Local Coverage Determination (LCD): MolDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer (L37899)

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CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
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Noridian Healthcare Solutions, LLC	A and B MAC	02102 - MAC B	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02201 - MAC A	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02202 - MAC B	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02301 - MAC A	J - F	Oregon
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LCD Information

Document Information

LCD ID
L37899

LCD Title
MolDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer

Proposed LCD in Comment Period
N/A

Source Proposed LCD
DL37899

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

Original Effective Date
For services performed on or after 06/03/2019

Revision Effective Date
N/A

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
04/18/2019

Notice Period End Date
06/02/2019

CMS National Coverage Policy

Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for items or services that "are not 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, §1833(e), prohibits Medicare payment for any claim lacking the necessary documentation to process the claim.

42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS On-Line Manual, Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, §§80.0, 80.1.1, 80.2. Clinical Laboratory services.

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Ch. 16, §50.5 Jurisdiction of Laboratory Claims, §60.12 Independent Laboratory Specimen Drawing, §60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes".

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

This test is a "liquid biopsy." It is intended to assist physicians caring for patients who suffer from a common form of lung cancer and who have advanced disease.

This policy provides limited coverage for InvisionFirst™ - Lung (Inivata, Research Triangle Park, NC) (hereafter InVision) a plasma-based, somatic comprehensive genomic profiling test (CGP) for patients with advanced (Stage IIIB/IV) non-small cell lung cancer (NSCLC):

- **At diagnosis and untreated**
  - When results for EGFR single nucleotide variants (SNVs) and insertions and deletions (indels); rearrangements in ALK and ROS1; and SNVs for BRAF are not available **AND**
  - When tissue-based CGP is infeasible [i.e., quantity not sufficient (QNS) for tissue-based CGP or invasive biopsy is medically contraindicated],

or

- **At progression**
  - For patients progressing on or after chemotherapy or immunotherapy who have not been tested for EGFR SNVs and indels; rearrangements in ALK and ROS1; and SNVs for BRAF, and for whom tissue-based CGP is infeasible;
  - For patients progressing on EGFR tyrosine kinase inhibitors (TKIs).

If no genetic alteration is detected by InVision or if circulating tumor DNA (ctDNA) is insufficient/not detected, tissue-based genotyping should be considered.

Summary of Evidence

Background

It is estimated that more than 222,500 new cases of lung cancer will be diagnosed in the United States (US) this year.[1] This represents roughly 13% of all new cancer diagnoses and 26% of cancer deaths.[1] At least 87% of lung cancer is NSCLC.[2] The estimated 5-year survival rate for all NSCLC cancer patients is 17%, and only 4% for patients with advanced (stage IIIB/IV) disease.[3]

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 alterations).

Among the best-studied genomic alterations are EGFR single nucleotide variants (SNVs) and insertions/deletions (indels) and EML4-ALK rearrangements/fusions. EGFR-mutated NSCLC comprises up to 15% of all NSCLC patients in the US, with higher prevalence in certain ethnic groups (e.g., 40% in Asian Americans and 26% in Latin Americans).[4] These mutations convey a more favorable prognosis and predict response to treatment with oral EGFR inhibitors such as erlotinib, gefitinib, osimertinib or afatinib. Rearrangements of ALK and EML4, or with other less common fusion partners, occur in approximately 4% of all NSCLC patients and predict response to treatment with oral ALK-targeted inhibitors such as crizotinib, ceritinib, or alectinib.[5] Recently, dabrafenib in combination with trametinib has been approved for BRAF V600E positive metastatic NSCLC.[6]

Genomic alterations in NSCLC vary by smoking history, ethnicity and age. Sequencing of tumor specimens in never-smokers demonstrates a higher mutation prevalence of EGFR than in smokers. Some non-smoking ethnic groups, such as Asian women, have a much higher mutation prevalence than their Caucasian counterparts.[7] Prevalence of ALK rearrangements is also higher in non-smokers.[8] In contrast, smokers have a higher prevalence of targetable alterations in the MET and BRAF genes.[9-10]

Tumor Tissue Genotyping

Failure of oncologists to order genotyping, inadequate quantity or quality of tissue specimen, and the necessity for repeat invasive biopsies with their associated complications and costs are just a few issues that confound tumor-tissue genotyping. Traditionally, tumor genotyping has been conducted by direct interrogation of tumor tissue obtained through invasive tissue sampling procedures. However, this diagnostic approach is limited by the availability of sufficient tumor tissue and the ability of patients to undergo invasive procedures.

