New Drug Overview

Hyrnuo (sevabertinib)

PDL 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 2024*).
- There are two subtypes of non-small cell carcinoma, including non-squamous carcinoma (adenocarcinoma and large cell carcinoma) and squamous cell carcinoma (*Eapen et al 2024*).
- It has been reported from real-world studies that mutations in human epidermal growth factor receptor 2 (HER2; which is also known as ErbB-2 receptor tyrosine kinase 2 [ERBB2] are found in about 2 to 4% of NSCLCs (*Heymach et al 2025*).
- Genetic predisposition and environmental exposures are listed as risk factors for NSCLC, but tobacco use is a main risk factor (*Eapen et al 2024*).
  - The Surgeon General has reported that both active smoking and second-hand smoke can cause lung cancer (*NCCN 2025*).
- 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 2024*).
- 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 2024*).
- Hyrnuo was FDA approved in 2025.

Pharmacology/Usage

- Hyrnuo (sevabertinib) is a kinase inhibitor.
  - It is a reversible kinase inhibitor of human epidermal growth factor receptor 2 (HER2).
  - It also exhibits activity against epidermal growth factor receptor (EGFR).

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Hyrnuo (sevabertinib)
• For the treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) whose tumors have *HER2* (*ERBB2*) tyrosine kinase domain (TKD) activating mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy. *	✔

***This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.**

(Prescribing information: Hyrnuo 2025)

- 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
Hyrnuo (sevabertinib)	Film-Coated Tablets -Swallow tablets whole; do not cut, crush, or chew tablets.	PO	BID with food, until disease progression or unacceptable toxicity.	• Select patients for treatment of locally advanced or metastatic non-squamous NSCLC based on the presence of *HER2* (*ERBB2)* TKD activating mutations in tumor specimens. Information on FDA-approved tests is available online. • If a dose is vomited, do not take an additional dose. Resume dosing at the next scheduled time. • There are recommended dosage reductions for adverse reactions.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Hyrnuo was assessed in an open-label, single-arm, multicenter, multicohort study (SOHO-01) where eligible patients (Groups D and E) were required to have previously treated locally advanced or metastatic NSCLC with *HER2* (*ERBB2*) activating mutations and have an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1.
  - Patients with treated, stable, and asymptomatic brain metastases were eligible.
- Patients received Hyrnuo 20mg twice daily until disease progression or unacceptable toxicity.
  - The efficacy population included patients from Group D (N=70) and from Group E (N=52), with advanced non-squamous NSCLC with *HER2* (*ERBB2*) TKD activating mutations based on prospective local testing.
    - Of the 122 patients in these combined cohorts, tumor tissue samples from 67.2% (82/122) of patients were tested retrospectively. While 92.7% (76/82) of samples were positive for *HER2* (*ERBB2*) TKD activating mutations, 7.3% (6/82) were unevaluable, and there were no samples with negative status for *HER2* (*ERBB2*) TKD activating mutations.
- *In NSCLC Previously treated, Naïve to HER2-Targeted Therapy: Group D:*
  - Efficacy was assessed in patients (N=70) with locally advanced or metastatic non-squamous NSCLC with *HER2* (*ERBB2*) TKD activating mutations who had received prior systemic therapy but were naïve to therapy targeting *HER2* mutations.
  - Baseline demographic and disease characteristics of the efficacy population included patients with a median age of 59 years (range 29 to 77 years), while 67% were female and 70% were Asian. Patients had an ECOG PS of either 0 (39%) or 1 (61%), while 69% were never-smokers, 29% were former smokers, and 2.9% were current smokers. Ninety-one percent of patients had stage IV disease and 20% had stable brain metastases. The median number of prior therapies was 1 (range 1 to 8).

- Efficacy results for SOHO-01 Group D are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

Efficacy Parameter	Hyrnuo
Objective Response Rate (ORR)	71%
Complete Response	2.9%
Partial Response	69%
Duration of Response (DOR)	N=50
Median, months	9.2
DOR ≥6 months	54%
DOR ≥12 months	18%

- *In NSCLC Previously treated, including Prior HER2 Targeted Antibody Drug Conjugates (ADCs): Group E:*
  - Efficacy was assessed in patients (N=52) with locally advanced or metastatic non-squamous NSCLC with *HER2* (*ERBB2*) TKD activating mutations who had received prior systemic therapy including HER2- targeted ADCs.
  - Baseline demographic and disease characteristics of the efficacy population included patients with a median age of 65 years (range 35 to 91 years), while 67% were female and 62% were Asian. Patients had an ECOG PS of either 0 (29%) or 1 (71%), while 65% were never-smokers and 35% were former smokers. Eighty-five percent of patients had stage IV disease and 29% had stable brain metastases. The median number of prior therapies was 2 (range 1 to 8).
  - The ORR was 38%, with 6% of patients having a complete response and 33% of patients having a partial response.
  - The median DOR was 7 months, ranging from 1+ to 17.2+ months based on the observed DOR.
  - The observed proportion of responding patients with DOR of ≥6 months and ≥12 months was 60% and 10%, respectively.

