zidesamtinib (Jideytro™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO352

Split Fill Management*

Description

Zidesamtinib (Jideytro) is an orally administered selective ROS1 tyrosine kinase inhibitor (TKI).

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
zidesamtinib (Jideytro)	Advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) after a prior ROS1 kinase inhibitor	100 mg tablets	30 tablets/30 days
		25 mg tablets	90 tablets/30 days

Initial Evaluation

I. **Zidesamtinib (Jideytro)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   B. Medication is not used in combination with any other oncology therapy; **AND**
   C. A diagnosis of **non-small cell lung cancer (NSCLC)** when the following are met:
      1. Confirmation of a ROS1-positive mutation; **AND**
      2. The disease is advanced (Stage III) or metastatic (IV); **AND**
         i. There is no evidence of central nervous system (CNS) metastases; **AND**
            a. Treatment with at least one agent from each group has been ineffective, not tolerated, or ineffective:
               i. Group 1: entrectinib (Rozlytrek)* or crizotinib (Xalkori)*
               ii. Group 2: repotrectinib (Augtyro)*
               iii. Group 3: taletrectinib (Ibtrozi)*; **OR**
         ii. There are central nervous system (CNS) metastases; **AND**
            a. Treatment with all of the following has been ineffective, contraindicated, or not tolerated:
               i. entrectinib (Rozlytrek)*
               ii. repotrectinib (Augtyro)*
               iii. taletrectinib (Ibtrozi)*

*Please note: medications notated with an asterisk may require additional review.

II. Zidesamtinib (Jideytro) is considered investigational when used for all other conditions, including but not limited to:
   A. First-line treatment of ROS1-positive NSCLC in a ROS1 TKI-naïve member
   B. NSCLC without a ROS1-positive gene fusion or rearrangement
   C. ROS1-positive solid tumors other than NSCLC
   D. Zidesamtinib (Jideytro) used in combination with another oncology therapy

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise; **AND**
III. Member has exhibited response to treatment defined by stabilization of disease or decrease in tumor size or tumor spread; **AND**
IV. Medication will not be used in combination with any other oncology therapy

Supporting Evidence

I. Zidesamtinib (Jideytro) is a selective ROS1 tyrosine kinase inhibitor (TKI), FDA-approved for the treatment of adult patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) who received a prior ROS1 kinase inhibitor. The recommended dosage is 100 mg orally once daily, with or without food, until disease progression or unacceptable toxicity. Dose reductions to 75 mg and 50 mg once daily may be used for adverse reactions.
II. The ROS1 gene fusions occur in approximately 1% to 3% of NSCLC. Acquired resistance to ROS1-directed therapy, including the solvent-front ROS1 G2032R mutation, and central nervous system (CNS) progression are important causes of treatment failure. These features create a need for subsequent ROS1-directed therapies with activity against resistance mutations and intracranial disease.
III. Zidesamtinib (Jideytro) was studied as monotherapy in ARROS-1. The pivotal efficacy population included adults with locally advanced or metastatic ROS1-positive NSCLC previously treated with at least one ROS1 TKI. There is insufficient evidence to support the safety and efficacy of zidesamtinib used in combination with other oncology therapies.
IV. ARROS-1 is a global, multicenter, Phase 1/2, open-label, single-arm study. The FDA efficacy population included 117 patients treated with zidesamtinib 100 mg once daily after at least one prior ROS1 TKI. Confirmed overall response rate (ORR) by blinded independent central review was 44% (95% CI, 34%-53%). Among responders, 82% maintained response for at least 6 months and 69% for at least 12 months. Overall response rate was 49% after one prior ROS1 TKI and 38% after two or more prior ROS1 TKIs. Intracranial ORR was 48% in patients with measurable CNS metastases, and responses were observed in 54% of patients with the ROS1 G2032R resistance mutation. The single-arm design and use of response-based endpoints limit conclusions regarding comparative efficacy or survival benefit.

V. In the ROS1-positive NSCLC safety population, serious adverse reactions occurred in 22%. Permanent discontinuation due to adverse reactions occurred in 2.3%, dose interruption in 30%, and dose reduction in 10%. Common adverse reactions included edema, peripheral neuropathy, constipation, fatigue, dyspnea, and dysgeusia. Warnings and precautions include CNS adverse reactions, QTc interval prolongation, interstitial lung disease/pneumonitis, skeletal fractures, myalgia with creatine phosphokinase elevation, pancreatic toxicity, and embryo-fetal toxicity.

