MEDICAL POLICY

POLICY TITLE	MOLECULAR ANALYSIS FOR TARGETED THERAPY FOR NON-SMALL CELL LUNG CANCER
POLICY NUMBER	MP- 2.241

Original Issue Date (Created):	**9/1/2011**
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I. POLICY

***EGFR* Gene**

Except as noted below, analysis of two types of somatic variants within the epidermal growth factor receptor (*EGFR*) gene – small deletions in exon 19 and a single-nucleotide variant in exon 21 (L858R) – may be considered **medically necessary** to predict treatment response to an EGFR tyrosine kinase inhibitor (TKI) therapy (e.g., erlotinib [Tarceva®], gefitinib [Iressa®], or afatinib [Gilotrif®]), in patients with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (see Policy Guidelines section). Analysis for the T790M variant in the gene for the EGFR is considered **medically necessary** as a technique to predict treatment response to osimertinib (Tagrisso™) in patients who have progressed on or after EGFR-TKI therapy.

Analysis of two types of somatic variants within the *EGFR* gene – small deletions in exon 19 and a point mutation in exon 21 (L858R) is considered **investigational** for patients with advanced non-small cell lung cancer (NSCLC) of squamous cell-type.

Analysis of other *EGFR* variants within exons 18 to 24, or other applications related to NSCLC, is considered **investigational**. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these procedures.

***ALK* Gene**

Analysis of somatic rearrangement variants of the anaplastic lymphoma kinase (*ALK)* gene may be considered **medically necessary** to predict treatment response to ALK inhibitor therapy (e.g., crizotinib [Xalkori®], ceritinib [Zykadia™], alectinib [Alecensa®], or brigatinib [Alunbrig™]) in patients with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (see Policy Guidelines section).

Analysis of somatic rearrangement variants of the *ALK* gene is considered **investigational** in all other situations. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these procedures.

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BRAF V600E TESTING

Analysis of the *BRAF* V600E variant may be considered **medically necessary** to predict treatment response to BRAF or MEK inhibitor therapy (e.g., dabrafenib [Tafinlar®] and trametinib [Mekinist®]), in patients with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (see Policy Guidelines section).

ROS1 TESTING

Analysis of somatic rearrangement variants of the *ROS1* gene may be considered **medically necessary** to predict treatment response to ALK inhibitor therapy (crizotinib [Xalkori®]) in patients with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded (see Policy Guidelines section).

KRAS Gene

Analysis of somatic variants of the *KRAS* gene is considered **investigational** as a technique to predict treatment non-response to anti-EGFR therapy with tyrosine-kinase inhibitors and for the use of the anti-EGFR monoclonal antibody cetuximab in NSCLC. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these procedures.

Other Genes

Testing for genetic alterations in the genes *HER2*, *RET*, and *MET* for targeted therapy in patients with NSCLC is considered **investigational.** There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these procedures.

Policy Guidelines

These tests are intended for use in patients with advanced non-small-cell lung cancer. Patients with either small deletions in exon 19 or a point mutation in exon 21 (L858R) of the tyrosine kinase domain of the epidermal growth factor receptor (*EGFR*) gene are considered good candidates for treatment with erlotinib, gefitinib or afatinib. Patients with wild-type variants are unlikely to respond to erlotinib or afatinib; for these patients, other treatment options should be considered.

The 2017 guidelines from the National Comprehensive Cancer Network recommend that *EGFR* variants and *ALK* rearrangement testing (category 1) as well as *ROS1* and *BRAF* testing (category 2A) be performed in the workup of non-small-cell lung cancer in patients with metastatic disease with histologic subtypes adenocarcinoma, large cell carcinoma, and non-small-cell lung cancer not otherwise specified.

The 2013 guidelines issued jointly by the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology have recommended the following:

- *EGFR* variants and *ALK* rearrangement testing in patients with lung adenocarcinoma regardless of clinical characteristics (eg, smoking history);

- In the setting of fully excised lung cancer specimens, *EGFR* and *ALK* testing is not recommended in lung cancers when an adenocarcinoma component is lacking (eg, pure squamous cell lacking any immunohistochemical evidence of adenocarcinomatous differentiation); and
- In the setting of more limited lung cancer specimens (eg, biopsies, cytology) where an adenocarcinoma component cannot be completely excluded, *EGFR* and *ALK* testing may be performed in cases showing squamous cell histology. Clinical criteria (eg, young age, lack of smoking history) may be useful to select a subset of these samples for testing.

