MedStar Health, Inc.
POLICY AND PROCEDURE MANUAL

Policy Number: MP.115.MH
Last Review Date: 02/04/2016
Effective Date: 03/01/2016
Renewal Date: 02/01/2017

MP.115.MH – Genetic Testing, Lung Cancer

This policy applies to the following lines of business:
- ✓ MedStar Employee (Select)
- ✓ MedStar MA – DSNP – CSNP
- ✓ MedStar CareFirst PPO

MedStar Health considers genetic testing to guide the treatment of lung cancer medically necessary for the following indications:

Vysis ALK Break Apart FISH test is indicated only for members who meet the following criteria:
1. Diagnosed advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) and
2. Treatment with Crizotinib (Xalkori) or Ceritinib (Zykadia) is being considered

therascreen EGFR RGQ PCR Kit is indicated only for members who meet the following criteria:
1. Diagnosed with advanced or metastatic NSCLC;
2. Treatment with XalkoriAfatinib (Giltrif) or Gefitinib (Iressa) is being considered.

cobas EGFR Mutation Test is indicated only for members who meet the following criteria:
1. Diagnosed with advanced or metastatic NSCLC;
2. Treatment with Erlotinib (Tarceva) is being considered.

Limitations for all testing:
- For in vitro diagnostic use by prescription only ;
- Not generally recommended for patients with NSCLC subtype of squamous cell carcinoma .

Note: All tests must be performed by laboratories/technologists with demonstrated proficiency in that specific technology.

Background
The Vysis ALK Break Apart FISH test (commercially known as Vysis ALK test) is a genetic test that determines the presence of the abnormal ALK (anaplastic lymphoma kinase) gene, which causes cancer development and growth. The Vysis ALK test is an

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FDA proven companion diagnostic test with Xalkori (Crizotinib) as a treatment for non-small cell lung cancer. Xalkori has proven to effectively block certain proteins (kinases) that are produced by the ALK gene. This abnormal ALK gene is present in certain patients with locally advanced or metastatic non-small cell lung cancer and is typically associated with patients who are non-smokers.

The Vysis ALK Break Apart FISH probe kit (currently manufactured by Abbott Molecular, Inc.) is considered the current standard for detecting ALK rearrangements via FISH tests in NSCLC tissue specimens. If the test result indicates that the patient's tumor is positive for ALK gene rearrangements, then the patient may benefit from treatment with Xalkori. The clinical interpretation of test results should be evaluated within the context of the patient's medical history and with any other diagnostic test results. Patients with these ALK gene abnormalities tend to be younger, have little or no exposure to tobacco and did not have mutations in KRAS (Kirsten Rat Sarcoma) or EGFR (epidermal growth factor receptor).

National Comprehensive Cancer Network's (NCCN) current guidelines recommend:

- ALK testing for patients with NSCLC subtypes of adenocarcinoma, large cell or NSCLC NOS (not otherwise specified).
- If ALK +, then Xalkori is the recommended treatment option.

The Food and Drug Adminsitration (FDA) defines the **cobas**® EGFR Mutation Test v2 as a real-time PCR test for the qualitative detection of defined mutations of the epidermal growth factor receptor (EGFR) gene in DNA derived from formalin-fixed paraffin-embedded tumor tissue (FFPET) from non-small cell lung cancer (NSCLC) patients. The test is intended to aid in identifying patients with NSCLC whose tumors have defined EGFR mutations and for whom safety and efficacy of a drug have been established as follows:

- Tarceva® (erlotinib) - Exon 19 deletions and L858R
- Tagrisso® (osimertinib) - T790M

The Food and Drug Adminsitration (FDA) defines the therascreen® EGFR RGQ PCR Kit as a real-time PCR test for the qualitative detection of exon 19 deletions and exon 21 (L858R) substitution mutations of the epidermal growth factor receptor (EGFR) gene in DNA derived from formalin-fixed paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC) tumor tissue. The test is intended to be used to select patients with NSCLC for whom GILOTRIF® (afatinib) or IRESSA® (gefitinib), EGFR tyrosine kinase inhibitors (TKIs), is indicated. Safety and efficacy of GILOTRIF (afatinib) and IRESSA (gefitinib) have not been established in the patients whose tumors have L861Q, G719X, S768I, exon 20 insertions, and T790M mutations, which are also detected by the therascreen EGFR RGQ PCR Kit.

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Specimens are processed using the QIAamp® DSP DNA FFPE Tissue Kit for manual sample preparation and the Rotor-Gene Q MDx instrument for automated amplification and detection.

Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes	
Code	Description
CPT Codes	
81235	*EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719S, L861Q)*
88271	*Molecular cytogenetics; DNA probe, each (e.g., FISH)*
88274	*Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells*
88291	*Cytogenetic and molecular cytogenetics, interpretation and report*
88367	*Morphometric analysis; in situ hybridization (quantitative or semi-quantitative), using compute-assisted technology*
ICD-9 codes covered if selection criteria are met:	
162.2	*Malignant neoplasm of trachea, bronchus, and lung, Main bronchus*
162.3	*Malignant neoplasm of trachea, bronchus, and lung, upper lobe, bronchus or lung*
162.4	*Malignant neoplasm of trachea, bronchus, and lung, Middle lobe, bronchus or lung*
162.5	*Malignant neoplasm of trachea, bronchus, and lung, Lower lobe, bronchus or lung*
162.8	*Malignant neoplasm of trachea, bronchus, and lung, Other parts of bronchus or lung*
162.9	*Malignant neoplasm of trachea, bronchus, and lung, Bronchus and lung, unspecified*
ICD-10 codes covered if selection criteria are met:	
C34.00-C34.92	Malignant neoplasm of bronchus and lung

References

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3. Hayes GTE Report. Anaplastic Lymphoma Kinase (ALK) Gene Rearrangement Testing in Non-Small Cell Lung Cancer (NSCLC). Published: 07/26/2012. Updated: 07/09/2014.
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6. KRAS Sequence Variant Analysis for predicting response to Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitors (TKIs) in the Treatment of Non-Small Cell Lung Cancer (NSCLC). Annual review April 13, 2015.
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