


MEDICAL POLICY	Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only)
Effective Date: 08/01/2021	Medical Policy Number: 193
 8/1/2021	Medical Policy Committee Approved Date: 5/18; 3/19; 3/2020; 6/2020; 07/2020; 12/2020; 3/2021; 7/2021
Medical Officer	Date

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

Medicare only

MEDICARE POLICY CRITERIA	
<p>The following Centers for Medicare & Medicaid Service (CMS) guidelines should be utilized for medical necessity coverage determinations. Click the link provided in the table below to access applicable medical necessity criteria. All listed guidelines apply.</p>	
Service	Medicare Guidelines
<i>EGFR Testing</i>	<ul style="list-style-type: none"> • Local Coverage Determination (LCD): MoIDX: Molecular Diagnostic Tests (MDT) (L36256)¹ • Local Coverage Article: Billing and Coding: MoIDX: FDA-Approved EGFR Tests (A54424)²
<i>Guardant360® (Guardant Health, Inc.; Redwood City, CA)</i>	<ul style="list-style-type: none"> • Local Coverage Article: Billing and Coding: Guardant360® (A58192)³ <ul style="list-style-type: none"> ○ Patient must also meet criteria in NCD for Next Generation Sequencing (NGS) (90.2)⁴
<i>Guardant 360® CDx (Guardant Health, Inc.; Redwood City, CA; CPT 0242U)</i>	<ul style="list-style-type: none"> • National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2)⁴

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<i>InVisionFirst®-Lung (Inivata; Research Triangle Park, NC)</i>	<ul style="list-style-type: none"> Local Coverage Determination (LCD): MoIDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer (L37899)⁵ Local Coverage Article: Billing and Coding: MoIDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer (A57665)⁶
<i>Resolution ctDx Lung™ (Resolution Bioscience; Kirkland, WA; CPT 0179U)</i>	<ul style="list-style-type: none"> Local Coverage Determination (LCD): MoIDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043)⁷ <i>According to the LCD, "Other liquid biopsies will be covered for the same indications if they display similar performance in their intended used applications to Guardant360®." The Resolution ctDx Lung™ (0179U) test is listed on the DEX™ Change Healthcare Registry website as a potentially covered test by MoIDX for Medicare.</i>
<i>Oncomine Dx Target Test</i>	<ul style="list-style-type: none"> Local Coverage Determination (LCD): MoIDX: Molecular Diagnostic Tests (MDT) (L36256)¹ Local Coverage Article: Billing and Coding: MoIDX: ThermoFisher Oncomine Dx Target Test for Non-Small Cell Lung Cancer (A55888)⁸
<i>Other Next Generation Sequencing</i>	<ul style="list-style-type: none"> National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2)⁴ Local Coverage Determination (LCD): MoIDX: Next-Generation Sequencing for Solid Tumors (L38121)⁹ Local Coverage Article: Billing and Coding: MoIDX: Next-Generation Sequencing for Solid Tumors (A57905)¹⁰

Per the [Medicare Policy Manual](#) commercial medical policies may be applied to Medicare coverage determinations in the absence of an appropriate NCD, LCD, LCA, or CMS Coverage Manual. Therefore, the commercial medical policy, **Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (All Lines of Business Except Medicare)**, applies to the following services:

- ALK gene rearrangements (*see criterion I. in commercial policy*)
- Testing for expression of the PD-L1 protein in tumor tissue (*see criterion II. in commercial policy*)
- Circulating Tumor DNA (also known as cell-free DNA or Liquid Biopsy) Testing not addressed above, including but not limited to, the following: (*see criterion VI. in commercial policy*)
 - Tests evaluating genetic alterations other than EGFR deletion of exon 19 and point mutations L858R and T790M
 - Oncomine™ Lung cfDNA Assay
 - SmartGenomics™ Complete
 - SmartGenomics™ Lung Profile
 - Target Selector™ Liquid Biopsy
- Proteomic Testing (e.g. VeriStrat®) (*see criterion VII. in commercial policy*)

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- Protogenomic testing (e.g. Biodesix Lung Reflex® (which includes VeriStrat® and GeneStrat®; GPS Cancer™ Test) (*see criterion VIII. in commercial policy*)

