New Drug Overview

Ensacove (ensartinib)

RDL Category: Antineoplastics

Introduction

Disease Background:

- The most common lung cancer, accountable for the greatest number of cancer deaths in the world, includes non-small cell lung cancers (NSCLC). This malignant tumor of the lung accounts for approximately 85-90% of lung cancer occurrences (*Eapen et al 2026*).
- Chromosomal rearrangements comprising the anaplastic lymphoma kinase (ALK) gene have been identified in approximately 3% to 11% of NSCLCs (*Horn et al 2021*).
- Genetic predisposition and environmental exposures are listed as risk factors for NSCLC, but tobacco use is a main risk factor (*Eapen et al 2026*).
  - The Surgeon General has reported that both active smoking and second-hand smoke can cause lung cancer (*NCCN 2026*).
- This cancer generally affects older adults ≥65 years of age, and men are more commonly diagnosed with lung cancer as compared with women (*Eapen et al 2026*).
- While roughly 25% of patients can be asymptomatic, common symptoms of lung cancer comprise of cough, dyspnea, chest pain, hemoptysis, wheezing, and nonspecific chest discomfort or pleuritic chest pain (*Eapen et al 2026*).
- Ensacove (ensartinib) was FDA approved in 2024

Pharmacology/Usage

- Ensacove (ensartinib) is a kinase inhibitor of anaplastic lymphoma kinase (ALK) and inhibits other kinases include MET and ROS1.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Ensacove (ensartinib)
• For the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive locally advanced or metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test who have not previously received an ALK-inhibitor.	✔

(Prescribing information: Ensacove 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Ensacove (ensartinib)	Capsules: 25mg and 100mg.	PO	225mg PO QD, with or without food until disease progression or unacceptable toxicity.	• Select patients for the treatment of locally advanced or metastatic NSCLC with Ensacove

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
	-Swallow capsules whole; do not crush or chew. Do not open or dissolve the contents of the capsule.		-Take at the same time each day.	based on the presence of ALK rearrangement(s) in tumor specimens. Information on FDA-approved tests for the detection of ALK rearrangements in NSCLC is available online. • Prior to starting Ensacove, evaluate liver function tests and fasting blood glucose. • If a dose is missed, then take the missed dose as soon as possible unless the next dose is due within 12 hours. Do not take 2 doses on the same day. • If vomiting occurs after taking a dose, do not take an additional dose and take the next dose at its scheduled time. • Dosage modifications for adverse reactions can be found in the prescribing information. • Avoid use of Ensacove for patients with severe hepatic impairment. Monitor patients with moderate hepatic impairment for increased adverse reactions and adjust Ensacove dosage as clinically indicated.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Ensacove was assessed in an open-label, randomized, active-controlled, multicenter study (eXALT3) that included adult patients with locally advanced (stage IIIB following prior chemotherapy or chemoradiation or not amenable to curative intent therapy) or metastatic ALK-positive NSCLC. Patients were required to have ALK-positive NSCLC in tumor specimens. Patients could have received one prior regimen of chemotherapy but could not have previously received an ALK-targeted therapy; patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2 were eligible. Patients with asymptomatic, untreated brain metastases who were not on corticosteroids and patients with asymptomatic, treated brain metastases who were on stable or decreasing dose of corticosteroids were eligible. Patients were required to have completed radiation therapy at least 2 weeks, or chemotherapy at least 4 weeks, prior to enrollment.
  - Patients were randomized to receive Ensacove 225mg QD or crizotinib 250mg PO BID in 28-day cycles until disease progression or unacceptable toxicity.
    - A total of 290 patients were randomized. The baseline demographic characteristics of the overall study population included a median age of 54 years (range 25-90), while 16% were >65 years of age. In addition, 51% were male, 56% were Asian, 62% were never smokers, 95% had ECOG performance status 0 or 1, 32% had received prior chemotherapy, and 17% had received prior radiation.
  - The main efficacy outcome measure was progression-free survival (PFS) as assessed by Blinded Independent Central Review (BICR) per RECIST version 1.1. The key secondary efficacy outcome measure was overall survival (OS), and other secondary outcome measures included CNS response rate, time to CNS progression, and overall response rate (ORR).
    - This study demonstrated a statistically significant improvement in PFS for patients randomized to Ensacove compared to patients randomized to crizotinib.
    - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

