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PHARMACY POLICY – 5.01.538

ALK Tyrosine Kinase Inhibitors

Effective Date:	May 1, 2026	RELATED MEDICAL POLICIES:
Last Revised:	Apr. 13, 2026	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

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Introduction

The anaplastic lymphoma kinase (ALK) gene provides instructions for making a specific kind of protein called ALK receptor tyrosine kinase. This protein helps cells communicate. When this gene is damaged, cell growth can get stuck in the "on" position and cells grow uncontrollably. Changes to the ALK gene can lead to non-small-cell lung cancer. Tyrosine kinase inhibitors block specific enzymes, essentially working to turn the cell growth to the "off" position. ALK tyrosine kinase inhibitors specifically target cancers caused by changes to the ALK gene. This policy describes when this specific form of chemotherapy may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity

Alecensa (alectinib)	**Alecensa (alectinib) may be considered medically necessary for the treatment of non-small cell lung cancer (NSCLC) when all the following are met:**
	• The individual is aged 18 years or older
	AND
	• Diagnosed with anaplastic lymphoma kinase (ALK)-positive NSCLC
	AND
	• Meets one of the following:
	  ○ Diagnosed with advanced or metastatic disease
	  ○ Requires adjuvant treatment following tumor resection with tumors at least 4 cm or node positive
	AND
	• The dose is limited to 1,200 mg daily
	
	Alecensa (alectinib) may be considered medically necessary for the treatment of metastatic or recurrent inflammatory myofibroblastic tumor (iMT) with ALK translocation when the individual has had treatment failure on prior Xalkori (crizotinib) therapy.

Alunbrig (brigatinib)	**Alunbrig (brigatinib) may be considered medically necessary for the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) when all the following are met:** • The individual is aged 18 years or older **AND** • Diagnosed with advanced or metastatic NSCLC that is anaplastic lymphoma kinase (ALK)-positive **AND** • The dose is limited to 180 mg daily **Alunbrig (brigatinib) may be considered medically necessary for the treatment of metastatic or recurrent inflammatory myofibroblastic tumor (iMT) with ALK translocation when the individual has had treatment failure on prior Xalkori (crizotinib) therapy.**

Drug	Medical Necessity
Ensacove (ensartinib)	**Ensacove (ensartinib) may be considered medically necessary for the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) when all the following are met:** • The individual is aged 18 years or older **AND** • Diagnosed with advanced or metastatic NSCLC that is anaplastic lymphoma kinase (ALK)-positive **AND** • Meets one of the following: ○ Has not previously received an ALK inhibitor **OR** ○ Is changing ALK inhibitor due to documented side effects (not due to a failure of ALK inhibitor therapy) **AND** • There is a documented contraindication to the use of Alecensa (alectinib) **AND** • The dose is limited to 225 mg daily
Lorbrena (lorlatinib)	**Lorbrena (lorlatinib) may be considered medically necessary for the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) when all the following are met:** • The individual is aged 18 years or older **AND** • Diagnosed with advanced or metastatic NSCLC that is anaplastic lymphoma kinase (ALK)-positive **AND** • The dose is limited to 100 mg daily **AND** • The quantity is limited to the following: ○ 25 mg tablets: 90 tablets per 30 days ○ 100 mg tablets: 30 tablets per 30 days **Lorbrena (lorlatinib) may be considered medically necessary for the treatment of metastatic or recurrent inflammatory myofibroblastic tumor (iMT) with ALK translocation when the individual has had treatment failure on prior Xalkori (crizotinib) therapy.**

Drug	Medical Necessity
Xalkori (crizotinib)	**Xalkori (crizotinib) may be considered medically necessary for the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) when all the following are met:** • The individual is aged 18 years or older **AND** • Diagnosed with advanced or metastatic NSCLC that is anaplastic lymphoma kinase (ALK)-positive or ROS proto-oncogene 1 receptor tyrosine kinase (ROS1)-positive **AND** • The dose is limited to 500 mg daily **Xalkori (crizotinib) may be considered medically necessary for the treatment of anaplastic large cell lymphoma (ALCL) when all the following are met:** • The individual is aged between 1 year and 21 years of age **AND** • Diagnosed with relapsed or refractory, systemic ALCL that is ALK-positive **Xalkori (crizotinib) may be considered medically necessary for the treatment of inflammatory myofibroblastic tumor (iMT) when all the following are met:** • The individual is aged 1 year or older **AND** • Diagnosed with unresectable, recurrent, or refractory iMT that is ALK-positive **AND** • The dose is limited to 500 mg daily
Zykadia (ceritinib)	**Zykadia (ceritinib) may be considered medically necessary for the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) when all the following are met:** • The individual is aged 18 years or older **AND** • Diagnosed with advanced or metastatic NSCLC that is anaplastic lymphoma kinase (ALK)-positive **AND** • The dose is limited to 450 mg per day