POLICY GUIDELINES

Companion Diagnostic Devices (In Vitro and Imaging Tools)

As of 6/14/2021, the following FDA-approved companion diagnostic tests would be covered as long as all of the medical necessity criteria in the NCD for Next Generation Sequencing (NGS) (90.2) were met:

Test	Diagnostic Manufacturer	FDA-Approved Indication(s) and Therapies
Therascreen EGFR RGQ PCR Kit	Qiagen Manchester Ltd.	Non-small cell lung cancer <ul style="list-style-type: none"> • Iressa (gefitinib) • Gilotrif (afatinib) • Vizimpro (dacomitinib)
Therascreen KRAS RGQ PCR Kit	Qiagen Manchester Ltd.	Non-Small Cell Lung Cancer (NSCLC) <ul style="list-style-type: none"> • Lumakras (sotorasib)
cobas EGFR Mutation Test v2	Roche Molecular Systems, Inc.	Non-small cell lung cancer (tissue and plasma) <ul style="list-style-type: none"> • Tarceva (erlotinib) • Tagrisso (osimertinib) • Iressa (gefitinib)
PD-L1 IHC 22C3 pharmDx	Dako North America, Inc.	Non-small cell lung cancer <ul style="list-style-type: none"> • KEYTRUDA (pembrolizumab)
PD-L1 IHC 28-8 pharmDx	Dako North America, Inc	Non-small cell lung cancer (NSCLC) OPDIVO (nivolumab) in combination with YERVOY (ipilimumab)
FoundationOne CDx (F1CDx)	Foundation Medicine, Inc.	Non-small cell lung cancer <ul style="list-style-type: none"> • Gilotrif (afatinib) • Iressa (gefitinib) • Tarceva (erlotinib) • Tagrisso (osimertinib) • Alecensa (alectinib) • Xalkori (crizotinib) • Zykadia (ceritinib) • Tafinlar (dabrafenib) - in combination with Mekinist (trametinib)

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FoundationOne® Liquid CDx	Foundation Medicine, Inc.	Non-small cell lung cancer (plasma) <ul style="list-style-type: none"> • Iressa (gefitinib) • Tagrisso (osimertinib) • Tarceva (erlotinib) • Alecensa (alectinib)
Oncomine Dx Target Test	Life Technologies Corporation	Non-small cell lung cancer <ul style="list-style-type: none"> • Tafenlar (dabrafenib) • Mekinist (trametinib) • Xalkori (crizotinib) • Iressa (gefitinib)
Ventana ALK (D5F3) CDx Assay	Ventana Medical Systems, Inc.	Non-small cell lung cancer <ul style="list-style-type: none"> • Zykadia (ceritinib) • Xalkori (crizotinib) • Alecensa (alectinib) • Lorbrina (lorlatinib)
VENTANA PD- L1(SP142) Assay	Ventana Medical Systems, Inc.	Non-small cell lung cancer (NSCLC) <ul style="list-style-type: none"> • TECENTRIQ (atezolizumab)
Vysis ALK Break Apart FISH Probe Kit	Abbott Molecular Inc.	Non-small cell lung cancer (NSCLC) <ul style="list-style-type: none"> • Xalkori (crizotinib) • Alunbrig (brigatinib)

Please see the FDA website “[List of Cleared or Approved Companion Diagnostic Devices](#)” for the most current information on these tests and new tests as they are approved.²

BILLING GUIDELINES

Next Generation Sequencing Tests

Based on Transmittal #215, included in NCD 90.2, the following CPT codes are considered appropriate for billing for the FDA-approved companion diagnostic tests for NSCLC.⁹

NGS Test	Code
FoundationOne CDx (F1CDx)	81455 (3/16/18 - 3/31/18) 0037U (4/1/18 to present)
Oncomine Dx Target Test	0022U

CPT CODES

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Note: Codes which may be billed for molecular testing addressed in this policy include, but are not limited to, the following:

