

Local Coverage Determination (LCD): MoIDX: Xpresys Lung (L37054)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Noridian Healthcare Solutions, LLC	A and B MAC	01111 - MAC A	J - E	California - Entire State
Noridian Healthcare Solutions, LLC	A and B MAC	01112 - MAC B	J - E	California - Northern
Noridian Healthcare Solutions, LLC	A and B MAC	01182 - MAC B	J - E	California - Southern American Samoa
Noridian Healthcare Solutions, LLC	A and B MAC	01211 - MAC A	J - E	Guam Hawaii Northern Mariana Islands American Samoa
Noridian Healthcare Solutions, LLC	A and B MAC	01212 - MAC B	J - E	Guam Hawaii Northern Mariana Islands
Noridian Healthcare Solutions, LLC	A and B MAC	01311 - MAC A	J - E	Nevada
Noridian Healthcare Solutions, LLC	A and B MAC	01312 - MAC B	J - E	Nevada American Samoa California - Entire State
Noridian Healthcare Solutions, LLC	A and B MAC	01911 - MAC A	J - E	Guam Hawaii Nevada Northern Mariana Islands

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LCD Information

Document Information

LCD ID L37054	Original Effective Date For services performed on or after 09/29/2017
LCD Title MoIDX: Xpresys Lung	Revision Effective Date N/A
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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.

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

42 Code of Federal Regulations (CFR) 410.32(a). 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, Chapter 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 Medicare contractor will provide limited coverage for the Xpresys Lung version 2 (XL2) test for the management of a lung nodule, between 8 and 30mm in diameter, in patients 40 years or older and with a pre-test cancer risk (as assessed by the Mayo Clinic Model for Solitary Pulmonary Nodules) of 50% or less. The intended use of the test is to assist physicians in the management of lung nodules by identifying those lung nodules with a high probability of being benign. These lung nodules would then be candidates for non-invasive computed tomography (CT) surveillance instead of invasive procedures.

Summary of Evidence

Lung nodules are rounded densities, under 30mm in diameter, detected by chest radiograph (CXR) or computer tomography (CT) scan. Nodules are mostly surrounded by lung tissue and are also called coin lesions, solitary pulmonary nodules or lesions, or a "spot" on the lung. The edges of a nodule can be described as smooth or irregular (stellate or spiculated) with irregular edges somewhat more indicative for cancer. Heavily calcified nodules with smooth edges are generally benign and solid nodules that have not shown growth over time are considered benign. For a comprehensive review of nodules and their evaluation see the 2-part series by Patel, et al.^{1, 2}

Lung nodules are detected incidentally or through lung cancer screening. Lung cancer screening now has Medicare coverage in the United States. As of April 26, 2016, there were 806 sites registered for screening (<http://www.acr.org/quality-safety/national-radiology-data-registry/lung-cancer-screening-registry> – see Core Documents, accessed June 20, 2016). The estimated number of new lung nodules incidentally detected annually in the US is 1.57 million whereas it is anticipated that another 1.5 million are detected by screening annually in the US.³

Early detection of lung nodules is an opportunity to reduce lung cancer mortality but it comes with significant risks. These risks are both for patients and health care delivery networks. For patients, a major problem is the risk of unnecessary invasive procedures to find the minority of nodules that are cancer. For health care delivery, the risks are both costs and overloading the health care system.

Of the expected 3 million nodules per year found incidentally or by lung cancer screening, the majority will be Medicare age. Four recent studies underscore the importance of lung cancer evaluations to the Medicare population:

- The mean age of 377 eligible patients in an 18 site retrospective chart review study was 65.4
- A prospective study across 12 sites and 475 patients found 62.5% of patients were 65 years of age or older.⁵
- A recent study reported that between Jan 2009 and Dec 2011, 8,979 Medicare patients from a random sampling of 5% of Medicare claims, underwent lung cancer evaluations because of an abnormal chest CT scan.⁶
- In the National Lung Screening Trial (NLST), over 57% of enrollees were over 65 years of age.⁷ Also the rates of nodule detection increased dramatically with age.³ Medicare enrollees are more likely to meet lung cancer screening criteria and have more nodules detected.