Clinical guidelines

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines): Non-Small Cell Lung Cancer** (*NCCN 2025*).
  - This guideline was last updated in December of 2025, but sevabertinib was added into the guideline in a prior version.
  - Sevabertinib was added into the review and listed as a preferred subsequent treatment option for advanced or metastatic NSCLC with *ERBB2* (*HER2*) mutations when have received prior systemic therapy.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**

- Hyrnuo can cause severe diarrhea that can lead to dehydration and electrolyte imbalances. The median time to first onset of any grade diarrhea was four days.
  - At the first sign of diarrhea or increased bowel movement frequency, instruct patients to start an antidiarrheal treatment (eg, loperamide [refer to full prescribing information]), and to increase their fluid and electrolyte intake. Interrupt, reduce the dose, or permanently discontinue Hyrnuo based on severity.
- Hyrnuo can cause severe hepatotoxicity described by elevations of liver function tests.
  - Monitor liver function tests including ALT, AST, and total bilirubin at baseline prior to the first administration of Hyrnuo, every 2 weeks for the first month, and then monthly thereafter as clinically indicated, with more frequent testing in patients who develop transaminase elevations. Interrupt, reduce the dose, or permanently discontinue Hyrnuo based on the severity of the adverse reaction.
- Hyrnuo can cause severe interstitial lung disease (ILD)/pneumonitis.
  - Monitor patients for new or worsening symptoms indicative of IDL/pneumonitis. Discontinue Hyrnuo upon confirmation of ILD/pneumonitis.
- Hyrnuo can cause ocular toxicity.
  - Promptly refer patients presenting with new or worsening eye symptoms to an ophthalmologist. Interrupt, reduce the dose or permanently discontinue Hyrnuo based on severity.
- Hyrnuo can cause elevations of amylase and lipase levels.
  - Monitor amylase and lipase regularly during treatment with Hyrnuo. Interrupt, reduce the dose, or permanently discontinue Hyrnuo based on severity.

- **Common adverse drug reactions**: Listed % incidence for adverse drug reactions= reported % incidence for drug (Hyrnuo) for all grades. Please note that there was no placebo data to compared with in the prescribing information.
  - The most frequently reported adverse events included diarrhea (87%), stomatitis (29%), nausea (21%), vomiting (15%), abdominal pain (10%), rash (66%), paronychia (33%), dry skin (20%), pruritus (14%), decreased appetite (18%), weight decreased (19%), fatigue (13%), ocular toxicity (16%), and dyspnea (10%).
  - Select laboratory abnormalities for all grades include hemoglobin decreased (47%), lymphocyte count decreased (32%), white blood cell decreased (21%), lipase increased (48%), potassium decreased (45%), aspartate aminotransferase increased (41%), magnesium decreased (40%), alanine aminotransferase increased (37%), glucose increased (36%), albumin decreased (32%), amylase increased (31%), calcium decreased (28%), creatinine increased (27%), sodium decreased (26%), alkaline phosphatase increased (24%), and triglycerides increased (22%).

- **Drug interactions:**
  - Sevabertinib is a CYP3A substrate.
    - Avoid concomitant use of Hyrnuo with strong CYP3A inhibitors. If concomitant use cannot be avoided, reduce Hyrnuo dosage.
    - Monitor patients for increased Hyrnuo-associated adverse reactions.
    - Avoid concomitant use of Hyrnuo with strong or moderate CYP3A inducers.
  - Sevabertinib is a weak to moderate CYP3A inhibitor.
    - Avoid concomitant use of Hyrnuo with CYP3A substrates where minimal increases in the concentration may lead to serious adverse reactions unless otherwise recommended in the prescribing information of the CYP3A substrate.
  - Sevabertinib is a P-gp inhibitor.
    - Refer to the prescribing information for P-gp substrates where minimal increases in the concentration may lead to serious adverse reactions.
  - Sevabertinib is an inhibitor of CYP1A1 in vitro.
    - Refer to the prescribing information of CYP1A1 substrates.

- **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, Hyrnuo 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.
    - As Hyrnuo can cause fetal harm when administered to a pregnant woman, verify pregnancy status in females of reproductive potential prior to starting Hyrnuo.
      - Advise females of reproductive potential and advise males with female partners of reproductive potential to use effective contraception during Hyrnuo treatment and for 1 week after the last dose.
  - The safety and efficacy of use have not been established in the pediatric population.

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 2024*).
- Hyrnuo is an oral kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic non-squamous NSCLC whose tumors have *HER2* (*ERBB2*) TKD activating mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.
  - This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Dosage modifications may be required for adverse reactions or drug interactions.
- Its efficacy was assessed in an open-label, single-arm, multicenter, multi-cohort study that included patients required to have previously treated locally advanced or metastatic NSCLC with *HER2* (*ERBB2*) activating mutations and have an ECOG PS of 0 or 1.
  - Efficacy was assessed in 70 patients with locally advanced or metastatic non-squamous NSCLC with *HER2* (*ERBB2*) TKD activating mutations who had received prior systemic therapy but were naïve to therapy targeting *HER2* mutations.
    - The ORR was 71%.
  - Efficacy was also assessed in 52 patients with locally advanced or metastatic non-squamous NSCLC with *HER2* (*ERBB2*) TKD activating mutations who had received prior systemic therapy including HER2-targeted antibody drug conjugates.
    - The ORR was 38%.
- NCCN guidelines have been updated to include Hyrnuo (sevabertinib).

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

- **PDL 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 08, 2024. Accessed February 3, 2026. Non-small Cell Lung Cancer - DynaMed.

- Heymach JV, Ruiter G, Ahn MJ, et al. Zongertinib in previously treated HER2-mutant non-small cell lung cancer. *NEJM*. 2025; 392(23): 2321-2333. doi:10.1056/NEJMoa2503704.
- Hyrnuo. Package insert. Bayer HealthCare Pharmaceuticals Inc; November 2025
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. V3.2026-December 24, 2025. Accessed February 3, 2026. nscl.pdf.

Publication Date: February 2026.