Local Coverage Determination (LCD): Genomic Sequence Analysis Panels in the Treatment of Non-Small Cell Lung Cancer (L36376)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
National Government Services, Inc.	MAC - Part A	06101 - MAC A	N/A	Illinois
National Government Services, Inc.	MAC - Part B	06102 - MAC B	N/A	Illinois
National Government Services, Inc.	MAC - Part A	06201 - MAC A	N/A	Minnesota
National Government Services, Inc.	MAC - Part B	06202 - MAC B	N/A	Minnesota
National Government Services, Inc.	MAC - Part A	06301 - MAC A	N/A	Wisconsin
National Government Services, Inc.	MAC - Part B	06302 - MAC B	N/A	Wisconsin
National Government Services, Inc.	A and B and HHH MAC	13101 - MAC A	J - K	Connecticut
National Government Services, Inc.	A and B and HHH MAC	13102 - MAC B	J - K	Connecticut
National Government Services, Inc.	A and B and HHH MAC	13201 - MAC A	J - K	New York - Entire State
National Government Services, Inc.	A and B and HHH MAC	13202 - MAC B	J - K	New York - Downstate
National Government Services, Inc.	A and B and HHH MAC	13282 - MAC B	J - K	New York - Upstate
National Government Services, Inc.	A and B and HHH MAC	13292 - MAC B	J - K	New York - Queens
National Government Services, Inc.	A and B and HHH MAC	14111 - MAC A	J - K	Maine
National Government Services, Inc.	A and B and HHH MAC	14112 - MAC B	J - K	Maine
National Government Services, Inc.	A and B and HHH MAC	14211 - MAC A	J - K	Massachusetts
National Government Services, Inc.	A and B and HHH MAC	14212 - MAC B	J - K	Massachusetts
National Government Services, Inc.	A and B and HHH MAC	14311 - MAC A	J - K	New Hampshire
National Government Services, Inc.	A and B and HHH MAC	14312 - MAC B	J - K	New Hampshire
National Government Services, Inc.	A and B and HHH MAC	14411 - MAC A	J - K	Rhode Island
National Government Services, Inc.	A and B and HHH MAC	14412 - MAC B	J - K	Rhode Island
National Government Services, Inc.	A and B and HHH MAC	14511 - MAC A	J - K	Vermont
National Government Services, Inc.	A and B and HHH MAC	14512 - MAC B	J - K	Vermont

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LCD Information

Document Information

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L36376

LCD Title
Genomic Sequence Analysis Panels in the Treatment of Non-Small Cell Lung Cancer

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CMS National Coverage Policy Language quoted from Centers for Medicare and Medicaid Services (CMS), National Coverage Determinations (NCDs) and coverage provisions in interpretive manuals is italicized throughout the policy. NCDs and coverage provisions in interpretive manuals are not subject to the Local Coverage Determination (LCD) Review Process (42 CFR 405.860[b] and 42 CFR 426 [Subpart D]). In addition, an administrative law judge may not review an NCD. See Section 1869(f)(1)(A)(i) of the Social Security Act.

Unless otherwise specified, *italicized* text represents quotation from one or more of the following CMS sources:

Title XVIII of the Social Security Act (SSA):
Section 1862(a)(1)(A) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1833(e) prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

Section 1862(a)(7) excludes routine physical examinations, unless otherwise covered by statute.

CMS Publications:
CMS Publication 100-02, *Medicare Benefit Policy Manual*, Chapter 15, Section 80.1 – Laboratory services must meet applicable requirements of CLIA

CMS Publication 100-04, *Medicare Claims Processing Manual*, Chapter 16, Section 40.7 Billing for Noncovered Clinical Laboratory Tests Section and 120.1 Clarification of the Use of the Term "Screening" or "Screen"

CMS Publication 100-04, *Medicare Claims Processing Manual*, Chapter 30, Section 50 Advance Beneficiary Notice of Noncoverage (ABN)

CMS Publication 100-08, *Medicare Program Integrity Manual*, Chapter 13, Local Coverage Determinations

CMS National Correct Coding Initiative (NCCI) *Policy Manual for Medicare Services*, Chapter 10, Pathology/Laboratory Services, (A) Introduction

CMS Publication 100-02, *Medicare Benefit Policy Manual*, Chapter 15, Section 80.6. 5 which describes the Surgical/Cytopathology Exception.