Drug	Medical Necessity
	Zykadia (ceritinib) may be considered medically necessary for the treatment of metastatic or recurrent inflammatory myofibroblastic tumor (iMT) with ALK translocation when the individual has had treatment failure on prior Xalkori (crizotinib) therapy.

Drug	Investigational
As listed	**All other uses of the medications listed in this policy are considered investigational.** **The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for all drugs listed in the policy may be approved up to 12 months.** **All other reviews for all drugs listed in policy may be approved up to 6 months.**
Re-authorization criteria	**Non-formulary exception reviews and all other reviews for re-authorization of all drugs listed in policy may be approved up to 12 months as long as the drug-specific coverage criteria are met, and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation, and medication history

Coding

N/A

Related Information

Benefit Application

This policy is managed through the pharmacy benefit.

Evidence Review

Background

ALK+ Non-Small Cell Lung Cancer

Lung cancer consists of two major types: non-small cell lung cancer (NSCLC) and small-cell lung cancer (SCLC). Approximately 85% to 90% of lung cancers are NSCLC. NSCLC is further categorized into three major histological subtypes: adenocarcinoma, squamous cell (epidermoid) carcinoma, and large cell (undifferentiated) carcinoma. Adenocarcinoma is the most common subtype of NSCLC in the United States (about 40% of lung cancers). Several biomarkers have emerged as prognostic and predictive makers for NSCLC. These biomarkers include epidermal growth factor receptor (EGFR), the 5′ endonuclease of the nucleotide excision repair complex (ERCC1), the k-ras oncogene, the regulatory subunit of ribonucleotide reductase (RRM1), and EML4-ALK fusion oncogene. Activation of ALK has been described as a primary oncogenic driver in about 2-7% of NSCLC individuals, or about 10,000 individuals in the United States. ALK-positive NSCLC is associated with distinct clinical features, including younger age of onset, absent or minimal smoking history, and adenocarcinoma histology.

In the United States, lung cancer is the second most common cancer and is the primary cause of cancer-related death in both men and women. It is estimated that 226,650 new cases of lung cancer (110,680 in men and 115,970 in women) are expected to be diagnosed in the US in 2025.

An estimated 124,730 deaths from lung cancer (64,190 in men and 60,540 in women) are expected to occur in the US in 2025. Lung cancer mainly occurs in older people. Most people diagnosed with lung cancer are 65 or older and a very small number of people diagnosed are younger than 45. The average age of people when diagnosed is about 70. Lung cancer is by far the leading cause of cancer death in the US, accounting for about 1 in 5 of all cancer deaths. Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined.

Description

The ALK Oncogene

Activation of ALK occurs through a chromosomal rearrangement that places one of several different 5′ fusion partners and their associated promoter upstream of the 3′ kinase domain of ALK. The most common 5′ fusion partner in non-small cell lung cancer (NSCLC) is EML4, but other, rarer 5′ fusion partners that cause oncogenic transformations have been described. The formation of ALK fusion proteins results in activation and dysregulation of gene expression and signaling which can contribute to increased cell proliferation and survival in tumors expressing these proteins. EML4-ALK translocations are usually mutually exclusive of epidermal growth factor receptor (EGFR) and KRAS mutations.

Alecensa (alectinib)

Alecensa (alectinib) is a tyrosine kinase inhibitor indicated for the treatment of individuals with ALK-positive metastatic NSCLC. In nonclinical studies, alectinib inhibited ALK phosphorylation and ALK-mediated activation of the downstream signaling proteins STAT3 and AKT, and decreased tumor cell viability in multiple cell lines harboring ALK fusions, amplifications, or activating mutations. The major active metabolite of alectinib, M4, showed similar in vitro potency and activity. Alectinib and M4 demonstrated in vitro and in vivo activity against multiple mutant forms of the ALK enzyme, including some mutations identified in NSCLC tumors in individuals who have progressed on crizotinib.

