in the NCIC Clinical Trials Group BR.21 trial. J Thorac Oncol. Nov 2012; 7(11): 1653-60. PMID 23059783
44. Gadgeel S, Goss G, Soria JC, et al. Evaluation of the VeriStrat (R) serum protein test in patients with advanced squamous cell carcinoma of the lung treated with second-line afatinib or erlotinib in the phase III LUX-Lung 8 study. Lung Cancer. Jul 2017; 109: 101-108. PMID 28577938
45. Buttigliero C, Shepherd FA, Barlesi F, et al. Retrospective Assessment of a Serum Proteomic Test in a Phase III Study Comparing Erlotinib plus Placebo with Erlotinib plus Tivantinib (MARQUEE) in Previously Treated Patients with Advanced Non-Small Cell Lung Cancer. Oncologist. Jun 2019; 24(6): e251-e259. PMID 30139835
46. Scagliotti G, von Pawel J, Novello S, et al. Phase III Multinational, Randomized, Double-Blind, Placebo-Controlled Study of Tivantinib (ARQ 197) Plus Erlotinib Versus Erlotinib Alone in Previously Treated Patients With Locally Advanced or Metastatic Nonsquamous Non-Small-Cell Lung Cancer. J Clin Oncol. Aug 20 2015; 33(24): 2667-74. PMID 26169611

47. Lee SM, Upadhyay S, Lewanski C, et al. The clinical role of VeriStrat testing in patients with advanced non-small cell lung cancer considered unfit for first-line platinum-based chemotherapy. Eur J Cancer. Oct 2019; 120: 86-96. PMID 31499384
48. Akerley WL, Nelson RE, Cowie RH, et al. The impact of a serum based proteomic mass spectrometry test on treatment recommendations in advanced non-small-cell lung cancer. Curr Med Res Opin. May 2013; 29(5): 517-25. PMID 23452275
49. Akerley WL, Arnaud AM, Reddy B, et al. Impact of a multivariate serum-based proteomic test on physician treatment recommendations for advanced non-small-cell lung cancer. Curr Med Res Opin. Jun 2017; 33(6): 1091-1097. PMID 28277859
50. Hanna NH, Robinson AG, Temin S, et al. Therapy for Stage IV Non-Small-Cell Lung Cancer With Driver Alterations: ASCO and OH (CCO) Joint Guideline Update. J Clin Oncol. Mar 20 2021; 39(9): 1040-1091. PMID 33591844
51. Hanna NH, Schneider BJ, Temin S, et al. Therapy for Stage IV Non-Small-Cell Lung Cancer Without Driver Alterations: ASCO and OH (CCO) Joint Guideline Update. J Clin Oncol. May 10 2020; 38(14): 1608-1632. PMID 31990617
52. Kalemkerian GP, Narula N, Kennedy EB, et al. Molecular Testing Guideline for the Selection of Patients With Lung Cancer for Treatment With Targeted Tyrosine Kinase Inhibitors: American Society of Clinical Oncology Endorsement of the College of American Pathologists/International Association for the Study of Lung Cancer/Association for Molecular Pathology Clinical Practice Guideline Update. J Clin Oncol. Mar 20 2018; 36(9): 911-919. PMID 29401004
53. Socinski MA, Evans T, Gettinger S, et al. Treatment of stage IV non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. May 2013; 143(5 Suppl): e341S-e368S. PMID 23649446