Cross-reference:

MP 2.150 Cetuximab (Erbitux)

II. PRODUCT VARIATIONS

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This policy is applicable to all programs and products administered by Capital BlueCross unless otherwise indicated below.

III. DESCRIPTION/BACKGROUND

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Non-Small-Cell Lung Cancer

Treatment options for non-small-cell lung cancer (NSCLC) depend on disease stage and include various combinations of surgery, radiotherapy, systemic therapy, and best supportive care. Unfortunately, in up to 85% of cases, the cancer has spread locally beyond the lungs at diagnosis, precluding surgical eradication. Also, up to 40% of patients with NSCLC present with metastatic disease.[1] When treated with standard platinum-based chemotherapy, patients with advanced NSCLC have a median survival of 8 to 11 months and a 1-year survival of 30% to 45%.[2,3] The identification of specific, targetable oncogenic "driver mutations" in a subset of NSCLCs has resulted in a reclassification of lung tumors to include molecular subtypes, which are predominantly of adenocarcinoma histology. Testing for epidermal growth factor receptor (*EGFR*) variants and anaplastic lymphoma kinase (*ALK*) rearrangements is routine in clinical decision making for the treatment of NSCLC. The use of testing for other variants to direct targeted therapy continues to evolve.

***EGFR* Gene**

EGFR, a receptor tyrosine kinase (TK), is frequently overexpressed and activated in NSCLC. Drugs that inhibit EGFR signaling either prevent ligand binding to the extracellular domain (monoclonal antibodies) or inhibit intracellular TK activity (small-molecule tyrosine kinase inhibitors [TKIs]). These targeted therapies dampen signal transduction through pathways downstream to the EGFR, such as the RAS/RAF/MAPK cascade. RAS proteins are G proteins that cycle between active and inactive forms in response to stimulation from cell surface receptors, such as EGFR, acting as binary switches between cell surface EGFR and downstream

signaling pathways. These pathways are important in cancer cell proliferation, invasion, metastasis, and stimulation of neovascularization.

Variants in 2 regions of the *EGFR* gene (exons 18-24)—small deletions in exon 19 and a point variant in exon 21 (L858R)—appear to predict tumor response to TKIs such as erlotinib. Likewise, tumors with an acquired exon 20 (T790M) substitution variant appear to respond to osimertinib following the failure of TKI therapy.

The prevalence of *EGFR* variants in NSCLC varies by population, with the highest prevalence in nonsmoking Asian women with adenocarcinoma, in whom *EGFR* variants have been reported to be up to 30% to 50%. The reported prevalence in the white population is approximately 10%.

***ALK* Gene**
ALK is a TK that, in NSCLC, is aberrantly activated because of a chromosomal rearrangement that leads to a fusion gene and expression of a protein with constitutive TK activity that has been demonstrated to play a role in controlling cell proliferation. The *EML4-ALK* fusion gene results from an inversion within the short arm of chromosome 2.

The *EML4-ALK* rearrangement ("*ALK*-positive") is detected in 3% to 6% of NSCLC patients, with the highest prevalence in never-smokers or light ex-smokers who have adenocarcinoma.

***BRAF* Gene**
RAF proteins are serine/threonine kinases that are downstream of RAS in the RAS-RAF-ERK-MAPK pathway. In this pathway, the *BRAF* gene is the most frequently mutated in NSCLC, in 1% to 3% of adenocarcinomas. Unlike melanoma, about 50% of the variants in NSCLC are non-V600E variants.[4] Most *BRAF* variants occur more frequently in smokers.

***ROS1* Gene**
ROS1 codes for a receptor TK of the insulin receptor family, and chromosomal rearrangements result in fusion genes. The prevalence of *ROS1* fusions in NSCLC varies from 0.9% to 3.7%.[4] Patients with *ROS1* fusions are typically never-smokers with adenocarcinoma.

***KRAS* Gene**
The *KRAS* gene (which encodes RAS proteins) can harbor oncogenic variants that result in a constitutively activated protein, independent of signaling from the EGFR, possibly rendering a tumor resistant to therapies that target the EGFR. Variants in the *KRAS* gene, mainly codons 12 and 13, have been reported in 20% to 30% of NSCLC, and occur most often in adenocarcinomas in heavy smokers.

EGFR, *ALK*, *ROS1*, and *KRAS* driver mutations are considered to be mutually exclusive.

