Local Coverage Determination (LCD): MolDX-CDD: NSCLC, Comprehensive Genomic Profile Testing (L36143)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Palmetto GBA	A and B and HHH MAC	11201 - MAC A	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11202 - MAC B	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11301 - MAC A	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11302 - MAC B	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11401 - MAC A	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11402 - MAC B	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11501 - MAC A	J - M	North Carolina
Palmetto GBA	A and B and HHH MAC	11502 - MAC B	J - M	North Carolina

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LCD Information

Document Information

LCD ID
L36143

Original ICD-9 LCD ID
N/A

LCD Title
MolDX-CDD: NSCLC, Comprehensive Genomic Profile Testing

Original Effective Date
For services performed on or after 10/01/2015

Revision Effective Date
For services performed on or after 11/27/2015

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
N/A

Notice Period End Date
N/A

CMS National Coverage Policy Title XVIII of the Social Security Act, §1862(a)(1)(A)allows coverage and payment for only those services that are considered to be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member

Title XVIII of the Social Security Act, §1862(a)(1)(D) items and services related to research and experimentation

Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim which lack the necessary information to process the claim.

42 CFR 410.32(a) Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions

42CFR411.15(k)(1) Particular services excluded from coverage

CMS On-Line Manual, Publication 100-08, Medicare Program Integrity Manual, Chapter 3, §3.4.1.3, diagnosis code requirements

Coverage Guidance
Coverage Indications, Limitations, and/or Medical Necessity

This policy provides limited coverage for comprehensive somatic genomic profiling on tumor tissue-only (hereafter called CGP) for patients with metastatic non-small cell lung cancer (NSCLC) who are lifetime non-smokers (also known as never-smokers) or former light smokers (=15 pack year history) and who tested negative for epidermal growth factor receptor (EGFR) mutations, EML4-ALK rearrangements, and ROS1 rearrangements when initial testing was done by an FDA-approved companion diagnostic (CDx) or by a laboratory developed test (LDT) for these genomic alterations. Alterations detected by CGP, if positive, may allow individuals to be treated with a targeted therapy for which they were previously ineligible. At the current time, CGP for germline (i.e. inheritable) mutations is not a Medicare benefit.

Background

It is estimated that more than 220,000 new cases of lung cancer will be diagnosed in the United States (US) this year. This represents roughly 13% of all new cancer diagnoses, and 27% of cancer deaths. Sadly, the estimated 5-year survival rate for all lung cancer patients is 17%, and only 4% for patients with metastatic disease.

The pathophysiological development of lung cancer is complicated, with several known genomic alterations found individually or in combination in many patients. These alterations may be due to toxic exposure or underlying genetic factors, and not all alterations have the same impact on disease development or prognosis. Some alterations appear to be integral to the transformation and ongoing growth of the tumor (driver mutations). Among the best studied in this class are point alterations and indels in EGFR and EML4-ALK translocations. EGFR mutated NSCLC is found in up to 15% of all lung cancers in the US. These mutations convey a more favorable prognosis and allow treatment with oral EGFR inhibitors such as erlotinib, gefitinib, or afatinib. Similarly, translocations of ALK and EML4 or other less common fusion partners occur in approximately 4% of all NSCLC patients and permit treatment with oral ALK-targeted inhibitors such as crizotinib and ceritinib.

The majority of NSCLC cases are diagnosed in patients with a smoking history. Lifetime non-smokers or light former smokers (=15 pack years) have different disease compared to their heavier smoking counterparts. Sequencing of tumor specimens in never-smokers has shown a higher mutation frequency of EGFR than smokers, with some non-smoking ethnic groups such as Asian women having a much higher mutation frequency than their Caucasian counterparts. Similar results have been shown with ALK translocations. For example, in one study involving never-smokers or light smokers with adenocarcinoma of the lung, 22% of patients' tumors harbored an ALK. When EGFR mutation carriers were excluded, 33% of patients had an ALK translocation. While ALK translocations and EGFR mutations certainly occur at a meaningful frequency in former smokers with more significant history of cigarette use, use of the enrichment approach described herein may allow a more efficient completion of this initial phase of study.

Currently, a variety of different techniques are used to test for these genomic alterations in tumor specimens including three FDA cleared/approved CDx tests for NSCLC to determine if a patient is a candidate for targeted therapy. For EGFR, there is the Cobas® EGFR Mutation Test for erlotinib and Therascreen EGFR RCQ PCR Kit for afatinib. For ALK, there is the Vysis ALK Break Apart FISH Probe Kit for crizotinib. These tests look at specific regions in the target gene to determine if the genomic alteration of interest is present.

In addition to these FDA-approved CDx test, there are a variety of laboratory-developed tests (LDTs) that are used to identify EGFR mutations and ALK translocations. These include bidirectional Sanger sequencing, direct DNA sequencing, hybridization sequencing, pyrosequencing and sequencing by denaturation to name a few. Some of these LDTs provide more extensive genetic analysis than their FDA-approved counterparts, but there are few head-to-head comparison studies demonstrating greater diagnostic accuracy or clinical utility of the various approaches.

For various reasons, CDx or LDT sequencing techniques may miss deleterious EGFR mutations and ALK translocations. For example, alterations may occur outside the sequenced region or involve complex alterations (e.g. insertions or deletions (indels), copy number alterations, or translocations) that are not detectable by the specific test. Newer techniques such as massively parallel sequencing, also known as next generation sequencing (NGS), offer the possibility of not only increased analytical sensitivity but also the ability to detect a broader range of genomic alterations than existing CDx and LDT techniques.

