ALK+ Non-Small Cell Lung Cancer
EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO002

Description
Crizotinib (Xalkori), ceritinib (Zykadia), alectinib (Alecensa), brigatinib (Alunbrig), and lorlatinib (Lorbrena) are orally administered anaplastic lymphoma kinase-positive (ALK+) tyrosine kinase inhibitors (TKI).

Length of Authorization
- Initial: Six months; first three months split fill for crizotinib (Xalkori), ceritinib (Zykadia), and brigatinib (Alunbrig).
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
crizotinib (Xalkori)	200 mg capsules	ALK+ NSCLC, metastatic	60 capsules/30 days	168671
	250 mg capsules	ROS1+ NSCLC, metastatic	60 capsules/30 days	168670
ceritinib (Zykadia)	150 mg capsules	ALK+ NSCLC, metastatic	84 capsules/28 days	183765
	150 mg tablets		84 tablets/28 days	206607
alectinib (Alecensa)	150 mg capsules		240 capsules/30 days	191329
brigatinib (Alunbrig)	30 mg tablets		180 tablets/30 days	197898
	90 mg tablets		30 tablets/30 days	201302
	90 mg and 180 mg tablet titration pack		30 tablets/30 days	201306
	180 mg tablets		30 tablets/30 days	201304
lorlatinib (Lorbrena)	25 mg tablets		90 tablets/30 days	204668
	100 mg tablets		30 tablets/30 days	204669

Initial Evaluation

I. Crizotinib (Xalkori), ceritinib (Zykadia), alectinib (Alecensa), brigatinib (Alunbrig), and lorlatinib (Lorbrena) may be considered medically necessary when the following criteria below are met:
   A. The medication is prescribed by, or in consultation with, an oncologist; **AND**
   B. The medication will not be used in combination with other agents and will be used as monotherapy for the diagnosis submitted; **AND**
   C. The member has metastatic (stage IV) disease; **AND**
   D. A diagnosis of one of the following:
      1. **ALK+ Non-Small Cell Lung Cancer as detected by an FDA-approved test**; **AND**
         i. Alectinib (Alecensa) is prescribed unless contraindicated or not tolerated; **AND**
            a. For alectinib (Alecensa);
               i. The member has not progressed on any other agent listed in this policy; **OR**
               ii. The member has progressed on or after use of crizotinib (Xalkori)
            b. For crizotinib (Xalkori);
               i. The member has not progressed on any other agent listed in this policy
            c. For ceritinib (Zykadia);
               i. The member has not progressed on any other therapy listed in this policy; **OR**
               ii. The member has progressed on crizotinib (Xalkori)
            d. For brigatinib (Alunbrig)
               i. The member has not progressed on any other therapy listed in this policy; **OR**
               ii. The member has progressed on crizotinib (Xalkori)
            e. For lorlatinib (Lorbrena);
               i. The member has progress on alectinib (Alecensa); **OR**
               ii. The member has progressed on ceritinib (Zykadia); **OR**
               iii. The member has progressed on crizotinib (Xalkori) AND one other agent in this policy.

      OR

      2. **ROS1+ Non-Small Cell Lung Cancer as detected by an FDA-approved test**; **AND**
         i. The request is for crizotinib (Xalkori)

II. Crizotinib (Xalkori), ceritinib (Zykadia), alectinib (Alecensa), brigatinib (Alunbrig), and lorlatinib (Lorbrena) are considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:

A. ROS1+ NSCLC for any agent in this policy except for crizotinib (Xalkori)
B. NSCLC prior to the metastatic setting, or outside of the ROS1+ or ALK mutation (e.g., RET-rearranged NSCLC)
C. NSCLC in combination with other therapies
D. Thyroid cancer
E. Melanoma
F. Gastrointestinal cancer
G. Prostate cancer
H. Leukemias or lymphomas
I. Urothelial cancer

Renewal Evaluation

I. The medication is prescribed by, or in consultation with, an oncologist; **AND**
II. The medication continues to be used as monotherapy for ALK+ or ROS1+ NSCLC; **AND**
III. There is documentation of disease response with treatment, defined by stabilization of disease or decrease in tumor size or tumor spread.