***HER2* Gene**
Human epidermal growth factor receptor 2 (*HER2*) is a member of the HER (EGFR) family of TK receptors and has no specific ligand. When activated, it forms dimers with other EGFR family members. *HER2* is expressed in approximately 25% of NSCLC. *HER2* variants are

detected mainly in exon 20 in 1% to 2% of NSCLC, predominantly in adenocarcinomas in nonsmoking women.[4]

***RET* Gene**
RET (rearranged during transfection) is a proto-oncogene that encodes a receptor TK growth factor. Translocations that result in fusion genes with several partners have been reported.[4] *RET* fusions occur in 0.6% to 2% of NSCLCs and 1.2% to 2% of adenocarcinomas.[4]

***MET* Gene**
MET amplification is one of the critical events for acquired resistance in *EGFR*-mutated adenocarcinomas refractory to EGFR TKIs.[4]

Targeted Therapies
Three orally administered EGFR-selective, small-molecule TKIs have been identified for treating NSCLC: gefitinib (Iressa®; AstraZeneca, Cambridge, England), erlotinib (Tarceva®; OSI Pharmaceuticals, Melville NY) and afatinib (Gilotrif™; Boehringer Ingelheim, Ingelheim, Germany). Gefitinib, erlotinib, and afatinib currently are approved by the U.S. Food and Drug Administration (FDA) for NSCLC.

Crizotinib is an oral small-molecule TKI that is FDA-approved for patients with locally advanced or metastatic NSCLC who are positive for the *ALK* or *ROS1* gene rearrangements. Ceritinib is a potent ALK inhibitor that is approved for *ALK*-positive patients who whose cancer has progressed while taking crizotinib or who could not tolerate crizotinib. Alectinib is a selective ALK inhibitor with high central nervous system penetration that is active against several secondary resistance variants to crizotinib. Brigatinib is also an ALK inhibitor that may be able to overcome a broad range of the resistance mechanisms in patients who have progressed on or are intolerant to crizotinib.

BRAF or MEK inhibition with TKIs (eg, vemurafenib/dabrafenib or trametinib) was originally approved by FDA for treatment of unresectable or metastatic melanoma with *BRAF* V600 variants. The combination of dabrafenib and trametinib was approved for treatment of metastatic NSCLC in 2017.

For the treatment of *KRAS*-mutated NSCLC, EGFR TKIs and anti-EGFR monoclonal antibodies have been investigated as treatment options. Anti-EGFR monoclonal antibodies include cetuximab and panitumumab. Cetuximab may be used in combination with chemotherapy in patients with advanced or recurrent NSCLC as first-line and maintenance therapy. Panitumumab is not used in NSCLC.

Proposed targeted therapies for the remaining genetic alterations in NSCLC addressed are trastuzumab and afatinib for *HER2* variants, crizotinib for *MET* amplification and cabozantinib for *RET* rearrangements.

Regulatory Status

Table 1 summarizes the FDA-approved targeted treatments for patients with NSCLC along with the concurrently approved diagnostic tests.[5-14]

Table 1. FDA-Approved Targeted Treatment for NSCLC and Companion Diagnostic Tests

Treatment	Indication	FDA Approval of Companion Diagnostic Test
Afatinib (Gilotrif)	• 2013: First line for patients with metastatic NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 (L858R) substitutions as detected by FDA-approved test • 2016: Second line for patients with metastatic squamous NSCLC	2013: therascreen® EGFR Rotor-Gene Q polymerase chain reaction (RGQ PCR) kit (Qiagen, Netherlands)
Alectinib (Alecensa)	• 2015: Second line for patients with *ALK*-positive metastatic NSCLC who have progressed on or are intolerant of crizotinib	
Ceritinib (Zykadia)	• 2014: Second line for patients with *ALK*-positive metastatic NSCLC who have progressed on or are intolerant of crizotinib	
Crizotinib (Xalkori)	• 2011: Patients with *ALK*-positive metastatic NSCLC as detected by FDA-approved test	• 2011: Vysis ALK Break Apart FISH Probe Kit (Abbott Laboratories, Lake Bluff, IL) • 2015: Ventana ALK (D5F3) CDx Assay (Ventana Medical Systems, Tucson, AZ)
Crizotinib (Xalkori)	• 2016: Patients with *ROS1*-positive metastatic NSCLC	• 2017: Oncomine™ Dx Target Test (Thermo Fisher Scientific, Waltham, MA)
Erlotinib (Tarceva)	• 2013: First line for patients with metastatic NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 (L858R) substitutions as detected by FDA-approved test • 2010: Maintenance for patients with locally advanced or metastatic NSCLC whose disease has not progressed after 4 cycles of platinum-based chemotherapy • 2004: Second line for patients with locally advanced or metastatic NSCLC	• 2013: cobas® EGFR Mutation Test (tissue test) (Roche Diagnostics, Indianapolis, IN) • 2016: cobas® EGFR Mutation Test v2 (tissue or blood test) (Roche, Diagnostics, Indianapolis, IN)
Gefitinib (Iressa)	• 2015: First line for patients with metastatic NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 (L858R) substitutions as detected by FDA-approved test • 2003: Second line for patients with locally advanced or metastatic NSCLC	2015: therascreen® EGFR Rotor-Gene Q polymerase chain reaction (RGQ PCR) kit 2017: Oncomine™ Dx Target Test
Necitumumab (Portrazza; Eli Lilly, Indianapolis, IN)	• 2015: In combination with gemcitabine and cisplatin, as first line for patients with squamous NSCLC	
Osimertinib (Tagrisso)	• 2015: Second line for patients with metastatic NSCLC whose tumors have *EGFR* T790M variants as detected by FDA-approved test, who have not responded to *EGFR*-blocking therapy	2015: cobas® EGFR Mutation Test v2 (blood test)
Dabrafenib (Tafinlar) and trametinib (Mekinist) combination	• 2017: Used in combination; for treatment of patients with metastatic NSCLC with *BRAF* V600E variant	2017: Oncomine™ Dx Target Test