Alunbrig (brigatinib)

Alunbrig (brigatinib) has in vitro activity against multiple kinases including ALK, ROS1, IGF-1R, and FLT-3, as well as EGFR deletion and point mutations. Brigatinib inhibited

autophosphorylation of ALK and ALK-mediated phosphorylation of the downstream signaling proteins STAT3, AKT, ERK1/2, and S6 in in vitro and in vivo assays. Brigatinib also inhibited the in vitro proliferation of cell lines expressing EML4-ALK and NPM-ALK fusion proteins. It inhibited the in vitro viability of cells expressing EML4-ALK and 17 mutant forms associated with resistance to ALK inhibitors EGFR-Del (E746-A750), ROS1-L2026M, FLT3-F691L, and FLT3-D835Y. Brigatinib exhibited in vivo anti-tumor activity against 4 mutant forms of EML4-ALK, including G1202R and L1196M mutants identified in NSCLC tumors in individuals who have progressed on crizotinib.

Ensacove (ensartinib)

Ensacove (ensartinib) is a kinase inhibitor of anaplastic lymphoma kinase (ALK) and inhibits other kinases including MET and ROS1. In vitro, ensartinib inhibited phosphorylation of ALK and its downstream signaling proteins AKT, ERK, and S6, thereby blocking ALK-mediated signaling pathways and inhibiting proliferation in cell lines harboring ALK fusions and mutations. In vivo, ensartinib showed anti-tumor activity in a mouse xenograft model of human NSCLC harboring an ALK fusion.

The safety and efficacy of ensartinib in the treatment of ALK positive NSCLC has been evaluated in one moderate quality Phase III trial (eXalt3). The eXalt3 study is a global, open-label, multicenter, randomized Phase III trial in adults with advanced or recurrent (stage III) or metastatic (stage IV), ALK positive, NSCLC. Patients were randomized 1:1 to receive ensartinib 225 mg orally once daily or crizotinib 250 mg orally twice daily. Patients were stratified by Eastern Cooperative Oncology Group (ECOG) performance status (PS) (0 or 1 vs 2), central nervous system (CNS) metastases at baseline, prior chemotherapy, and geographic region (Asia vs all others). Patients continued treatment until disease progression, unacceptable toxicity, or withdrawal of consent. Key inclusion criteria included patients aged 18 or older with advanced or recurrent (stage IIIB not amenable for multimodality treatment) or metastatic (stage IV) NSCLC that is ALK positive as determined by local testing (or central lab after a protocol amendment) and may have received up to one prior chemotherapy regimen for metastatic disease. Patients with asymptomatic brain metastasis were permitted.

Key exclusion criteria included having received cancer treatment within 4 weeks or radiotherapy within 14 days of study entry, or prior ALK tyrosine kinase inhibitors, programmed cell death 1 (PD1), or programmed cell death ligand 1 (PD-L1) treatment. The primary endpoint was progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST), v1.1 in the ITT population as accessed by blinded independent review committee. Secondary endpoints included overall survival, CNS response rate, and CNS time to progression.

Results demonstrated a median PFS of 25.8 months with ensartinib compared to 12.7 months with crizotinib (hazard ratio [HR], 0.56; P = 0.0007). Ensartinib showed superior intracranial efficacy, achieving a response rate of 63.6% versus 21.1% with crizotinib, and significantly reduced CNS progression rates at 12 months (4.2% vs. 23.9%). However, there was not a statistically significant difference in the secondary endpoint of overall survival between the two drugs (HR = 0.88; 95% CI, 0.63–1.23).

The most common adverse reactions (incidence ≥20%) with ensartinib were rash, musculoskeletal pain, constipation, pruritus, cough, nausea, edema, vomiting, fatigue, and pyrexia. The most common Grade 3-4 laboratory abnormality (incidence ≥2%) were increased uric acid, decreased lymphocytes, increased alanine aminotransferase, decreased phosphate, increased gamma glutamyl transferase, increased magnesium, increased amylase, decreased sodium, increased glucose, decreased hemoglobin, increased bilirubin, decreased potassium, and increased creatine phosphokinase.