	Ensacove N=143	Crizotinib N=147
Progression-free survival		
Number of events, n (%)	59 (41%)	80 (54%)
Progressive disease, n (%)	51 (36%)	77 (52%)
Death, n (%)	8 (6%)	3 (2%)
Median, months	25.8	12.7
Hazard Ratio; p-value	0.56; p=0.0008	
Overall response rate		

	Ensacove N=143	Crizotinib N=147
Overall response rate, %	74%	67%
Complete response, %	12%	5%
Partial response, %	62%	61%
Duration of response		
Number of responders, n	106	98
Median, months	Not estimable	27.3

- At the time of the primary PFS analysis, OS results were immature. At the time of final analysis of OS, there was no statistically significant difference (p=0.4570) between Ensacove and crizotinib. Median OS was 63.2 months in the Ensacove arm and 55.7 months in the crizotinib arm, with the HR of 0.88.
- Results of the pre-specified analyses of CNS response rate by BICR in patients with baseline measurable CNS disease are presented in the table below, which was adapted from the prescribing information.

Table 4. Efficacy results

Efficacy parameter	Ensacove N=17	crizotinib N=24
CNS overall response rate, %	59%	21%
Complete response, %	24%	8%
Partial response, %	35%	13%
Duration of Response (DOR)		
Number of responders, n	10	5
Patients with DOR ≥12 months	30%	40%

Clinical guidelines

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer** (*NCCN 2026).*
  - Ensartinib has been added to the updated NSCLC guideline.
  - For ALK gene fusion discovered prior to first-line systemic therapy, ensartinib (category 1) is listed as preferred first-line therapy. If ALK gene fusion is discovered during first-line systemic therapy, interrupt current therapy and start a preferred treatment. Ensartinib is listed as a preferred treatment.
  - For ALK gene fusion, with progression, ensartinib is listed, as well as with progression on crizotinib, as subsequent therapy.

Safety summary

- **Contraindications:**
  - In patients who have experienced a severe hypersensitivity reaction to Ensacove, FD&C Yellow No. 5 (tartrazine), or to any of its components.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Ensacove can cause severe interstitial lung disease (ILD)/pneumonitis.
    - Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis during Ensacove treatment. Immediately withhold Ensacove in patients with suspected ILD/pneumonitis. Permanently discontinue Ensacove if ILD/pneumonitis is confirmed.
  - Ensacove can cause hepatotoxicity including drug-induced liver injury. The median time to first onset of increased ALT or AST was 5.3 weeks.
    - Monitor liver function tests including ALT, AST, and total bilirubin at baseline and every 2 weeks during the first cycle of treatment with Ensacove, and then monthly and as clinically indicated. Withhold, reduce the dose, or permanently discontinue Ensacove based on the severity of the adverse reaction.
  - Ensacove can cause dermatologic adverse reactions, including drug reaction with eosinophilia and systemic symptoms (DRESS), rash, pruritus, and photosensitivity.
    - Monitor patients for dermatologic adverse reactions during Ensacove treatment. If dermatologic adverse reactions occur, treat with antihistamine, topical or systemic steroids based on the severity. Advise patients to limit direct sun exposure while taking Ensacove and for at least 1 week after discontinuation. Withhold, reduce the dose, or permanently discontinue Ensacove based on the severity of the adverse reaction.
  - Ensacove can cause symptomatic bradycardia.
    - Monitor heart rate regularly during Ensacove treatment. Withhold, reduce the dose, or permanently discontinue Ensacove based on severity.
  - Ensacove can cause hyperglycemia.
    - Assess fasting serum glucose at baseline and monitor serum glucose periodically during treatment with Ensacove. Withhold, reduce the dose, or permanently discontinue Ensacove based on severity.
  - Ensacove can cause visual disturbances including blurred vision, diplopia, photopsia, vitreous floaters, visual impairment, visual field defect, and reduced visual acuity.
    - Obtain an ophthalmologic evaluation in patients with new or worsening visual symptoms during Ensacove treatment. Withhold, reduce the dose, or permanently discontinue Ensacove based on severity.
  - In the pooled safety population, of the 203 patients with creatine phosphokinase (CPK) laboratory data available, increased CPK occurred in 43% of patients who received Ensacove. The incidence of Grade 3 increased CPK was 1.5% and 0.5% were Grade 4. The median time to onset of increased CPK was 123 days. Increased CPK leading to dose interruption occurred in 0.2% and dose reduction in 0.4%.
    - Advise patients to report any unexplained muscle pain, tenderness, or weakness. Monitor CPK levels during treatment with Ensacove. Withhold, reduce the dose, or permanently discontinue Ensacove based on severity.
  - Ensacove can cause hyperuricemia.
    - Monitor serum uric acid levels prior to starting Ensacove and periodically during treatment. Initiate treatment with urate-lowering medications as clinically indicated. Withhold, reduce the dose, or permanently discontinue Ensacove based on severity.

