Pharmacy Policy Bulletin: J-0877 ALK-Targeting Kinase Inhibitors - Commercial and Healthcare Reform	
Number: J-0877	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes with Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0877-013	**Original Date:** 06/04/2003
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Alecensa (alectinib) • Alunbrig (brigatinib) • Ensacove (ensartinib) • Lorbrena (lorlatinib) • Xalkori (crizotinib) • Zykadia (ceritinib)

FDA-Approved Indication(s):	• Alecensa (alectinib)
	  ○ Treatment of adult patients with anaplastic lymphoma kinase (*ALK*)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.
	  ○ Adjuvant treatment in adult patients following tumor resection of *ALK*-positive NSCLC (tumors ≥ 4 cm or node positive) as detected by an FDA-approved test.
	• Alunbrig (brigatinib)
	  ○ Treatment of adult patients with *ALK*-positive metastatic NSCLC as detected by an FDA-approved test.
	• Ensacove
	  ○ Treatment of adult patients with *ALK*-positive locally advanced or metastatic NSCLC who have not previously received an ALK-inhibitor.
	• Lorbrena (lorlatinib)
	  ○ Treatment of adult patients with metastatic NSCLC whose tumors are *ALK*-positive as detected by an FDA-approved test.
	• Xalkori (crizotinib)
	  ○ Treatment of adult patients with metastatic NSCLC whose tumors are *ALK*– or *ROS1*-positive as detected by an FDA-approved test.
	  ○ Treatment of pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is *ALK*-positive.
	  ○ Treatment of adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is *ALK*-positive.

	• Zykadia (ceritinib) ○ Treatment of adults with metastatic NSCLC whose tumors are *ALK*-positive as detected by an FDA-approved test.

Background:	• Alecensa (alectinib) is a tyrosine kinase inhibitor that blocks the activity of the ALK protein, which may prevent NSCLC cells from growing and spreading.
	• Alunbrig (brigatinib) is a kinase inhibitor with activity against multiple kinases including ASLK, ROS1, insulin-like growth factor-1 receptor, FLT-3 as well as EGFR deletion and point mutations. Alunbrig inhibited the viability of cell expressing EML4-ALK and 17 mutant forms associated with resistance to ALK inhibitors including crizotinib.
	• Ensacove is an inhibitor of ALK and other kinases including Mesenchymal Epithelial Transition (MET) and ROS proto-oncogene 1 (ROS1). Ensacove inhibits the phosphorylation of ALK and its downstream signaling proteins. This blocks ALK-mediated signaling pathways and inhibits proliferation in cell lines harboring ALK fusions and mutations.
	• Xalkori (crizotinib) inhibits the ALK and mesenchymal endothelial transition factor tyrosine kinases. It inhibits the proliferation of ALK-positive cells, resulting in gap1-S-phase cell cycle arrest and cellular apoptosis. Xalkori was evaluated in Study ADVL0912 (NCT00939770), in which patients were 1 to ≤ 21 years of age with relapsed or refractory, systemic ALK-positive ALCL after at least one systemic treatment.
	• Zykadia (ceritinib) is a kinase inhibitor. Targets of ceritinib inhibition identified in either biochemical or cellular assays at clinically relevant concentrations include ALK, insulin-like growth factor 1 receptor (IGF-1R), insulin receptor (InsR), and ROS1. Among these, ceritinib is most active against ALK. Ceritinib inhibited auto-phosphorylation of ALK, ALK-mediated phosphorylation of the downstream signaling protein STAT3, and proliferation of ALK-dependent cancer cells in in vitro and in vivo assays.
	• Lorbrena (lorlatinib) is a kinase inhibitor active against multiple kinases, including multiple mutant forms of ALK and ROS1. *ALK* and *ROS1* gene rearrangements have been identified as predictive biomarkers in a subset of patients with NSCLC. This activity may prevent NSCLC cells from growing and spreading.
	• FDA-approved tests for *ALK*-positive tumor specimens include FoundationOne CDx and VENTANA ALK (D5F3) CDx Assay. Oncomine Dx Target Test is an FDA-approved test for *ROS1*-positive fusions. For additional information regarding FDA-approved companion diagnostics, please visit: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools.
	• Prescribing Considerations:
	  ○ Alunbrig
	  ▪ Avoid co-administration of Alunbrig with strong or moderate CYP3A inhibitors. If co-administration of a strong or moderate CYP3A inhibitor is unavoidable, reduce the dose of Alunbrig.
	  ▪ Avoid co-administration of Alunbrig with strong or moderate CYP3A inducers. If co-administration of a moderate CYP3A inducer is unavoidable, increase the dose of Alunbrig.
	  ○ Ensacove
	  ▪ Ensacove should be avoided with strong or moderate CYP3A inhibitors, strong or moderate CYP3A inducers and P-gp inhibitors.
	  ○ Lorbrena
	  ▪ *CYP3A Inducers*: Lorbrena is contraindicated in patients taking strong CYP3A inducers. There is a risk of serious hepatotoxicity if Lorbrena is used with a strong CYP3A inducer. Concomitant