A set of guidelines for lung nodule management is published and updated by the American College of Chest Physicians (ACCP). The ACCP guidelines for lung nodules, updated in 2013, is the primary reference used by pulmonologists in the United States.⁸ The ACCP Guidelines state: "Although clinical and radiographic [CT scans] characteristics cannot reliably distinguish between benign and malignant nodules in most individuals, it is nevertheless important to estimate the clinical probability of malignancy before ordering imaging tests or biopsy procedures". The pretest probability of malignancy (pCA) is estimated by using clinical judgment or with a quantitative risk model.^{9, 10} Establishing a pCA creates three risk stratification groups, namely, Low, Intermediate, and High probability, with Low risk having pCA below 5% and High risk having pCA above 65%. The general concept is that Low risk patients will be observed with CT surveillance to watch for growth if a nodule is malignant. Conversely, the guidelines suggest those patients in the High risk group go directly to surgery. The logic is that the probability of cancer is high enough that a negative biopsy will not change the care pathway. The Intermediate risk group (5-65% pCA) are recommended to enter the diagnostic odyssey that often includes PET scanning as the next step. A negative PET suggests a benign nodule, so the patient is followed with CT scans. A positive PET scan goes on to surgery or biopsy. This is the overall concept, but PET has sensitivity and specificity challenges. In particular, current estimates of PET sensitivity from 72% to 94% and is reviewed in the 2013 ACCP Guidelines in section 4.2.3.8 False positive PET scans for nodules are an additional problem with estimates of the false positive PET scan rate of 39%.⁴

A pulmonary community practice observational chart review of 18 practices and 377 patients found a wide variation in management of nodules.⁴ The surgery rate for benign nodules was 35% and the rate of surgery was the same for Low, Intermediate and High risk patients. The risk categories were calculated by the study and despite a Low risk, 28% had biopsies and 17% had surgery. The rates of surgery for benign nodules range between 10% and 55%. A survey of 196 pulmonologists supports the potential of a non-invasive biomarker to positively improve lung nodule management decisions.¹¹

Biopsies can be obtained through a bronchoscope or a needle passed through the chest wall with CT image guidance. A community practice chart review found 38% of patients had a form of biopsy.⁴ Complications with biopsies or surgery are increased with age, smoking history, and other lung disease. Biopsy through the

bronchoscope has the lowest risk with a 2-4% risk of bleeding or pneumothorax.⁸ A disadvantage of this procedure is inaccurate sampling of the nodule. Correct sampling averages about 50%.⁸ The correct sampling rate may improve with modern navigation techniques that are being adopted. Bronchoscopic biopsy use for nodules is currently about 20% of nodules.⁶ Needle biopsies are done in about 15% of patients with nodules with a 1% risk of bleeding, and a 15-19% risk of pneumothorax.¹² About half (7%) of patients with a pneumothorax require chest tube placement with a significant period of hospitalization.¹² Most needles biopsies are diagnostic but the risk of a non-diagnostic result with a malignant nodule is about 20%.⁸ Biopsies (combined bronchoscopy and needle) are performed in about 25% of nodules (200,000) and the procedures are for benign nodules in 42-62% (104,000). Complications from biopsies result in hospitalization in 2-7% of cases.^{6, 12} That translates into 4,680 excess hospitalizations per year that are potentially avoidable.

Eventually, most malignant nodules go to surgery for resection and about 15-25% of patients have biopsy attempts before surgery. The overall surgery rate is about 34% (270,000 per year) for benign and malignant nodules in the nodule population.⁴ Complications include death (2% in Medicare population),¹³ prolonged lung air leak (3-5%), and pneumonia (1-8%).⁸ Published rates for surgery for benign nodules range from 31-44%.^{4, 7, 17} This translates into an estimated 102,000 surgeries and 2,052 deaths per year that are avoidable for patients that do not have lung cancer.