In a recent study of more than 100 community-based oncologists, nearly one-third of NSCLC patients were not tested for EGFR or ALK mutations, and more than 75% were not tested for ROS1 fusions. Fewer than 10% of NSCLC patients were tested for all guideline-recommended alterations.[11] These results are similar to a study in a single academic center where 58% of non-squamous NSCLC were tested for EGFR and 40% for ALK fusions, despite repeat invasive biopsies to obtain sufficient tissue for genomic testing in 13% of patients.[12-13] Tissue availability was similarly limited in several recent series, some of which reported that more than 50% of NSCLC patients had insufficient or unobtainable material for tissue-based CGP.[14-16]

Even when adequate tissue for NGS testing is available for testing, many specimens do not yield a complete result

for a variety of reasons. Pre-analytical variables in tissue preservation are known to impact the quality and success of the NGS testing. Some of these variables include tissue fixation and processing variables, the volume of tissue (needle biopsy or resection specimen) available for testing, and the fraction of tumor cells within the specimen. Evaluating somatic mutations in FFPE (formalin-fixed, paraffin-embedded) tissue below 5% allele frequency is challenging due to these pre-analytical variables.[17-19]

Recently, the Oncomine™ Dx Target Test (Thermo Fisher Scientific Inc., Waltham, MA) and FoundationOne CDx™ (Foundation Medicine, Cambridge, MA) tissue-based NGS panel assays received FDA approval and Medicare coverage as alternatives to multiple, individual FDA approved companion diagnostics (CDx).[20,21] The Oncomine panel is considered the least tissue intensive of the CGP tissue profiling panels. In the Oncomine clinical validation studies submitted for FDA approval, only 60% of samples had sufficient tissue for successful testing. The Oncomine validation set included surgical resections specimens that generally have a higher tumor load than diagnostic biopsies and may represent an over-estimate of successful testing specimens.[20]

Currently, a variety of techniques are used to test for genomic alterations in plasma specimens to determine if a patient is a candidate for targeted therapy, including the FDA-approved Cobas® EGFR Mutation Test (tissue or plasma samples) for erlotinib and osimertinib. This assay interrogates specific regions in EGFR to determine whether the genomic alteration of interest is present.[22] For various reasons, these companion diagnostics (CDx) and other existing lab developed test (LDT) techniques may miss deleterious EGFR mutations, ALK rearrangements, and other genomic alterations that can be targeted with FDA-approved drugs, though efficacy data for the patient's specific indication may be limited. For example, alterations may occur outside the sequenced region or involve complex alterations (e.g. indels, copy number alterations, or rearrangements) that are not detectable by certain tests.[22]

Within the InVision clinical validation studies, only 33% of the prospectively recruited NSCLC patients had sufficient tissue for complete CGP. The remaining 67% either had no tissue for genomic analysis (31%) or had only enough tissue for some but not all markers required (36%). This data underscores the marked limitation of available tissue specimens for tissue CGP testing and emphasizes the importance of plasma-based CGP testing.

Even when successful, tissue acquisition procedures pose a significant morbidity and mortality risk to Medicare patients. In a recent report, 19% of all lung tissue acquisition procedures resulted in a serious adverse event.[23] The National Lung Cancer Screening Trial reported 1-2% mortality rates in their cohorts.[24]

Given that the majority of lung cancer diagnoses are based on needle biopsy, and that only 30%-60% of tissue specimens provide full informative results by CGP, plasma-based CGP (ctDNA testing) identifies genetic alternations for use of targeted therapies without delay in therapy,[25] and without the risks and costs of repeat invasive biopsy.[23,26] InVision detects genomic targets linked to targeted drug therapies used at diagnosis and/or progression with response rates similar to those patients identified using tissue-based CGP and tissue-based CDx.