Supporting Evidence

I. There is currently no evidence for safety and efficacy of any of these agents in combination with another ALK inhibitor, or in combination with any other therapies for the treatment of non-small-cell lung cancer. Any open prior authorizations for other ALK-inhibitors will be closed if coverage is approved an agent in this policy. These agents have only been studied in the metastatic and adult populations in clinical trials.
II. Alectinib (Alecensa) has been evaluated in the first-line setting for metastatic ALK+ NSCLC, or after progression on crizotinib (Xalkori). A class review was done in 2018 which revealed advantages with alectinib (Alecensa) including superior head-to-head progression-free survival (PFS), intracranial response compared to crizotinib, and a more favorable safety profile via indirect comparison. Alectinib (Alecensa) is the preferred agent for first-line treatment per the National Comprehensive Cancer Network (NCCN) for the treatment of ALK-positive NSCLC. Alectinib (Alecensa) has been evaluated after progression on crizotinib (Xalkori) or lorlatinib (Lorbrena); however, safety and efficacy after progression on ceritinib (Zykadia) and/or brigatinib (Alunbrig) are unknown.
III. In the second line setting, several agents have been evaluated after progression on crizotinib (Xalkori). Lorlatinib (Lorbrena) is the only agent at this time that has been evaluated in the third line setting following progression on crizotinib (Xalkori) and one other ALK+ TKI for NSCLC.
IV. Lorlatinib (Lorbrena) received its FDA-approval for second or greater line therapy in the metastatic setting of non-small cell lung cancer. As of July 2019, a phase III clinical trial was in the enrollment stage to determine the comparative efficacy against crizotinib (Xalkori).

V. Crizotinib (Xalkori) is currently FDA-approved for ROS1+ NSCLC. Several other agents are being evaluated in clinical trials; however, safety and efficacy data was not available as of July 2019.
VI. Brigatinib (Alunbrig) was evaluated in an open-label, Phase 3, randomized trial against crizotinib (Xalkori) in metastatic ALK+ NSCLC. The study included 275 subjects, and those receiving brigatinib (Alunbrig) had a greater PFS (12-month PFS was 67% versus 43%; HR 0.49, p<0.001). The intracranial response was 78% for brigatinib (Alunbrig) and 29% for crizotinib (Xalkori). The data is not considered of high quality due to open label trial design, and lack of clinical significant outcomes such as overall survival and quality of life parameters.
VII. There is currently no evidence that ALK-inhibitors improve clinical outcomes (e.g., overall survival, quality of life) in patients with NSCLC. Although PFS data is promising, PFS is a surrogate endpoint in NSCLC that has not been correlated with improved outcomes.

Investigational or Not Medically Necessary Uses

I. The agents in this policy have not been sufficiently evaluated in the following settings. There may be NCCN recommendations or low quality data available; however, safety and efficacy have not been established for:
   A. ROS1+ NSCLC for any agent in this policy except for crizotinib (Xalkori)
   B. NSCLC prior to the metastatic setting, or outside of the ROS1+ or ALK mutation (e.g., RET-rearranged NSCLC)
   C. NSCLC in combination with other therapies
   D. Thyroid cancer
   E. Melanoma
   F. Gastrointestinal cancer
   G. Prostate cancer
   H. Leukemias or lymphomas
   I. Urothelial cancer

References

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Policy Implementation/Update:

Date Created	December 2011
Date Effective	December 2011
Last Updated	July 2019
Last Reviewed	12/2012, 09/2014, 12/2015, 06/2017, 01/2018, 02/2019, 07/2019

Action and Summary of Changes	Date
Criteria update: Transitioned prior authorization criteria to policy format and consolidated all agents into one policy. Brigatinib now allowed for first-line setting if member has CI or intolerance to preferred therapy. Quantity level limits updated to reflect currently available products and package sizes. Addition of Zykadia tablets that are available in addition to the capsules.	07/2019
Criteria updates: Crizotinib updated criteria to new format, moved new start versus continuation question up. Updated prescriber question to fit current format, updated and added a question regarding both of the FDA-approved indications. Added a question regarding other therapies tried and failed or contraindicated. Zykadia updated to new format, deleted try and fail crizotinib question as this agent can now be used first line, added try and fail alectinib question, as per class review this is Moda Health's preferred agent. Removed age question, removed LFT question, QT prolongation question, and placed new versus continuation question up front. Alecensa criteria updated criteria to new format, deleted try and fail crizotinib question as this agent can now be used first line, removed age question. Alunbrig criteria updated to add question regarding prescribed and preferred therapy.	01/2018