Test Description and Intended Use

XL2 is a proteomic risk predictor that integrates the expression levels of two proteins with five clinical risk factors. The XL2 assay is performed on fresh-frozen EDTA plasma samples using mass spectrometry.^{15, 16} Results are reported as "Likely Benign" when the post-test probability that a lung nodule is benign is 90% or higher. Otherwise, the test reports "Indeterminate" when the post-test probability is less than 90%. "Likely Benign" test reports also include the post-test probability that the lung nodule is benign, ranging from 90% to 98%. This is further detailed in Table 1 below along with the performance of the test at each post-test probability.

The intended use of the test is to assist physicians in the management of lung nodules by identifying those lung nodules with a high post-test probability of being benign. These lung nodules would then be candidates for non-invasive computed tomography (CT) surveillance instead of invasive diagnostic procedures such as biopsy or surgery.

Clinical Validation

The discovery, clinical validation and analytical performance of earlier versions of Xpresys Lung were previously reported.¹⁵⁻¹⁷ The current version of Xpresys Lung (XL2) is a refinement that incorporates clinical risk factors (nodule size, age, smoking history, nodule location and nodule spiculation). XL2 was retrospectively validated on the prospective observational PANOPTIC study (NCT01752114) of lung nodule management. PANOPTIC enrolled 685 subjects across 33 sites in the US and Canada. Validation of XL2 followed the National Academy of Medicine's guidelines for rigorous test development.¹⁸

In the PANOPTIC study, 178 subjects met the intended use population of XL2. This consisted of 149 benign lung nodules (as determined by histopathology after biopsy or surgery, or by stable CT surveillance of a lung nodule after at least 1 year) and 29 malignant lung nodules (as determined by histopathology after biopsy or surgery), yielding a cancer prevalence of 16.3%. Per protocol, this cohort of patients was split into separate verification (n = 69) and validation (n = 109) subsets, with pre-specified interim and final analyses on each subset, respectively, to determine the performance characteristics of the test. Since the test system and clinical endpoints were unchanged between the interim and final analyses, all analyses were blinded, and the 2 patient cohorts were mutually exclusive, the 69 and 109 patients are combined below.

For these 178 subjects, XL2 yielded a sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of 97% (CI: 82%-100%), 44% (CI: 36%-52%), 98% (CI: 92%-100%), and 25% (CI: 17%-34%), respectively. We note that the post-test probability of XL2 is equivalent to its NPV.

Procedure use and clinical factors were collected in the PANOPTIC study permitting the comparison of XL2 performance to:

- current practice, as characterized by physician pre-test risk assessment, denoted as pCA, which is based on the physician's clinical assessment of risk using a clinical risk model and/or clinical judgement,
- PET, and
- clinical risk factor models including the 'Mayo', 'VA', 'Brock' and 'Herder' models (9, 10, 19, 20).

Using AUC as a general performance measure, the respective AUCs for XL2, pCA, PET, and these four clinical factor models were: 76% (CI: 69%-82%), 69% (CI: 62% - 76%), 58% (CI: 46%-69%), 69% (CI: 62%-76%), 60% (CI: 53%-67%), 71% (CI: 63%-77%), and 67% (CI: 56%-78%). XL2 had statistically significant improved

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performance over all above diagnostic modalities with p-values 2.1xE-11 (pCA), 0.001 (PET), 0.0009 (Mayo), 2.7xE-7 (VA), 0.005 (Brock) and 0.02 (Herder).