InVision Test Description and Performance

InVision is a plasma-based circulating tumor DNA (ctDNA) NGS assay for detection of genomic alterations consisting of 36 commonly mutated genes. It utilizes technology first developed by the Cancer Research UK (CRUK)-funded Cambridge Institute at the University of Cambridge.[27-29] The group was first to publish industry standard ctDNA methods, including hybrid capture and the highly sensitive tagged amplicon, deep sequencing or TAm-Seq™ technology. The InVision assay utilizes an enhanced version of the TAm-Seq method developed by Inivata to detect clinically relevant cancer mutations of low allele fractions in cell free DNA (cfDNA) including substantial improvements and optimizations to maximize sensitivity and specificity of the assay.[28]

Approximately 76% of patients with NSCLC are known to have a genomic alteration in tumor tissue for 1 of 8 genes

(EGFR, ALK, ROS1, BRAF, MET, ERBB2, KRAS, STK11).[30] These alterations constitute actionable driver alterations (EGFR, ALK, ROS1, BRAF, MET, ERBB2 - rule-ins) associated with FDA approved therapies or are recognized as mutually exclusive for actionable changes (STK 11 and KRAS-rule-outs). These alterations have not been described as significant mutations contributing to clonal hematopoiesis of indeterminate potential.[31]

Analytical Validation

The analytical validation of the InVision assay was conducted according to the deliverables outlined in the MolDx document M00135 v2.0. Using contrived samples and tested with multiple users, multiple reagent lots and across multiple days, the sensitivity, specificity, reproducibility and level of detection (LoD) is summarized for all four variant types in the test system: SNV, Structural Variants (SV), Indel, and CNV. Using patient samples, orthogonal comparison to digital PCR/fluorescent in-situ hybridization (dPCR/FISH) techniques was generated for SNVs, Indels and SVs. Interference of somatic mutation detection was investigated with both spiked EDTA or Streck BCT plasma with fragmented cell line DNA and detection was shown to be comparable.

In the analysis of the contrived sample sets (Table 1), the PPA is 96.6% for SVs, 100% for SNVs, 97.4% for Indels and 100% for CNVs. The PPV is 100% for SVs, 99.8% for SNVs, 100% for Indels and 98.3% for CNVs. Specificity was shown to be acceptable for all variants. One CNV false positive was seen. No false positives were seen with Indels or SVs. In normal donor analysis, one SNV is considered to be a false positive. Specific variants described in M00135 were further analyzed for specificity and were shown to be of high specificity (>99% NPA). Reproducibility for all variants as analyzed at the LoD region was shown to be acceptable within reagent lots, within operators, and overall.

Table 1. Analytical Performance for the InVisionFirst assay

Platform	Actionable Alterations	Sensitivity		Specificity	
		Alteration	**Result**	**Alteration**	**Result**
InvisionFirst™ amplicon-based 36 gene panel	EFGR ALK ROS1 BRAF ERRBB2 MET KRAS STK11	SNVs	100% @ >0.25AF	SNVs	99.9 @ >0.25%AF
		Indels	97.4% @ >0.25AF	Indels	100% @ >0.25%AF
		Fusions	96.6% @ >0.5%	Fusions	100% @ >0.5%
		CNVs	98.3% @ 1.5x CNAR	CNVs	99.8 @ 1.5x CNAR

Sensitivity for both the detection of contrived samples and patient samples is shown in Table 2. The goals for meeting the lower 95% CI for the M00135 guidance was met at both the LoD region and at the region >3x or 2x LoD. Specific variants described in M00135 were further analyzed for sensitivity and were shown to be of high sensitivity (>97% PPA) in all variants (Table 3). Orthogonal testing,[32] Table 4, showed very good agreement with dPCR with the region of greatest disagreement between the two technologies occurring at the LoD90-3xLoD90 region. Above the 3xLoD90 region the agreement between dPCR and NGS was 100%. 8/9 ALK or ROS1 fusions were detected where the tissue was shown to be FISH positive for the fusions.[32]