	use of Lorbrena with moderate CYP3A inducers should be avoided. ▪ *CYP3A Inhibitors*: Concomitant use of Lorbrena with moderate CYP3A inhibitors should be avoided. If concomitant use cannot be avoided, starting dose of Lorbrena should be reduced from 100 mg orally once daily to 75 mg orally once daily. • In patients who have had a dose reduction to 75 mg orally once daily due to adverse reactions and who start a strong CYP3A inhibitor, dose of Lorbrena should be reduced to 50 mg orally once daily. ○ Xalkori ▪ The safety and efficacy of Xalkori have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL. ▪ A recommended dose of Xalkori oral capsules has not been established in patients with a body surface area < 1.34 m^2.

Approval Criteria

I. Initial Authorization

A. Alecensa

When a benefit, coverage of Alecensa may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member meets one (1) of the following criteria **(a. or b.)**:

a. The member has a diagnosis of metastatic NSCLC (ICD-10: C34).

b. The member has a diagnosis of NSCLC (ICD-10: C34) and meets all of the following **(i. and ii.)**:

i. Tumors ≥ 4 cm or node positive

ii. The member is using Alecensa as adjuvant treatment following tumor resection.

3. Disease is *ALK*-positive, as detected by an FDA-approved test.

B. Alunbrig

When a benefit, coverage of Alunbrig may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of metastatic NSCLC (ICD-10: C34).

3. Disease is *ALK*-positive, as detected by an FDA-approved test.

C. Ensacove

When a benefit, coverage of Ensacove may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of locally advanced or metastatic NSCLC (ICD-10: C34).

3. Disease is *ALK*-positive.

4. The member has not previously received an ALK-inhibitor.

D. Lorbrena

When a benefit, coverage of Lorbrena may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of metastatic NSCLC (ICD-10: C34).

3. Disease is *ALK*-positive, as detected by an FDA-approved test.

E. Xalkori

1. **NSCLC** (ICD-10: C34)
   When a benefit, coverage of Xalkori may be approved when all of the following criteria are met **(a. through d.)**:
   - **a.** The member is 18 years of age or older.
   - **b.** The member has a diagnosis of metastatic non-small cell lung cancer (NSCLC).
   - **c.** The member meets one (1) of the following criteria **(i. or ii.)**:
     - **i.** Disease is *ALK*-positive as detected by an FDA-approved test.
     - **ii.** Disease is *ROS1*-positive as detected by an FDA-approved test.
   - **d.** If the request is for Xalkori oral pellets, the member has an inability to swallow oral capsules.

2. **ALCL** (ICD-10: C84.6)
   When a benefit, coverage of Xalkori may be approved when all of the following criteria are met **(a. through d.)**:
   - **a.** The member is 1 to 21 years of age.
   - **b.** The member has a diagnosis of relapsed or refractory systemic ALCL.
   - **c.** Disease is *ALK*-positive.
   - **d.** If the request is for Xalkori oral pellets, the member meets one (1) of the following **(i. or ii.)**:
     - **i.** The member has a body surface area < 1.34 m^2.
     - **ii.** The member has an inability to swallow oral capsules.

3. **IMT** (ICD-10 D48.7)
   When a benefit, coverage of Xalkori may be approved when all of the following criteria are met **(a. through d.):**
   - **a.** The member is 1 year of age or older.
   - **b.** The member has a diagnosis of unresectable, recurrent, or refractory IMT.
   - **c.** Disease is *ALK*-positive.
   - **d.** If the request is for Xalkori oral pellets, the member meets one (1) of the following **(i. or ii.)**:
     - **i.** The member has a body surface area < 1.34 m^2.
     - **ii.** The member has an inability to swallow oral capsules.

F. Zykadia
When a benefit, coverage of Zykadia may be approved when all of the following criteria are met **(1., 2., and 3.)**:
1. The member is 18 years of age or older.
2. The member has a diagnosis of metastatic NSCLC (ICD-10: C34).
3. Disease is *ALK*-positive as detected by an FDA-approved test.

II. Reauthorization
When a benefit, reauthorization of an ALK-targeting kinase inhibitor may be approved when the following criterion is met **(A.)**:
- **A.** The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:
  1. Disease improvement
  2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology drug(s) listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

Refer to J-879 and J-699 and J-848 for previous versions.

References:

1. Alecensa [package insert]. South San Francisco, CA: Genentech; April 2024.
2. Alunbrig [package insert]. Cambridge, MA: Ariad Pharmaceuticals, Inc.; February 2022.
3. Ensacove [package insert]. Miami, FL: Xcovery Holdings, Inc. December 2024.
4. Lorbrena [package insert]. New York, New York: Pfizer, Inc.; March 2021.
5. Xalkori [package insert]. New York, New York: Pfizer, Inc.; September 2023.
6. Zykadia [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2021.
7. U.S. Food and Drug Administration. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). Available at: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools. Accessed June 30, 2025.