VI. National Comprehensive Cancer Network Non-Small Cell Lung Cancer Guidelines Version 8.2026 list zidesamtinib (Jideytro) as a subsequent therapy option for ROS1 gene fusion-positive advanced or metastatic NSCLC. For symptomatic brain progression, zidesamtinib is listed as a preferred option. National Comprehensive Cancer Network also recognizes repotrectinib, taletrectinib, or zidesamtinib as options for resistant mutations such as ROS1 G2032R. Jideytro is not listed as a first-line ROS1 therapy.

VII. There are no head-to-head trials comparing zidesamtinib with repotrectinib (Augtyro) or taletrectinib (Ibtrozi). Indirect comparisons show broadly comparable post-TKI activity, while Jideytro has a higher annual WAC. Therefore, requiring treatment with Augtyro or Ibtrozi before Jideytro is reasonable when clinically appropriate. Exceptions are appropriate when Jideytro is selected for NCCN-concordant subsequent therapy, particularly for symptomatic brain progression or a documented ROS1 resistance mutation such as G2032R.

Investigational or Not Medically Necessary Uses

I. Zidesamtinib (Jideytro) has not been FDA-approved, or sufficiently studied for safety and efficacy, for the conditions or settings listed below:
   - A. First-line treatment of ROS1-positive NSCLC in a ROS1 TKI-naïve member
     - i. The FDA-approved indication requires prior treatment with a ROS1 kinase inhibitor. A TKI-naïve cohort of ARROS-1 remains under evaluation; current evidence does not support routine first-line use.
   - B. NSCLC without a ROS1-positive gene fusion or rearrangement
     - i. Jideytro is a biomarker-directed ROS1 inhibitor and has not been sufficiently studied to support treatment of NSCLC without a ROS1-positive gene fusion or rearrangement.
   - C. ROS1-positive solid tumors other than NSCLC
     - i. Although ARROS-1 includes patients with other ROS1-positive solid tumors, Jideytro is currently FDA-approved only for ROS1-positive NSCLC after a prior ROS1 kinase inhibitor. Evidence is insufficient to support routine use in other ROS1-positive solid tumors.
   - D. Zidesamtinib (Jideytro) used in combination with another oncology therapy
     - i. Jideytro is FDA-approved as monotherapy, and the pivotal ARROS-1 efficacy data evaluated zidesamtinib as monotherapy. There is insufficient evidence supporting safety or efficacy in combination with other oncology therapies.

** The Moda Split Fill program is a physician-centric, patient engagement program intended to provide enhanced patient and physician support while accomplishing the goals of minimizing waste and avoiding incremental healthcare costs due to*

medication intolerance and unexpected change or termination of therapy regimen. Under the Split Fill program, the identified medications are programmed for fills of up to a 14 or 15-day supply for the duration of the first three months (86 or 90 days) of therapy. This program affords additional interactions with a specialty pharmacist, allowing more frequent assessments of side effects and barriers to adherence. Each fill is administered at half of the member cost-share, thereby reducing the economic burden if they must discontinue therapy mid-month.

References

1. Jideytro (zidesamtinib) [prescribing information]. Cambridge, MA: Nuvalent, Inc.; July 2026.
2. Drilon AE, et al. Pivotal ARROS-1 efficacy and safety data: zidesamtinib in TKI-pretreated patients with advanced/metastatic ROS1-positive non-small cell lung cancer. J Thorac Oncol. 2025;20(10 suppl 1):S3. doi:10.1016/j.jtho.2025.09.018.
3. Liu G, et al. Zidesamtinib in patients with ROS1-positive NSCLC previously treated with repotrectinib or taletrectinib. Cancer Res. 2026;86(8 suppl):CT248.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 8.2026. September 11, 2026.
5. ClinicalTrials.gov. A Phase 1/2 study of zidesamtinib (NVL-520) in patients with advanced ROS1-positive NSCLC and other solid tumors (ARROS-1). NCT05118789. Accessed September 13, 2026.
6. IPD Analytics. RxInsights New Drug Review: Jideytro (zidesamtinib). August 2026.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
taletrectinib (Ibtrozi™)	Advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC)
repotrectinib (Augtyro™)	Advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC)
	Neurotrophic receptor tyrosine kinase (NTRK) gene fusion positive solid tumors
entrectinib (Rozlytrek®)	Neurotrophic receptor tyrosine kinase gene fusion positive solid tumors
	NSCLC, metastatic, ROS1-positive
ALK+ Inhibitors	NSCLC, metastatic, ALK-positive
	NSCLC, metastatic, ROS1- positive
	Recurrent, refractory, Inflammatory myofibroblastic tumors, ALK-positive, unresectable
	Relapsed, refractory systemic anaplastic large cell lymphoma, ALK-positive

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	11/2026