ALK: anaplastic lymphoma kinase; *EGFR*: epidermal growth factor receptor; FDA: Food and Drug Administration; FISH: fluorescence in situ hybridization; NSCLC: non-small-cell lung cancer; PCR: polymerase chain reaction.

IV. RATIONALE

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Summary of Evidence

For individuals who have advanced-stage NSCLC who are being considered for targeted therapy who receive testing for *EGFR* variants and *ALK* rearrangements, the evidence includes phase 3 studies comparing TKIs with chemotherapy. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, quality of life, and treatment-related morbidity. Studies have shown that TKIs are superior to chemotherapy regarding tumor response rate and progression-free survival, with a reduction in toxicity and improvement in quality of life. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have advanced-stage NSCLC who are being considered for targeted therapy who receive testing for *BRAF* variants and *ROS1* rearrangements, the evidence includes nonrandomized trials and observational studies of BRAF and MEK inhibitors and crizotinib or ceritinib, respectively. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, quality of life, and treatment-related morbidity. Studies have shown that combination therapy with dabrafenib and trametinib for *BRAF* V600E variant NSCLC and crizotinib for NSCLC with *ROS1* rearrangements result in response rates of 60% and 70%, respectively, with acceptable toxicity profiles. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have advanced-stage NSCLC who are being considered for targeted therapy who receive testing for *KRAS* or *HER2* variants, *RET* rearrangements, or *MET* amplifications, the evidence includes for *KRAS* post hoc analyses trials, observational studies, and meta-analyses; for the other variants, the evidence includes a phase 2 trial with preliminary data, and retrospective analyses of very small case series and case reports. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, quality of life, and treatment-related morbidity. Studies have shown that *KRAS* variants in patients with NSCLC confer a high level of resistance to TKIs; data are insufficient to assess any additional benefit to testing for *KRAS* variants to select for EGFR TKIs beyond *EGFR* testing. In 2 randomized trials with post hoc analyses of *KRAS* variant status and use of the anti-EGFR monoclonal antibody cetuximab with chemotherapy, *KRAS* variants did not identify patients who would benefit from anti-EGFR antibodies, because outcomes with cetuximab were similar regardless of *KRAS* variant status. In two randomized controlled trials of advanced *KRAS*-variant positive disease, MEK inhibitors did not improve progression-free survival compared with docetaxel. Studies for *HER2*, *RET*, and *MET* variant testing have reported response rates and progression-free survival in numbers of patients too small from which to draw conclusions. The evidence is insufficient to determine the effects of the technology on health outcomes.

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V. DEFINITIONS

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NA

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER

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Capital BlueCross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore not covered for KRAS testing for NSCLC when used to predict treatment non-response to anti-EGFR therapy:

CPT Codes®								
81275	81276	88363						

Investigational; therefore not covered when used to test for genetic alterations in the genes ROS, RET, MET, BRAF, and HER2, for targeted therapy in patients with NSCLC:

CPT Codes®								
81404	81405	81479	0022U					

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Covered when medically necessary:

CPT Codes®								
81235	81401	81406	88342					

ICD-10-CM Diagnosis Codes	Description
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
D38.1	Neoplasm of uncertain behavior of trachea, bronchus and lung

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X. POLICY HISTORY

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MP 2.241	**CAC 4/26/11** New Policy. Adopted BCBSA (medically necessary).
	CAC 6/26/12 Consensus review; no changes, references updated. FEP variation added.
	12/20/2013 2013 Codes added
	05/20/13 Administrative code review completed.
	8/1/13 Administrative change. Add Medicare variation referencing LCD L33142.