Lorbrena (lorlatinib)

Lorbrena (lorlatinib) received FDA approval in November 2018 for the treatment of ALK-positive metastatic NSCLC for individuals whose disease has progressed on other targeted therapies. In March 2021 Lorbrena was approved for first-line therapy based on results of the CROWN study. In this study patients were randomized 1:1 to receive lorlatinib 100 mg orally once daily or crizotinib 250 mg orally twice daily. Results from the study demonstrated a significant improvement in progression-free survival for the lorlatinib arm over the crizotinib arm. Lorlatinib has in vitro activity against ALK and ROS1 as well as TYK1, FER, FPS, TRKA, TRKB, TRKC, FAK, FAK2, and ACK. Lorlatinib demonstrated in vitro activity against multiple mutant forms of the ALK enzyme, including some mutations detected in tumors at the time of disease progression on crizotinib and other ALK inhibitors.

Xalkori (crizotinib)

Xalkori (crizotinib) is a small-molecule tyrosine kinase receptor inhibitor, which inhibits ALK, Hepatocyte Growth Factor Receptor (HGFR, c-MET), and Recepteur d'Origine Nantais (RON). ALK gene abnormalities due to mutations or translocations may result in expression of oncogenic fusion proteins (i.e., EML4-ALK fusion protein) which alter signaling and expression and result in increased cellular proliferation and survival in tumors which express these fusion proteins.

Crizotinib selectively inhibits ALK tyrosine kinase, which reduces proliferation of cells expressing the genetic alteration.

Xalkori (crizotinib) efficacy was demonstrated in two multicenter, single-arm studies that enrolled 255 patients with locally advanced or metastatic ALK-positive NSCLC: a phase II study (Study A [PROFILE 1005]) and a part two expansion cohort of a phase I dose-escalation study (Study B [Study 1001]). Patients enrolled into these studies had received prior systemic therapy, with the exception of 15 patients in Study B who had no prior systemic treatment for locally advanced or metastatic disease. The primary efficacy endpoint in both studies was investigator-determined Objective Response Rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST). Patients received 250 mg of crizotinib orally twice daily until disease progression or until intolerable side effects were reported. In Study A, there was 1 complete and 67 partial responses for an ORR of 50% (95% CI: 42%, 59%). In Study B, there were 2 complete and 69 partial responses for an ORR of 61% (95% CI: 52%, 70%). The median response duration was 41.9 weeks and 48.1 weeks in Studies A and B, respectively.

Xalkori (crizotinib) was studied in individuals with ALK-positive inflammatory myofibroblastic tumors in two trials, ADVL0912 for pediatric patients and A8081013 for adults. The overall response rates were 86% (95% CI: 57%, 98%) for pediatric patients and 71% for adult patients.

Adverse effects were less than would be expected with conventional cytotoxic chemotherapy, but serious adverse events and treatment-related deaths related to crizotinib have been observed. Adverse events led to dosage reductions in 44% and 29% of patients in Studies A and B, respectively. Most adverse events were mild to moderate (Grade 1 or Grade 2). The most common (≥ 25%) adverse events were vision disorder, nausea, vomiting, diarrhea, edema, and constipation. Grade 3 or Grade 4 adverse events observed in ≥ 2% of patients included dyspnea, increased ALT levels, and neutropenia. Severe or fatal pneumonitis was reported in a small number of patients on crizotinib therapy.

Zykadia (ceritinib)

Zykadia (ceritinib) is a small-molecule tyrosine kinase receptor inhibitor similar to crizotinib. Ceritinib was approved for treatment of ALK+ NSCLC on the basis of one single-arm, open-label, dose-finding Phase I study. This study started with 59 patients in the dose-escalation phase and recruited an additional 71 patients in the expansion phase, for a total of 130 patients. All patients had ALK-mutated tumors, with the majority (94%) with NSCLC; 68% of patients had previous progression of cancer while receiving crizotinib. The primary outcome was the finding the maximum tolerated dose and secondary outcome was tumor response as measured

according to RECIST v1.0 by investigators and a blinded independent review committee (BIRC). The drop-out rate was not reported. There was a partial response in less than half of the patients (41.1% as evaluated by BIRC) and a complete response in only 2.5% of patients. The average progression free survival was 7 months. Previously approved second line agents (docetaxel, pemetrexed, erlotinib) did not have response rates greater than 10% and had progression free survival time of at most 12.3 weeks.