Table 2- Performance Characteristics - All Variants Tested Contrived Samples

Variant Type	Detail	Unique Samples	Unique Variants	No Calls	Unique Variants by ctDNA	Concordant Unique Variants	Variant-level PPA (95% CI)	Variant-level TPPV (95% CI)	Variant-level Reproducibility (95% CI)
SNVs	VAF=>0.75%	41	519	0	519	519	**100% (CI:0.9963 to 1,000)**	**99.8% (CI: 0.9911 to 0.9998)**	N/A
SNVs	Expected VAF - 0.25%-0.75% VAF	4	76	0	76	76	**100% (CI: 0.9751 to 1,000)**	**98.7% (CI: 0.9409 to 0.9986)**	98.8% (0.9706-0.9958)
Indels	≤ 20 bp >0.75% VAF	29	74	2	72	72	**97.3% (CI: 0.9161 to 0.9943)**	**100.0% (CI: 0.9738 to 1.000)**	N/A
Indels	≤20 bp Expected VAF = 0.25%-0.75%	6	41	1	40	40	**97.6% (CI: 0.8916 to 0.9974)**	**100.0% (CI: 0.9575 to 1.000)**	85.6% (0.7987-0.9011)
CNAs	>2x CNA	28	28	0	28	28	**100.0% (CI: 0.9484 to 0.9999)**	**97.3% (CI: 0.8806 to 0.9971)**	N/A
CNAs	Expected CN AR = 1.5x - 2x CN AR	21	24	0	23	23	**95.8% (CI: 0.8213 to 0.9995)**	**95.8% (CI: 0.8213 to 0.9995)**	93.8% (0.8143 - 0.9868)
SVs	VAF>1.5%	19	38	0	38	38	**100.0% (CI: 0.9510 to 1.000)**	**100.0% (CI: 0.9510 to 1.000)**	N/A
SVs	Expected VAF = 0.5%-1.5% VAF	25	50	3	47	47	**94.0% (CI: 08485)**	**100.0% (CI: 0.9705)**	90.0% (0.7946-0.9608)

Table 3- Performance Characteristics – Specific Variants Tested Contrived Samples

Variant Type	Unique Samples	Samples with Specified Variant Expected	No Calls	Samples with Specified Variant Detected by ctDNA	Concordant "Positive" Samples	Concordant "Negative" Samples	Sample-level PPA (95% CI)[2]	Sample-level NPA (95% CI)[2]
AKL (SVs)	54	54	2	52	52	95	98.1% (0.8865 - 0.9922)	100% (0.9800 - 1.000)
BRAF (V600E and V600K)	43	43	0	43	43	109	100% (0.9566 - 1.000)	100% (0.9826 - 1.000)
EGFR (G719A, G719C, G719S, S768I, T791M, L858R, L861Q)	43	43	0	83	83	436	100% (0.9772 - 1.000)	100% (0.9956 - 1.000)
EGFR (ex on 19 deletions and exon 20 insertions)	43	30	1	40	40	217	97.6% (0.8916 - 0.9974)	99.5% (0.9788 - 0.9995)
ERBB2 (CNAs)	14	14	0	14	14	109	100% (0.8739 - 1.000)	100% (0.9826 - 1.000)
ERBB2 (exon 20 insertions)	47	5	0	5	5	109	100 (0.6943 - 1.000)	100% (0.9826 - 1.000)
KIT (exon 9, 11, 13, 17, and 18 SNVs)	43	17	0	17	17	109	100% (0.8747 - 1.000)	100% (0.9826 - 1.000)
KRAS (codon 12, 13, 61, and 146 SNVs)	43	43	0	158	158	436	100% (0.9879 - 1.000)	100% (0.9956 - 1.000)
MET (CNAs and exon 14 skipping mutation)	43	18	0	18	18	109	100% (0.9001 - 1.000)	100% (0.9826 - 1.000)

Table 4- Performance Characteristics - Orthogonal Testing[1] (dPCR SNV/Indel; FISH SV), All Variants Tested[1]

Variant Type	Detail	Unique Samples	Unique Variants Expected by non-NGS method	No Calls	Unique Variants by ctDNA	Concordant Unique Variants	Variant - level PPA (95% CI)	Variant level APPV (95% CI)
SNVs	VAF=>0.75%	97	43	0	43	43	100%	100%

							(CI: 0.9566 to 1.000	(CI: 0.9566 to 1.000)
SNVs	Expected VAF = 0.25% - 0.75% VAF	77	15	0	17	12	80% (CI: 0.5564 to 0.9402)	70.6% (CI: 0.4702 to 0.8778)
Indels	≤ 20bp >0.75% VAF	56	31	0	31	31	100% (CI: 0.9404 to 0.9999)	100.0% (CI:0.9404 to 0.9999)
Indels	≤ 20 bp Expected VAF = 0.25% - 0.75%	32	7	0	6	6	85.7% (CI: 0.4992 to 0.9841)	100.0% (CI: 0.7358 to 0.9997)
SVs[2]	Any Detection	9	9	0	8	8	88.9% CI: 0.5855 to 0.9877	100.0% CI: 0.7925 to 0.9998

[1] CNA not tested with orthogonal method

[2] Neither non-NGS method or NGS method returns quantitative values.