CMS National Correct Coding Initiative (NCCI) *Policy Manual for Medicare Services*, Chapter 10 Pathology/Laboratory Services which addresses reflex testing.

Code of Federal Regulations:
42 CFR, Section 410.32, indicates that diagnostic tests may only be ordered by the treating physician (or other treating practitioner acting within the scope of his or her license and Medicare requirements) who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem. Tests not ordered by the physician (or other qualified non-physician provider) who is treating the beneficiary are not reasonable and necessary (see Sec. 411.15(k)(1) of this chapter).

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

Abstract
The American Cancer Society estimates that over 220,000 new cases of lung cancer will be diagnosed in 2015, with over 85% of those cancers being classified as non-small cell lung cancer. Lung cancer represents approximately 13% of all new cancer diagnoses, and approximately 27% of cancer deaths. The estimated 5yr survival rate for all lung cancer patients is 17% and is only 4% for patients with metastatic disease.

Most lung cancers are epithelial in origin, with squamous cell carcinomas, adenocarcinomas, and small cell carcinomas being the predominant histologic types. The first two, squamous and adenocarcinomas, have been traditionally grouped as non-small cell lung cancer (NSCLC). Surgery remains the cornerstone of treatment for early stage NSCLC of either type, however treatment of advanced stage disease is based primarily on drugs. Distinctive response patterns to specific therapeutic drugs have been demonstrated over the past 12 years, necessitating the distinction between squamous cell and adenocarcinoma morphology. Consequently the most recent WHO guidelines advocate sub-classification of all NSCLC in to a more specific subtype whenever possible. This is typically accomplished by histologic evaluation with support from specific immunohistochemical studies, which are particularly useful in the evaluation of small biopsies.

Adenocarcinomas account for approximately 40% of all lung cancers, and are the most common lung cancer in never- or light smokers. Adenocarcinomas are characterized by glandular differentiation, mucin production, or pneumocyte marker expression. Certain genomic alterations are more commonly found in lung adenocarcinomas (when compared to squamous or small cell carcinomas) and clinical laboratory testing to identify these alterations is important in two respects: First, some mutations are now recognized as "driver mutations," which are essential for tumor cell survival. Inhibition of these mutated proteins results in tumor cell death, making them attractive therapeutic targets. While not all driver mutations have specific therapies at this time, an important corollary of this concept is that with rare exception, such driver mutations are mutually exclusive, i.e. the identification of one driver mutation in a tumor effectively makes the likelihood that another driver mutation is present extremely unlikely.

The second reason clinical laboratory testing for specific driver mutations in lung adenocarcinomas is important is the association of specific genomic alterations with response to specific drugs. Different driver mutations respond to different targeted therapies, and only genetic testing can clearly identify which mutation is present and, therefore, which treatment should be administered. While some of the genetic alterations that affect response to targeted inhibitors are found in a higher proportion of adenocarcinomas from patients with certain clinical risk factors (i.e., low to no history of tobacco exposure, female gender, young age, Asian ethnicity) , these clinical associations are not sufficiently predictive of mutation status to appropriately determine therapy without genetic testing. Accordingly, professional practice guidelines from CAP-IASLC-AMP, WHO, and NCCN all advise against using smoking history, or other clinical risk factors, to exclude testing patients for specific genomic alterations.

NCCN Guidelines (v 7.2015) for Non-Small Cell Lung Cancer recommend testing all non-squamous NSCLCs (i.e. adenocarcinomas, large cell carcinomas, and NSCLC not otherwise specified) for specific alterations in EGFR and ALK and recommend consideration of such testing in tumors with mixed squamous and adeno histology, and in the rare squamous cell carcinomas in never smokers. The NCCN NSCLC Panel "strongly endorses broader molecular profiling to identify rare driver mutations using multiplex/NGS to ensure that patients receive the most appropriate treatment". In addition to testing for alterations in EGFR and ALK, NCCN Guidelines explicitly recognize the prognostic and predictive value of KRAS mutations as well as alterations in the BRAF, MET, and ROS1 genes to select a therapeutic agent, the use of which may be "off-label" but which also meets Medicare coverage requirements for off-label cancer drugs (CMS Publication Pub 100-02, Medicare Benefit Policy Manual, Chapter 15, §50.4.5).