Common adverse events experienced with ceritinib include nausea, elevated liver function tests, diarrhea, and vomiting. Uncommon but serious events reported include interstitial lung disease, hyperglycemia, dyspnea, and prolonged QT interval. Fatal reactions occurred in 5% of patients in clinical trials due to pneumonia, respiratory failure, pneumonitis, pneumothorax, gastric hemorrhage, pulmonary tuberculosis, cardiac tamponade, and sepsis.

2013 Update

Added treatment of inflammatory myofibroblastic tumor with ALK translocation (NCCN category 2A).

2014 Update

Policy updated with new ALK tyrosine kinase inhibitor, ceritinib.

2015 Update

Added treatment of ROS1-positive non-small-cell lung cancer with crizotinib (NCCN category 2A).

2016 Update

Policy updated with new ALK tyrosine kinase inhibitor, alectinib.

2017 Update

Policy updated with literature review for the previous year. A statement outlining the length of therapy for initial and subsequent approval has been added to the policy.

2018 Update

Policy updated with no changes. Third-generation inhibitor loratinib is currently in phase III clinical trials, expecting FDA approval in August 2018. Added reauthorization criteria and documentation statement.

2019 Update

Reviewed prescribing information for all drugs. No new evidence was identified that would require changes to drugs listed in this policy.

2020 Update

Reviewed prescribing information for all drugs. No new evidence was identified that would require changes to drugs listed in this policy. Added a Documentation Requirements table to policy.

2021 Update

Reviewed prescribing information for all drugs. Based on results from the CROWN study in previously untreated ALK-positive NSCLC, Lorbrena (lorlatinib) coverage criteria were updated removing requirement for prior treatment with an alternative ALK kinase inhibitor. Coverage criteria for Alecensa (alectinib), Alunbrig (brigatinib), Xalkori (crizotinib), and Zykadia (ceritinib) for the treatment of NSCLC were updated limiting use to adult individuals. Quantity limits were also added to all drugs for the treatment of NSCLC following the prescribing information. Per the NCCN Guidelines Version 2.2021 for Soft Tissue Sarcoma, for the treatment of inflammatory myofibroblastic tumor (iMT) with the ALK translocation Alunbrig (brigatinib), Xalkori (crizotinib), and Zykadia (ceritinib) are all listed as preferred ALK inhibitors with a category 2A recommendation. Based on NCCN Guidelines, coverage criteria were expanded for Alunbrig

(brigatinib) and Zykadia (ceritinib) to include treatment of iMT with the ALK translocation. References and background information were revised.

2022 Update

Reviewed prescribing information for all drugs. Reviewed new indication for Xalkori (crizotinib) and related pivotal trials. Added coverage for Xalkori (crizotinib) for ALK-positive inflammatory myofibroblastic tumors.

2023 Update

Reviewed prescribing information for all drugs in the policy. No new evidence was found that could change the policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.

2024 Update

Reviewed prescribing information for all drugs in the policy. Updated Alecensa (alectinib) coverage criteria to include treatment of certain adults requiring adjuvant treatment for non-small cell lung cancer (NSCLC).

2025 Update

Reviewed prescribing information for all drugs in the policy and no new evidence was found that could change the policy statements. Added coverage for Ensacove (ensartinib) for the treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced or metastatic non-small cell lung cancer (NSCLC) who have not previously received an ALK-inhibitor. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

2026 Update

Reviewed prescribing information for all drugs in the policy. Updated coverage criteria for Lorbrena (lorlatinib) adding a prescribed quantity limit per 30 days. Updated coverage criteria for Alunbrig (brigatinib) and Zykadia (ceritinib) for the treatment of inflammatory myofibroblastic tumor (iMT) to include it is for metastatic or recurrent disease and the individual has had treatment failure on prior Xalkori (crizotinib) therapy. Added coverage criteria for Alecensa (alectinib) and Lorbrena (lorlatinib) for the treatment of metastatic or recurrent inflammatory myofibroblastic tumor (iMT) with ALK translocation when the individual has had treatment failure on prior Xalkori (crizotinib) therapy.

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19. Lorbrena (lorlatinib). Prescribing Information. Pfizer Inc., New York, New York. Revised August 2024.
20. Ensacove (ensartinib). Prescribing Information. Xcovery Holdings, Inc. Miami, FL. Revised December 2024.