Clinical Validation

The InVision test was investigated prospectively in advanced untreated patients with non-squamous NSCLC blood samples.[33] Clinical validation data consists of combined analysis of three studies. Two prospective multicenter studies (NCT02906852 and NCT03116633) demonstrated the concordance of the InVision assay with tissue-based CGP in 254 patients with untreated advanced (stage IIIB/IV) non-squamous NSCLC. A third study consisted of a small group of banked matched tissue and plasma samples (n=10) from an equivalent patient population that were procured from a commercial bio-repository and used to supplement the prospective collections. Across the 264 patients, only 165 patients (62.5%) had tissue available for testing for any point mutations/ indels. For 159 patients (60.2%), tissue was tested for ROS1 and/or ALK fusions. 119 patients (45% of patients) underwent CGP.

The performance of InVision is highlighted by the following factors:

- High Sensitivity: for each of the key 8 genes used for therapeutic treatment decision with an overall plasma sensitivity of 73.9% (73.9% of tissue results are identified in plasma);
- High Proportion of Informative Results: based on the utilization of 8 specific genes (present in tumors independently of each other occurring in 53% of NSCLC) each with individual high gene sensitivity;
- High Specificity: for each of the 8 panel genes that supports correct therapeutic determination (CTD) in the 53% of patients with informative results.

Based on literature evidence of the prevalence of the genetic alterations in the 8 genes of most interest (76%) and an assumed 70% clinical sensitivity for ctDNA testing, the authors predicted an informative result in 50% of patients

with untreated advanced NSCLC (0.76x0.7). Clinical CTD performance based on InVision profiling results yielded actionable genes in 18.2% of patients and rule out findings in 35.6%, an informative result in 53.8% of patients (95%; CI 41%-56.2%) (Table 5). Of the plasma positive gene results, when either a molecular change in the 6 actionable driver genes (rule-in) or, a non-targetable gene (rule-out) was detected, the correct therapeutic determination (CTD) was 100%. This clinical validity is consistent across the entire intended use population (n=264), both those with and without tissue for profiling.

Table 5: InVision - ctDNA Clinical Validity

Class	Alterations	Total Enrolled (n=264)	Plasma (%)	Total Enrolled (n=264)	Tissue (%)
		Plasma		Tissue	
Rule-In		48	18.18	38	14.39
	EGFR exons 18-21	26	9.85	18	6.82
	ALK-ROS1 fusions	5	1.89	5	1.89
	ERBB2 exon 20 insertions	4	1.52	2	0.76
	BRAF V600E	6	2.27	7	2.65
	MET exon 14 splice	7	2.65	6	2.27
Rule-Out	KRAS/STK11	94	35.61	70	26.52

Performance characteristics for clinically actionable alterations in 8 genes that effect clinical patient management were: PPV-97.8%, NPV-97.1%, sensitivity-73.9% and specificity-99.8% (Table 6).

Table 6: Concordance of Combined and Individual Actionable Driver Genomic Alterations

	Tissue and liquid	Tissue only	Liquid only	No call	PPV	NPV	Sensitivity	Specificity
ALK/ROS1 fusions	2	3	0	292	100.0	99.0	40.0	100.0
BRAF V600E	5	2	0	140	100.0	98.6	71.4	100.0
EGFR (exons 18.21)	13	5	0	146	100.0	96.7	72.2	100.0
ERBB2 exon 20 ins	2	0	0	137	100.0	100.0	100.0	100.0
KRAS	48	12	1	86	98.0	87.8	80.0	98.9
MET exon 14 splice	3	3	0	133	100.0	97.8	50.0	100.0
STK11	15	6	1	93	93.8	93.9	71.4	98.9
Key 8 genes*	88	31	2	1027	97.8	97.1	73.9	99.8
All Genes	156	65	32	4135	83.0	98.5	70.6	99.2

*"Key 8 genes" refers to the combination of all directly actionable mutations (ALK/ROS1 fusions, BRAF V600E, EGFR exons 18-21, ERBB2 insertions, MET exon 14 splice) and KRAS and STK11 variants.