Clinical Utility

Current practice has been previously characterized^{4,11} as well as the potential clinical utility of an earlier version of Xpresys Lung.⁵ The clinical utility of XL2 is measured in terms of its potential to reduce unnecessary invasive procedures, such as biopsies and surgeries, on benign lung nodules while not significantly increasing the number of malignant lung nodules routed to CT surveillance thereby delaying surgical resection. Assuming strict adherence to management recommendations based on assay results (i.e., active surveillance if “likely benign”), an earlier version of Xpresys Lung demonstrated a potential 32% reduction in invasive procedures on benign lung nodules without increasing the number of malignant nodules routed to CT surveillance⁵ based on a retrospective analysis of a prospective observational study of lung nodule management (NCT01752101). Similarly, in the PANOPTIC study, the potential clinical utility of the current version of Xpresys Lung (XL2) was assessed retrospectively. Specifically, if XL2 were used to guide lung management (and assuming a post-test probability of 98%), then invasive procedures on benign lung nodules would have been reduced 36% (CI: 22%-52%) with only 3% (CI: 0%-18%) of malignant nodules routed to CT surveillance (compared to 45% with current practice in the PANOPTIC study).

Summary of Analytical and Clinical Performance

General

Intended Use	XL2 is intended for the evaluation of 8-30 mm lung nodules in patients 40 years or older with a pre-test cancer risk (as assessed by the Mayo Clinic Model for Solitary Pulmonary Nodules) of 50% or less.
Validated Specimen Type(s)	Plasma from K2 EDTA vacutainer tubes

Analytical Performance

Description	Results (with 95% Confidence Intervals if applicable)
Repeatability (within run precision) 8 samples tested three times within a run, 1 instrument, 2 operators, 3 runs, 3 non-consecutive days, 1 manufacturing reagent lot for critical reagents. Qualitative results represent only 2 possible final results (i.e., indeterminate and likely benign) with post-test probabilities for the latter from 90 to 98%.	<p>Analytes (analytical repeatability): ARR_{LG3BP} CV = 7.0% (3.6%-10.3%) ARR_{C163A} CV = 5.9% (3.6%-8.2%)</p> <p>Score (analytical repeatability): Score CV = 9.0% (3.4%-14.6%)</p> <p>Qualitative (clinical concordance): 62.5% (5/8; 24.5%-91.5%)</p> <p>ARR is defined as the ratio between the peak area for the endogenous quantifier peak and the peak area of the corresponding SIS peptide, multiplied by a calibration factor that is specific for each SIS lot.</p> <p>Score is defined as $\text{Log}_2[\text{ARR}_{LG3BP} / \text{ARR}_{C163A}]$</p>
Intermediate precision (between run precision)	<p>Analytes (analytical repeatability): ARR_{LG3BP} CV = 14.5% (10.1%-18.9%) ARR_{C163A} CV = 12.8% (9.1%-16.6%)</p> <p>Score (analytical repeatability):</p>

7 samples tested once in three different runs, 1 instrument, 2 operators, 3 runs, 3 non-consecutive days, 1 manufacturing reagent lot for critical reagents. Qualitative results represent only 2 possible final results (i.e., indeterminate and likely benign) with post-test probabilities for the latter from 90 to 98%.	Score CV = 6.0% (3.7%-8.4%)
Reproducibility (between sites)	Qualitative (clinical concordance): 85.7% (6/7; 42.1%-99.6%)
Minimum input quantity	Not applicable
Limit of blank (LOB)	20 µL plasma
Limit of detection (LOD)	Defined as the upper 99.5% confidence interval (CI) for the response ratio (ARR) observed in negative controls. The lower limit of response for each analyte in samples and positive controls is defined as the lower limit of quantification. The lower limit of quantification (LLOQ) is defined as the lowest response ratio within the linear range where the coefficient of variation (CV) was equal to or below 0.20, where linearity was established using five replicate measures at each concentration.
Limits of quantitation (LOQ)	The upper limit of quantification (ULOQ) is defined as the highest response ratio within the linear range where the coefficient of variation (CV) was equal to or below 0.20, where linearity was established using five replicate measures at each concentration. LG3BP: ULOQ = 42 LLOQ = 0.043 C163A: ULOQ = 71 LLOQ = 0.053
Linearity	Not applicable for qualitative interpretation (i.e., likely benign or indeterminate) For individual analytes, the linear response range was established between the LLOQ and ULOQ Visual inspection to detect hemolysis (&ge 100 mg/dL of hemoglobin rejected).
Interfering substances	MRM-MS chromatograms for each analyte in every sample are inspected for interference, with any interference resulting in QC failure.
Specimen stability, primary (EDTA whole blood)	3 hours at 2-8 °C based on validation study (manuscript in preparation) 24 months at -70 °C based on validation study (manuscript in preparation)
Specimen stability, intermediate (plasma)	2 freeze-thaw cycles when stored at -70 °C based on validation study (manuscript in preparation) 24 months at -70 °C for 2 critical reagents (i.e., Human Plasma Samples (HPS) and SIS peptides). ARR for 623 samples evaluated with slope not significantly different from zero (p = 0.77).
Reagent closed/shelf-life stability	Non-critical (general purpose) reagents are stored and expired per manufacturer recommendations. Critical reagents: Not applicable since single use aliquots
Reagent open/in use stability	Non-critical reagents are stored and expired per manufacturer recommendations.