Genomic alterations contribute to the development of non-small cell lung carcinoma. Two of the best studied alterations are EGFR mutations and ALK (e.g., EML4-ALK) gene fusions. EGFR mutations are permissive for the use of oral EGFR inhibitors, such as erlotinib. Similarly, activating fusions of ALK permit treatment with oral ALK inhibitors, such as crizotinib. Gene alterations for which a targeted therapeutic agent is available and the use of which meets Medicare coverage requirements (outside of a clinical trial) are listed in Table 1.

Table 1

Gene	**NCCN Category 1 or 2A Recommended Therapeutic Option**
ALK	crizotinib, ceritinib, and alectinib
EGFR	afatinib, erlotinib hydrochloride, and gefitinib
ROS 1	crizotinib
KRAS	Avoid TKI
BRAF	dabrafenib and vemurafib
MET	crizotinib

In total, there are over 40 single nucleotide or small insertion/deletion variants occurring at numerous specific loci in ten genes. These variants represent potential therapeutic targets and, as therapeutic agents aimed at these targets are proven safe and effective and meet Medicare coverage guidelines, additional genes may be added to the above table. In addition, gene fusions can involve five different genes, and amplification is the significant recognized alteration in at least one gene. Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5-50 genes (CPT 81445) is a useful representation of the aggregate of these gene tests, and may be used as long as the panel contains, at a minimum, 5 or more gene tests for molecular biomarkers determined to meet Medicare coverage criteria as listed above. Evaluation of other genes or genomic sequences not addressed by NCCN or other professional guidelines are not precluded, but their inclusion in panels recognized by this code should not be interpreted as endorsement of such testing by genomic sequencing procedures and laboratories and users of such testing are advised to adhere to traditional regulatory and institutional oversight mechanisms to assure their clinical validity and utility.

Indications and Limitations of Coverage
Genomic Sequential Analysis Panel represented by CPT 81445 will be considered reasonable and necessary in the evaluation of tumor tissue in the following clinical circumstances:

- Newly diagnosed patients with advanced (stage IIIB or IV) NSCLC, who are not treatable by resection or radiation with curative intent, and who are suitable candidates for therapy at the time of testing.
- Previously diagnosed patients with advanced (stage IIIB or IV) NSCLC, who have not responded to at least one systemic therapy, or who have progressed following resection. The patient must be a candidate for treatment at the time of the testing.
- Previously diagnosed patients with advanced (stage IIIB or IV) NSCLC, who have been resistant to at least one targeted therapy, are able to undergo tumor tissue biopsy for testing, and who are suitable candidates for additional treatment at the time of testing.

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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.

012x Hospital Inpatient (Medicare Part B only)
013x Hospital Outpatient

014x Hospital - Laboratory Services Provided to Non-patients
022x Skilled Nursing - Inpatient (Medicare Part B only)
023x Skilled Nursing - Outpatient

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.

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.

Revenue codes only apply to providers who bill these services to the Part A MAC. Revenue codes do not apply to physicians, other professionals and suppliers who bill these services to the Part B MAC.

Please note that not all revenue codes apply to every type of bill code. Providers are encouraged to refer to the FISS revenue code file for allowable bill types. Similarly, not all revenue codes apply to each CPT/HCPCS code. Providers are encouraged to refer to the FISS HCPCS file for allowable revenue codes.

0300 Laboratory - General Classification
0310 Laboratory Pathology - General Classification

CPT/HCPCS Codes
Group 1 Paragraph: CPT code 81445 Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5-50 genes, may be used as long as the panel contains, at a minimum, 5 or more gene tests for molecular biomarkers determined to meet Medicare coverage criteria as listed above.