Clinical Utility

Clinical utility has been demonstrated with prospective outcome collection from within the clinical validation study and within additional studies at the Institute Gustave Roussy (Paris, France) and Centre Leon Berard (Lyon, France), and in 3 groups of patients; namely,

1. Patients not exposed to any prior therapy and receiving targeted therapy directed by the assay
2. Patients with no prior targeted therapy but other therapy and targeted directed by the assay, and
3. Patients with prior anti-EGFR targeted therapy and now progressing with the specific osimertinib sensitive mutation T790M detected by the assay.

As detailed recently by the FDA, time on treatment was used as the endpoint for clinical impact of targeted therapy.[34] When targeted therapies are used in patients without a specific target, average time on treatment is well under 2 months.[35] With current directed targeted treatment in NSCLC, it is unusual to come off therapy before 3 months.[29] Regardless of which group mentioned above was assessed, disease control at 3 months was approximately 80% or more, which is equivalent to the best outcomes of any target agent reported. This is strong evidence that therapeutic determination based on InVision results is equivalent to outcomes reported in clinical trials, and most importantly unlikely to be causing patient harm (Table 7).

Implied clinical utility of Inivata's prospective clinical validation study (NCT02906852) and three unpublished internal studies identified actionable alterations in patients who received FDA approved drugs and tracked clinical outcomes (Table 7).

Table 7: Actionable Genomic Alterations Detected by InVision:

Patients Treated with Appropriate Targeted Therapy and Remaining on Therapy at 3 Months

Prior therapy for advanced disease	Genomic alteration	n	Number still on targeted therapy at 3 months	% still on targeted therapy at 3 months
Untreated for advanced disease	All	9	7/9	78%
	EGFR mutation	6	5/6	83%
	BRAF V600 mutation	2	1/2	50%
	ALK/ROS1 fusion	1	1/1	100%
Prior cytotoxic chemotherapy for advanced disease but no targeted therapy	All	21	17/19	89%
	EGFR mutation	9	8/9	89%
	BRAF V600 mutation	3	1/2	50%

	ALK/ROS1 fusion	9	7/7	100%
	All	62	48/58	82.7%
Prior therapy with targeted therapy	EGFR mutation (49 with T790)	52	42/49	85.7%
	ALK/ROS1 fusion	7	6/6	100%
Overall		93	72/86	83.7%

Professional Society Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN) clinical practice guidelines (v4.2018) for non-small cell adenocarcinoma recommend a broad molecular profile panel. NCCN recommends molecular testing in never-smokers regardless of histology or mixed histology, and in small biopsies with the goal of identifying rare driver mutations for which effective drugs may be available. Tissue profiling is recommended to include EGFR and ERBB2 point mutations and indels; BRAF mutations; ALK, ROS1, and RET rearrangements; and MET amplification and deletion/skipping of exon. The guidelines indicate that if tissue biopsy is not feasible, plasma biopsy should be considered. If plasma biopsy is negative, then repeat tissue biopsy is recommended, if feasible.[36]

Analysis of Evidence
(Rationale for Determination)

Level of Evidence:

Quality – Moderate
Strength –Limited
Weight – Limited

The InVision assay provides a minimally invasive methodology to detect actionable mutations with an informative test rate of 50-70% for providing valuable guidance for patient genomic profile stratification. Clinical utility has been demonstrated equivalent to tissue-based profiling outcomes. Patients are limited to one test assay per primary diagnosis.

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:

CODE	DESCRIPTION
81479	UNLISTED MOLECULAR PATHOLOGY PROCEDURE

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:

N/A

Group 1 Codes:

ICD-10 CODE	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

ICD-10 CODE	DESCRIPTION
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
C38.1	Malignant neoplasm of anterior mediastinum
C38.2	Malignant neoplasm of posterior mediastinum
C38.4	Malignant neoplasm of pleura
C38.8	Malignant neoplasm of overlapping sites of heart, mediastinum and pleura

ICD-10 Codes that DO NOT Support Medical Necessity

N/A

Additional ICD-10 Information

N/A

General Information

Associated Information

N/A

Sources of Information

N/A

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Revision History Information

N/A

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)
A56410 - Response to Comments: MolDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer
LCD(s)
DL37899 - MolDX: Inivata, InVisionFirst, Liquid Biopsy for Patients with Lung Cancer

Related National Coverage Documents

N/A

Public Version(s)

Updated on 04/11/2019 with effective dates 06/03/2019 - N/A

Keywords

- Inivata
- InVisionFirst
- Liquid Biopsy
- Lung cancer
- EGFR
- single nucleotide variants
- SNVs
- 81479