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Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 19, 2025
Subject:	Hyrnuo	**Page:**	1 of 5

Last Review Date: March 6, 2026

Hyrnuo

Description

Hyrnuo (sevabertinib)

Background
Hyrnuo (sevabertinib) is a reversible kinase inhibitor of human epidermal growth factor receptor 2 (HER2). It also exhibits activity against epidermal growth factor receptor (EGFR). In vitro, Hyrnuo inhibited the phosphorylation of HER2 and downstream signaling in cancer cells with HER2 alterations and proliferation of cancer cells overexpressing wild-type HER2 or harboring HER2 mutations. In vivo, Hyrnuo demonstrated antitumor activity in subcutaneous mouse xenograft models derived from human NSCLC tumors harboring an activating HER2 exon 20 mutation (1).

Regulatory Status
FDA-approved indications: Hyrnuo is a kinase inhibitor indicated 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 (1).

Hyrnuo carries warnings regarding diarrhea, hepatotoxicity, interstitial lung disease (ILD)/pneumonitis, ocular toxicity, and pancreatic enzyme elevation. Monitor liver function tests including ALT, AST, and total bilirubin at baseline prior to administration, every 2 weeks for the first month, and then monthly thereafter as clinically indicated, with more frequent testing in patients who develop transaminase elevations. Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis. Patients with new or worsening eye symptoms should be promptly referred to an ophthalmologist. Monitor amylase and lipase regularly during treatment with Hyrnuo. Interrupt, reduce the dose, or permanently discontinue Hyrnuo based on severity (1).

Hyrnuo can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Hyrnuo and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Hyrnuo and for 1 week after the last dose (1).

The safety and effectiveness of Hyrnuo in pediatric patients less than 18 years of age have not been established (1).

Related policies
Hernexeos

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Hyrnuo may be considered **medically necessary** if the conditions indicated below are met.

Hyrnuo may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC)
    a. Tumors have HER2 (ERBB2) tyrosine kinase domain activating mutations, as detected by an FDA-approved test
    b. Patient has received a prior systemic therapy

AND ALL of the following:

1. Prescriber agrees to monitor for signs and symptoms of interstitial lung disease (ILD)/pneumonitis

2. Prescriber agrees to monitor liver function tests including ALT, AST, and total bilirubin prior to initiation, every 2 weeks during the first month, and then monthly thereafter as clinically indicated
3. Prescriber agrees to monitor patient for new or worsening eye symptoms and refer to an ophthalmologist if needed
4. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Hyrnuo and for 1 week after the last dose
5. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Hyrnuo and for 1 week after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for signs and symptoms of interstitial lung disease (ILD)/pneumonitis
3. Prescriber agrees to monitor liver function tests including ALT, AST, and total bilirubin monthly as clinically indicated
4. Prescriber agrees to monitor patient for new or worsening eye symptoms and refer to an ophthalmologist if needed
5. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Hyrnuo and for 1 week after the last dose
6. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Hyrnuo and for 1 week after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 40 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Hyrnuo (sevabertinib) is a kinase inhibitor indicated in patients for the treatment of locally advanced or metastatic non-squamous NSCLC whose tumors have HER2 (ERBB2) tyrosine kinase domain activating mutations. Hyrnuo carries warnings regarding diarrhea, hepatotoxicity, ILD/pneumonitis, ocular toxicity, pancreatic enzyme elevation, and embryo-fetal toxicity. The safety and effectiveness of Hyrnuo in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Hyrnuo while maintaining optimal therapeutic outcomes.

References

1. Hyrnuo [package Insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; November 2025.
2. NCCN Drugs & Biologics Compendium® Sevabertinib 2026. National Comprehensive Cancer Network, Inc. Accessed on November 20, 2026.

Policy History

Date	Action
December 2025	Addition to PA
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.