Clinical Performance: Validity

XL2 integrates the relative abundance of two plasma proteins (LG3BP and C163A) with five clinical risk factors (age, smoking status, nodule diameter, nodule spiculation status and nodule location). From these seven markers, a numerical value, XL₂(k), for a patient k, is calculated.

XL₂(k) ranges between 0 and 1 and its value is used to index the post-test probability (i.e., NPV) validated in the PANOPTIC study (see Table 1 below).

XL ₂ (k) Value	Post-Test Benign Probability (i.e. NPV) (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	Test Report
0 to 0.131	98% (92% - 100%)	97% (82% - 100%)	44% (36% - 52%)	25% (17% - 34%)	Likely Benign
>0.131 to 0.1613	97% (91% - 100%)	93% (77% - 99%)	49% (41% - 57%)	26% (18% - 36%)	Likely Benign
0.1613 to 0.172	96% (90% - 99%)	90% (73% - 98%)	54% (45% - 62%)	27% (19% - 37%)	Likely Benign
>0.172 to 0.176	95% (89% - 99%)	86% (68% - 96%)	55% (47% - 63%)	27% (18% - 37%)	Likely Benign
>0.176 to 0.1785	94% (87% - 98%)	83% (64% - 94%)	56% (47% - 64%)	27% (18% - 37%)	Likely Benign
>0.1785 to 0.193	93% (86% - 98%)	79% (60% - 92%)	57% (44% - 65%)	26% (18% - 37%)	Likely Benign
>0.193 to 0.195	92% (85% - 96%)	76% (56% - 90%)	58% (49% - 66%)	26% (17% - 37%)	Likely Benign
>0.195 to 0.2306	91% (84% - 96%)	69% (49% - 85%)	64% (56% - 72%)	27% (18% - 39%)	Likely Benign
>0.2306 to 0.354	90% (84% - 95%)	55% (36% - 74%)	83% (75% - 88%)	38% (24% - 54%)	Likely Benign
>0.354	-	-	-	-	Indeterminate

Clinical Performance: Utility

PANOPTIC was a non-interventional study; however, the potential clinical utility of XL2 can be estimated by evaluating how many benign (benefit) and malignant (harm) nodules would have been routed away from invasive procedures into CT surveillance if XL2 had been used to guide patient management in the study (and assuming complete compliance). Table 2 summarizes the potential clinical utility of XL2 at each post-test probability.