POLICY TITLE	MOLECULAR ANALYSIS FOR TARGETED THERAPY FOR NON-SMALL CELL LUNG CANCER
POLICY NUMBER	MP- 2.241

	CAC 11/26/13 Consensus. No change to policy statements. Added rationale section. References updated**.**
	7/24/14 Administrative change for the Medicare variation - For Novitas MAC jurisdictions, the LCD has been assigned a new number. Biomarkers for Oncology LCD changed from L33124 to L34796
	CAC 1/27/15 Minor revision. ▪ Policy title revised to "Molecular Analysis for Targeted Therapy for Non-Small Cell Lung Cancer" for this review. ▪ First policy statement revised to state analysis of two types of somatic mutation within the epidermal growth factor receptor (EGFR) gene -- small deletions in exon 19 and a point mutation in exon 21 (L858R) – may be considered medically necessary to predict treatment response to erlotinib or afatinib in patients with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded. Previously, afatinib was not included and the medically necessary indication as for non-small cell lung cancer. ▪ A new statement was added that testing for ROS, RET, MET, BRAF and HER2 mutations is considered investigational. ▪ Policy MP-2.240 KRAS Mutation Analysis in Non-Small Cell Lung Cancer (NSCLC) merged with this policy. Background, rationale, references, and guidelines updated. FEP variation updated to reflect combining two policies. (MP 2.240 Info added into this policy). Cellular and histologic classification of NSCLC added to policy guidelines. No coding changes.
	11/2/15 Administrative change. LCD number changed from L34796 to L35396 due to Novitas update to ICD-10.
	CAC 3/29/16 Minor revision**.** Policy updated only to address *ALK* rearrangement testing. Policy statement added that analysis of somatic rearrangement mutations of the *ALK* gene is considered medically necessary to predict treatment response to crizotinib in patients with advanced lung adenocarcinoma or in whom an adenocarcinoma component cannot be excluded. Policy statement added that testing for *ALK* gene rearrangements is investigational for all other clinical situations. Reference and rationale update. Coding reviewed.
	Admin update 1/1/17: Product variation section reformatted.
	CAC 3/28/17 Minor revision. Added testing for T790M mutation in patients who have progressed on or after EGFR-TKI therapy to the EGFR Gene medically necessary statement. The medically necessary statement language for the EGFR and ALK Genes were revised to reference the gene inhibitor therapy with examples of therapy types/drugs. FEP variation

POLICY TITLE	MOLECULAR ANALYSIS FOR TARGETED THERAPY FOR NON-SMALL CELL LUNG CANCER
POLICY NUMBER	MP- 2.241

	updated. Policy Guidelines, Description/Background, Rationale and Reference sections updated. Appendix added. Coding Reviewed
	1/1/18 Admin Update: Medicare variations removed from Commercial Policies.
	1/25/18 Minor revision. Policy section updates: • Genetics nomenclature update 'mutation' to 'variant'; • 'Point mutation' replaced with 'single-nucleotide variant' within the EGFR Gene policy statement; • *ROS1* and *BRAF* testing added as medically necessary when criteria is met; and • Genes within the 'Other Genes' statement updated. FEP variation removed as policy was archived December 2015. Policy Guidelines, Description/Background, Rationale and Reference sections updated. Coding revised to mirror policy statements.

APPENDIX

Appendix Table 1. Categories of Genetic Testing Addressed in MP-2.241

Category	Addressed
1. Testing of an affected individual's germline to benefit the individual	
1a. Diagnostic	
1b. Prognostic	
1c. Therapeutic	
2. Testing cancer cells from an affected individual to benefit the individual	
2a. Diagnostic	
2b. Prognostic	
2c. Therapeutic	X
3. Testing an asymptomatic individual to determine future risk of disease	
4. Testing of an affected individual's germline to benefit family members	
5. Reproductive testing	
5a. Carrier testing: preconception	
5b. Carrier testing: prenatal	
5c. In utero testing: aneuploidy	
5d. In utero testing: mutations	
5e. In utero testing: other	
5f. Preimplantation testing with in vitro fertilization	

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