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Prior Authorization Required	
0009U	Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin-fixed paraffin-embedded tissue isolated using image-based dielectrophoresis (DEP) sorting, reported as ERBB2 gene amplified or non-amplified
0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes, interrogation for sequence variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider
0242U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 55-74 genes, interrogation for sequence variants, gene copy number amplifications, and gene rearrangements
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
0179U	Oncology (non-small cell lung cancer), cell-free DNA, targeted sequence analysis of 23 genes (single nucleotide variations, insertions and deletions, fusions without prior knowledge of partner/breakpoint, copy number variations), with report of significant mutation(s)
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
81404	Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT,

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	KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
No Prior Authorization Required	
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)
81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)
88271	Molecular cytogenetics; DNA probe, each
88272	Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)
88273	Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)
88274	Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells
88275	Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells
88291	Cytogenetics and molecular cytogenetics, interpretation and report
88341	Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)
88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure
88360	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; manual
88363	Examination and selection of retrieved archival (ie, previously diagnosed) tissue(s) for molecular analysis (eg, KRAS mutational analysis)
88366	In situ hybridization (eg, FISH), per specimen; each multiplex probe stain procedure
88367	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; initial single probe stain procedure
88368	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; initial single probe stain procedure
88374	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; each multiplex probe stain procedure

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88377	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; each multiplex probe stain procedure
88381	Microdissection (ie, sample preparation of microscopically identified target); manual
Not Covered	
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival
Unlisted Codes	
All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then prior-authorization is required.	
81479	Unlisted molecular pathology procedure
81599	Unlisted multianalyte assay with algorithmic analysis

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

MEDICAL POLICY CROSS REFERENCES

Providence Health Plans Medical Policies

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- Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (All Lines of Business Except Medicare)
- Circulating Tumor Cell and DNA Assays For Cancer Management
- Genetic Testing: Non-Covered Genetic Panel Tests (Medicare Only)
- Genetic Studies and Counseling

Providence Health Plans Pharmacy Policies

- Injectable ANTI-Cancer Medications. Antineoplastics, ORPTCONC102
- Oral ANTI-Cancer Medications. Antineoplastics, ORPTCONC103

REFERENCES

1. Centers for Medicare & Medicaid Services. LCD L36256. LCD Title: MoIDX: Molecular Diagnostic Tests (MDT). <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36256>. Published 2019. Accessed 6/15/2021.
2. Centers for Medicare & Medicaid Services. LCA A54424. LCA Title: MoIDX: FDA-Approved EGFR Tests Billing and Coding Guidelines. <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=54424>. Published 2015. Accessed 6/15/2021.
3. Centers for Medicare & Medicaid Services. Local Coverage Article: Billing and Coding: Guardant360® (A58192). Original Effective Date: 05/15/2020. <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=58192>. Accessed 6/15/2021.
4. Centers for Medicare & Medicaid Services. NCD 90.2. NCD Title: Next Generation Sequencing (NGS). <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=372>. Published 2018. Accessed 6/15/2021.
5. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD): MoIDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer (L37899). <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37899>. Published 2019. Accessed 6/15/2021.
6. Centers for Medicare & Medicaid Services. Local Coverage Article: Billing and Coding: MoIDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer (A57665). <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=57665&ver=3&LCDId=37899>. Published 2019. Accessed 6/15/2021.
7. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD): MoIDX: Plasma-Based Genomic Profiling in Solid Tumors (L38043). Revision Effective Date: For services performed on or after 03/05/2020. <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38043>. Accessed 6/15/2021.
8. Centers for Medicare & Medicaid Services. LCA A55888. LCA Title: MoIDX: ThermoFisher Oncomine Dx Target Test For Non-Small Cell Lung Cancer Billing and Coding Guidelines. <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=55888>. Published 2017. Accessed 6/15/2021.

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- 9. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD): MoIDX: Next-Generation Sequencing for Solid Tumors (L38121). Published 5/17/2020. <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38121>. Accessed 6/15/2021.
- 10. Center for Medicare & Medicaid Services. Local Coverage Article: Billing and Coding: MoIDX: Next-Generation Sequencing for Solid Tumors (A57905). Published 5/17/2020. <https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=57905>. Accessed 6/15/2021.