Group 1 Codes:

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, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), INTERROGATION FOR SEQUENCE VARIANTS AND COPY NUMBER VARIANTS OR REARRANGEMENTS, IF PERFORMED

ICD-10 Codes that Support Medical Necessity
Group 1 Paragraph: The following ICD-10- diagnosis codes are considered medically necessary:

Group 1 Codes:

ICD-10 Codes	Description
C33 - C34.92	Malignant neoplasm of trachea - Malignant neoplasm of unspecified part of left bronchus or lung
C38.4	Malignant neoplasm of pleura
C45.0	Mesothelioma of pleura

ICD-10 Codes that DO NOT Support Medical Necessity
Group 1 Paragraph: Any diagnosis code not listed above does not support medical necessity.

Group 1 Codes:

ICD-10 Codes	Description
XX000	Not Applicable

ICD-10 Additional Information

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General Information

Associated Information
Documentation Requirements

Documentation must be adequate to verify that coverage guidelines listed above have been met. Thus, the medical record must contain documentation that the testing is expected to influence treatment of the condition toward which the testing is directed. The laboratory or billing provider must have on file the physician requisition which sets forth the diagnosis or condition (ICD-10-CM code) that warrants the test(s).

Examples of documentation requirements of the ordering physician/nonphysician practitioner (NPP) include, but are not limited to, history and physical or exam findings that support the decision making, problems/diagnoses, relevant data (e.g., lab testing, imaging results).

Documentation requirements of the performing laboratory (when requested) include, but are not limited to, lab accreditation, test requisition, test record/procedures, reports (preliminary and final), and quality control record.

Documentation requirements for LDT(s)/protocols (when requested) include diagnostic test/assay, lab/manufacturer, names of comparable assays/services (if relevant), description of assay, analytical validity evidence, clinical validity evidence, and clinical utility.

Providers are required to code to specificity however, if CPT 81479 (unlisted molecular pathology procedure) is used the documentation must clearly identify the unique molecular pathology procedure performed. When multiple procedure codes are submitted on a claim (unique and/or unlisted) the documentation supporting each code should be easily identifiable. If on review the contractor cannot link a billed code to the documentation, these services will be denied based on Title XVIII of the Social Security Act, §1833(e).

For these tests, the ordering provider must provide to the laboratory copies of the signed informed consent documentation.

An Advance Beneficiary Notice of Noncoverage (ABN) is required before furnishing a beneficiary a test which the physician or laboratory believes to be noncovered by Medicare as not reasonable or necessary. *The physician or laboratory must obtain a signed ABN from the beneficiary (or representative) that the physician or laboratory has informed him/her on the non-coverage of the test and that there will be a charge for the test.*

When the documentation does not meet the criteria for the service rendered or the documentation does not establish the medical necessity for the services, such services will be denied as not reasonable and necessary under Section 1862(a)(1)(A) of the Social Security Act.

Utilization Guidelines

Screening services such as pre-symptomatic genetic tests and services used to detect an undiagnosed disease or disease predisposition are not a Medicare benefit and are not covered. Similarly, Medicare may not reimburse the costs of tests/examinations that assess the risk of a condition unless the risk assessment clearly and directly effects the management of the patient.

Title XVIII of the Social Security Act (SSA) §1862(a)(1)(A) states that no Medicare payment shall be made for items and services which are not reasonable and necessary for the diagnosis or treatment of illness or injury. Based on this statute, CMS states that *"tests that are performed in the absence of signs, symptoms, complaints, or personal history of disease or injury are non-covered unless explicitly authorized by statute."*

A specific genetic test may only be performed once in a lifetime per beneficiary for inherited conditions; however, when medically reasonable and necessary, genetic testing may be done on acquired conditions such as malignancies (including separate malignancies developing at different times) as they are treated and are being followed, in order to assess response or other relevant clinical criteria. Likewise, there are situations where medical record and literature documentation are able to demonstrate that serial testing can be reasonably predicted to provide additional clinically useful information. When the record documents that this information, such as confirmed significant response to current therapy, is likely to assist in modifying treatment, serial testing can be considered reasonable and necessary and eligible for coverage.

Sources of Information and Basis for Decision

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Revision History Information

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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) A54845 - Response to Comments: Genomic Sequence Analysis Panels in the Treatment of Non-Small Cell Lung Cancer

Related National Coverage Documents N/A

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Keywords

- Molecular
- Genes
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- Lab
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