BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ENSACOVE™ (ensartinib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for ENSACOVE (ensartinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
-
- Anaplastic lymphoma kinase (ALK) positive locally advanced or recurrent (stage IIIB not amenable for multimodality treatment) metastatic (stage IV) nonsmall cell lung cancer (NSCLC) who have not previously received an ALK inhibitor

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- Other oncologic direct treatment use listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Documentation of presence of ALK rearrangement(s) in tumor specimens
- Liver function tests
- Fasting blood glucose
- Negative pregnancy test in a woman of childbearing potential
- Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety
- **NONE** of the following:
  - Concomitant drug use with:
    1. Strong or moderate CYP3A inhibitors
    2. Strong or moderate CYP3A inducers
    3. P glycoprotein (P gp) inhibitors
  - Hypersensitivity reaction to Ensacove, FD&C Yellow No. 5 (tartrazine), or any of its components
  - Severe hepatic impairment (total bilirubin greater than 3 times ULN and any AST)
  - Primary central nervous system (CNS) tumor and leptomeningeal disease

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (ALK rearrangement, liver function, fasting glucose, pregnancy test, ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

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Prescriber Qualifications
- Continues to be seen by a physician specializing in or is in consultation with an Oncologist

Clinical Response
- No disease progression or unacceptable drug toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented
- Requested dose is at least 150 mg once daily

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- **NONE** of the following:
  - Concomitant drug use with:
    4. Strong or moderate CYP3A inhibitors
    5. Strong or moderate CYP3A inducers
    6. P glycoprotein (P gp) inhibitors
  - Hypersensitivity reaction to Ensacove, FD&C Yellow No. 5 (tartrazine), or any of its components
  - Severe hepatic impairment (total bilirubin greater than 3 times ULN and any AST)
  - Primary central nervous system (CNS) tumor and leptomeningeal disease
- No development of any of the following adverse effects:
  - Pneumonitis
  - Interstitial lung disease
  - Hepatotoxicity
  - Severe dermatologic reaction (drug reaction with eosinophilia systemic syndrome, rash, pruritus)
  - Bradycardia (heart rate less than 60 bpm) with life threatening consequences
  - Hyperglycemia greater than 250 mg/dL not controlled with medical management
  - Severe visual disturbances
  - Increased creatine phosphokinase (CPK)
  - Hyperuricemia
  - Other recurrent severe adverse reaction

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

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Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

Description:

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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 4.2025 – Updated May 23, 2025

ALK Rearrangement

- First-line therapy
  - Alectinib – category 1
  - Brigatinib – category 1
  - Ceritinib – category 1
  - Crizotinib – category 1
  - Ensartinib – category 1
  - Lorlatinib – category 1
- Subsequent therapy
  - Alectinib
  - Brigatinib
  - Ceritinib
  - Ensartinib
  - Lorlatinib

Patients who are intolerant to crizotinib may be switched to alectinib, brigatinib, ceritinib, ensartinib, or lorlatinib

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Resources:

Ensacove (ensartinib) product information, revised by Xcovery Holdings, Inc. 12-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 20, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 4.2025 – Updated May 23, 2025. Available at https://www.nccn.org. Accessed June 20, 2025.

Horn L, Wang Z, Wu G, et al.: Ensartinib vs Crizotinib for Patients With Anaplastic Lymphoma Kinase−Positive Non–Small Cell Lung Cancer A Randomized Clinical Trial. Available at JAMA Oncology 2021; 7(11):1617-1625. Accessed June 20, 2025

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT02767804: Phase 3 Randomized Study Comparing X-396 (Ensartinib) to Crizotinib in Anaplastic Lymphoma Kinase (ALK) Positive Non-Small Cell Lung Cancer (NSCLC) Patients. Available from: http://clinicaltrials.gov. Last update posted August 20, 2024. Last verified August 2024. Accessed June 20, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.