History

Date	Comments
06/12/12	New policy, add to Prescription Drug section.
07/08/13	Minor Update – Clarification was added to the policy that it is managed through the member's pharmacy benefit; this is now listed in the header and within the coding section.
10/14/13	Replace policy. Medically necessary indications for crizotinib expanded to include treatment of inflammatory myofibroblastic tumor (iMT) with the ALK translocation.
11/10/14	Annual Review. Policy updated with literature review; medically necessary policy statement added for the new ALK tyrosine kinase inhibitor, ceritinib. References 12-15 added.
09/08/15	Annual Review. Policy updated with literature review; reference 16 added. Medically necessary policy statement for Xalkori (crizotinib) updated to include the indication of ROS proto-oncogene 1 receptor tyrosine kinase (ROS1)-positive.
04/01/16	Interim update, changes approved March 8, 2016. Medically necessary policy statement added for the new ALK tyrosine kinase inhibitor, alectinib.

Date	Comments
05/01/17	Annual Review, changes approved April 11, 2017. A statement outlining the length of therapy for initial and subsequent approval has been added to the policy.
07/01/17	Interim update. approved June 13, 2017. Policy moved into the new format. Added coverage criteria for Alunbrig (brigatinib).
10/01/17	Interim review approved September 21, 2017. Alecensa, Zykadia, Alunbrig changed to first-line.
07/01/18	Annual Review, approved June 22, 2018. Added reauthorization criteria and documentation statement.
03/01/19	Interim Review, approved February 12, 2019. Added coverage criteria for Lorbrena (lorlatinib).
12/01/19	Annual Review, approved November 21, 2019. Literature review through October 2019; no change to policy statements.
01/01/21	Annual Review, approved December 1, 2020. No changes to policy statements.
03/01/21	Interim Review, approved February 18, 2021. Added a new indication to Xalkori (crizotinib) for the treatment of anaplastic large cell lymphoma that is ALK-positive.
06/01/21	Annual Review, approved May 20, 2021. Updated coverage criteria for Lorbrena (lorlatinib) for the treatment of NSCLC removing requirement for prior treatment with an ALK kinase inhibitor and adding a daily dose limit. Updated coverage criteria for Alecensa (alectinib), Alunbrig (brigatinib), Xalkori (crizotinib), and Zykadia (ceritinib) for the treatment of NSCLC limiting use to adults and adding a daily dose limit. Expanded coverage for Alunbrig (brigatinib) and Zykadia (ceritinib) to include treatment of inflammatory myofibroblastic tumor (iMT) with the ALK translocation.
04/01/22	Annual Review, approved March 7, 2022. No changes to policy statements.
10/01/22	Interim Review, approved September 13, 2022. Updated coverage for Xalkori (crizotinib) for ALK-positive inflammatory myofibroblastic tumors (IMT) to limit use to patients 1 year of age and older with unresectable, recurrent, or refractory IMT.
09/01/23	Annual Review, approved August 7, 2023. Reviewed prescribing information for all drugs in the policy. No new evidence was found that could change the policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.
07/01/24	Annual Review, approved June 11, 2024. Updated Alecensa (alectinib) coverage criteria to include treatment of certain adults requiring adjuvant treatment for non-small cell lung cancer (NSCLC).
04/01/25	Annual Review, approved March 11, 2025. Added coverage for Ensacove (ensartinib) for the treatment of advanced or metastatic NSCLC. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

Date	Comments
03/01/26	Annual Review, approved February 10, 2026. Updated coverage criteria for Lorbrena (lorlatinib) adding a prescribed quantity limit per 30 days. Updated coverage criteria for Alunbrig (brigatinib) and Zykadia (ceritinib) for the treatment of inflammatory myofibroblastic tumor (iMT) to include it is for metastatic or recurrent disease and the individual has had treatment failure on prior Xalkori (crizotinib) therapy. Added coverage criteria for Alecensa (alectinib) and Lorbrena (lorlatinib) for the treatment of metastatic or recurrent inflammatory myofibroblastic tumor (iMT) with ALK translocation when the individual has had treatment failure on prior Xalkori (crizotinib) therapy.
05/01/26	Interim Review, approved April 13, 2026. Updated initial authorization for all other reviews for all drugs listed in the policy from 3 months to 6 months.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.