- This product contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Ensacove) minus reported % incidence for crizotinib for all grades. Please note that an incidence of 0% means the incidence was the same as or less than comparator.
    - The most frequently reported adverse events included rash (56%), pruritus (25.9%), alopecia (6.2%), dry skin (9.3%), musculoskeletal pain (16%), cough (15%), constipation (5%), nausea (0%), vomiting (0%), edema (0%), pyrexia (12%), fatigue (7%), decreased appetite (3%), respiratory tract infection (3%), dizziness (0%), dysgeusia (0%), and hemorrhage (5.2%).
    - Laboratory abnormalities include alanine aminotransferase increased (0%), alkaline phosphatase increased (14%), aspartate aminotransferase increased (2%), glucose increased (14%), albumin decreased (0%), phosphate decreased (0%), urate increased (12%), creatinine increased (10%), calcium decreased (0%), sodium decreased (0%), lymphocytes decreased (10%), and hemoglobin decreased (12%).

- **Drug interactions:**
  - Avoid concomitant use of strong or moderate CYP3A inhibitors with Ensacove.
  - Avoid concomitant use of strong or moderate CYP3A inducers with Ensacove.
  - Avoid concomitant use of P-gp inhibitors with Ensacove.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that based on findings from animal studies and its mechanism of action, Ensacove can cause fetal harm when administered to a pregnant woman. There are no available data on use in pregnant women to inform a drug-associated risk. Advise pregnant women of the potential risk to a fetus.
    - Verify the pregnancy status of females of reproductive potential prior to starting Ensacove.
    - Advise females of reproductive potential to use effective contraception during treatment with Ensacove and for 1 week after the last dose.
    - Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Ensacove and for 1 week after the last dose.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- The most common lung cancer, accountable for the greatest number of cancer deaths in the world, includes non-small cell lung cancers (NSCLC). This malignant tumor of the lung accounts for approximately 85-90% of lung cancer occurrences (*Eapen et al 2026*).
- Ensacove is a kinase inhibitor indicated for the treatment of adult patients with ALK-positive locally advanced or metastatic NSCLC as detected by an FDA-approved test who have not previously received an ALK-inhibitor.
- Prior to starting Ensacove, assess liver function tests and fasting blood glucose.
- The efficacy of Ensacove was assessed in an open-label, randomized, active-controlled study that included patients required to have ALK-positive NSCLC.
  - The main efficacy outcome measure was PFS, and results demonstrated a statistically significant improvement in PFS for patients randomized to Ensacove compared to patients randomized to crizotinib.

- NCCN guidelines have been updated to include Ensacove (ensartinib).

- It is recommended that Ensacove should be non-recommended with conditions in order to confirm the appropriate diagnosis and clinical parameters for use.

- **RDL Placement:**
  - ☐ Recommended
  - ☒ Non-Recommended with conditions

References

- Eapen GA, Weiss KS, Ko YJ, et al. Non-small cell lung cancer. Dynamed Web site. Updated May 1, 2026. Accessed June 2, 2026. www.dynamed.com.
- Ensacove. Package insert. Xcovery Holdings, Inc; February 2026.
- 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. *JAMA Oncol.* 2021; 7(11): 1617-1625.
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. V5.2026-March 13, 2026. Accessed June 2, 2026. nscl.pdf.

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