Probability of Being Benign	of Benign Nodules (95% CI)	CT Surveillance (95% CI)
98%	15/42 = 36% (22% - 52%)	1/29 = 3% (0% -18%)
97%	17/42 = 40% (26% - 57%)	2/29 = 7% (1% -23%)
96%	19/42 = 45% (30% - 61%)	2/29 = 7% (1% -23%)
95%	20/42 = 48% (32% - 64%)	2/29 = 7% (1% -23%)
94%	20/42 = 48% (32% - 64%)	2/29 = 7% (1% -23%)
93%	22/42 = 52%	3/29 = 10%

	(36% - 68%)	(2% -27%)
92%	22/42 = 52% (36% - 68%)	4/29 = 14% (4% -32%)
91%	25/42 = 60% (43% - 74%)	4/29 = 14% (4% -32%)
90%	32/42 = 76% (61% - 88%)	7/29 = 24% (10% -44%)

Table 2: Potential Clinical Utility of XL2v

In the PANOPTIC study, there were 178 intended use subjects (when the verification and validation sets are combined) of whom 29 had malignant lung nodules and 149 had benign lung nodules. Of the 149 benign lung nodules, 42 had at least one invasive procedure. Hence the denominator of "42" in column 2 of Table 2. Of the 29 malignant lung nodules, 13 were routed to CT surveillance. That is, 13/29 = 45% of malignant nodules were routed to CT surveillance in PANOPTIC. This is substantially larger than the largest corresponding value in Table 2 (i.e. 24%).

Coverage Summary

The XL2 assay is reasonable and necessary to assist physicians in the management of lung nodules by identifying those lung nodules with a high probability of being benign. This assay is only covered when the following conditions are met:

- Patient is at least 40 years of age and has a lung nodule of diameter 8 to 30mm, and
- The pre-test risk of cancer as determined by the Mayo risk prediction algorithm (10) is 50% or less, and
- The test is ordered by a physician certified in the XL2 Certification and Training Registry (CTR), and
- The following information is recorded: all clinical risk factors to calculate the Mayo, VA, and Brock cancer risk predictors; PET result (if used), physician pre-test risk assessment, physician post-test lung nodule management recommendation, any subsequent procedures (non-invasive or invasive), and clinical diagnosis based on those procedures (i.e., benign or malignant)

Note: The XL2 test should not be ordered if a physician does not intend to act upon the test result. It is expected that physicians will advise nodule surveillance for at least 80% of patients with a post-test probability of 98% or higher.

Analysis of Evidence (Rationale for Determination)

Level of evidence

Quality – Moderate

Strength – Limited

Weight - Limited

This contractor recognizes that evidence of clinical utility for the Xpresys Lung, version 2 (XL2) assay for ≥40 year old patients with an 8 to 30mm lung nodules and a pre-test cancer risk (as assessed by the Mayo Clinic Model for Solitary Pulmonary Nodules) of ≤50% is promising at the current time. Clinical studies underway at this time are expected to demonstrate clinical utility. These studies are designed to show a statistically significant reduction in the number of benign lung nodules experiencing invasive procedures between a prospective group of patients managed by XL2 and a contemporaneous group not managed by XL2. A secondary end-point will show that the management of lung nodules by XL2 does not (i.e., is statistically non-inferior to) the number of malignant nodules routed to CT surveillance (determined at one year interval) as compared to current practice without XL2. Continued coverage for XL2 testing will be dependent on annual review of prospective data and peer-reviewed studies.

[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:

81599 UNLISTED MULTIANALYTE ASSAY WITH ALGORITHMIC ANALYSIS

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph: N/A

Group 1 Codes:

ICD-10 Codes	Description
R91.1	Solitary pulmonary nodule

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

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[General Information](#)

Associated Information

N/A

Sources of Information

N/A

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Revision History Information

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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) [A55661 - Response to Comments: MoIDX: Xpresys Lung](#) LCD(s) [DL37054 - MoIDX: Xpresys Lung](#)

Related National Coverage Documents N/A

Public Version(s) Updated on 07/25/2017 with effective dates 09/29/2017 - N/A [Back to Top](#)

[Keywords](#)

- Xpresys
- XL2
- lung
- pulmonary
- nodule
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