In a recent study by Drilon, lifetime non-smokers or light smokers who tested negative for alterations in various target genes (including EGFR and ALK) in a broad "focused panel of a variety of non-NGS" tests developed at a major academic institution were studied using a specific type of NGS, namely CGP. Despite robust non-NGS (and CGP) testing using multiple techniques, CGP testing identified EGFR mutations in 7% more patients than had been identified by prior combined methodologies, and 6% more ALK translocations than by previous FISH analysis. Although some of the EGFR mutated malignancies found by NGS are less likely to respond to available EGFR tyrosine kinase inhibitors (TKIs) (e.g. exon 20 insertions), others such as complex double mutations and exon 18 mutations (which are typically undetectable with so-called "hotspot" panels), are likely to benefit from targeted therapy. CGP analysis was equally compelling for ALK translocations. In two patients, where FISH analysis was clearly negative, translocations were identified using CGP. These patients would likely benefit from treatment with crizotinib.

Although the study population is small, the significant number of potentially actionable genomic alterations that were missed by non-NGS methodologies is compelling, and demonstrates that CGP can identify a group of non-small cell lung cancer patients who are likely to benefit from targeted therapy.

Comprehensive Genomic Profiling (CGP) Test Description:

CGP analysis is defined as a single test using tumor tissue only (i.e., not matched tumor and normal) that does not distinguish between somatic and germline alterations and can detect the following classes of alterations:

1. Base pair substitutions (including single nucleotide variants (SNVs))
2. Insertions and deletions (Indels; up to 70 bp)
3. Copy number variations (CNVs; including both amplifications (ploidy < 4 with copy number = 8) and homozygous deletions (ploidy < 4 with copy number = 0)
4. Translocations

Other non-NGS testing platforms may be considered if they can similarly detect all four classes of alterations with comparable test performance as CGP.

MolDX CGP Analysis Coverage

CGP analysis is covered only when the following conditions are met:

- Patient has been diagnosed with advanced (Stage IIIB or IV) NSCLC; **and**
- Patient is a lifetime non-smoker or former light smoker with =15 pack year history of smoking; **and**
- Patient previously tested negative for EGFR mutations, ALK rearrangements, and ROS1 rearrangements through non-CGP methods; **and**

- Testing is performed by a lab that satisfies Palmetto GBA's published AV criteria.

Palmetto GBA expects participating laboratories to:

- Prior to CGP testing, verify that each patient has previously tested negative for EGFR mutations, ALK rearrangements, and ROS1 rearrangements
- Report the following to MolDX every six months on an individual patient basis but de-identified (i.e., no protected health information):
    - Patient demographics including patient age when the specimen was collected, and gender;
    - Sample information including whether CGP testing was performed on the same specimen DNA as the original test result, a re-biopsy from the same tumor site, or a re-biopsy from a different tumor site, and the dates of biopsy for the original non-CGP and CGP tests;
    - Non-CGP test methodology resulting in a negative EGFR mutations, or ALK or ROS1 rearrangements;
    - Alterations in the following genes: ALK, BRAF, EGFR, HER2, KRAS, MET, ROS1, and RET.
    - Any treatment received after CGP testing, the current response status and duration of response
- Reports will be delivered in every 6 months in a mutually acceptable format.

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Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

N/A

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

N/A

CPT/HCPCS Codes

Group 1 Paragraph: N/A

Group 1 Codes:

81445 TARGETED GENOMIC SEQUENCE ANALYSIS PANEL, SOLID ORGAN NEOPLASM, DNA ANALYSIS, 5-50 GENES (EG, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, 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 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

81479 UNLISTED MOLECULAR PATHOLOGY PROCEDURE

ICD-10 Codes that Support Medical Necessity
Group 1 Paragraph: N/A

Group 1 Codes:

ICD-10 Codes	Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung

ICD-10 Codes that DO NOT Support Medical Necessity N/A
ICD-10 Additional Information

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General Information

Associated Information
Documentation Requirements

The patient's medical record must contain documentation that fully supports the medical necessity for services included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available to the J11 MAC upon request.

Sources of Information and Basis for Decision

References

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Revision History Information

Please note: Most Revision History entries effective on or before 01/24/2013 display with a Revision History Number of "R1" at the bottom of this table. However, there may be LCDs where these entries will display as a separate and distinct row.

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
11/27/2015	R3	added "-CDD" after the word MolDX in the title	• Other (added "-CDD" after the word MolDX in the title)
10/01/2015	R2	Per CMS Internet-Only Manual, Pub 100-08, Medicare Program Integrity Manual, Chapter 13, §13.1.3 LCDs consist of only "reasonable and necessary" information. All bill type and revenue codes have been removed.	• Other (Bill type and/or revenue code removal)
10/01/2015	R1	Added Bill Type codes, ICD-10 codes and references that were left off ICD-10 version in error.	• Typographical Error

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Associated Documents

Attachments N/A

Related Local Coverage Documents N/A

Related National Coverage Documents N/A

Public Version(s) Updated on 11/20/2015 with effective dates 11/27/2015 - N/A Updated on 06/03/2015 with effective dates 10/01/2015 - 11/26/2015 Updated on 05/18/2015 with effective dates 10/01/2015 - N/A Updated on 05/14/2015 with effective dates 10/01/2015 - N/A Back to Top

Keywords

N/A Read the **LCD Disclaimer** Back to Top