# repotrectinib (Augtyro™)

EOCCO POLICY

## Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO304

### Description

Repotrectinib (Augtyro) is an orally administered selective tyrosine kinase inhibitor (TKI).

### Length of Authorization

- Initial: Six months
- Renewal: 12 months

### Quantity Limits

| Product Name | Indication | Dosage Form | Quantity Limit |
|---|---|---|---|
| repotrectinib (Augtyro) | Advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) | 40 mg capsules | 240 capsules/ 30 days |

### Initial Evaluation

I. **Repotrectinib (Augtyro)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. Medication is not used in combination with any other oncology therapy; **AND**
   D. A diagnosis of **non-small cell lung cancer (NSCLC); AND**
      1. Confirmation of ROS1-postive mutation; **AND**
      2. The disease is advanced (Stage III); **OR**
      3. The disease is metastatic (IV); **AND**
         i. There is no evident CNS metastases; **AND**
            a. Treatment with entrectinib (Rozlytrek) or crizotinib (Xalkori) have been ineffective, contraindicated, or not tolerated; **OR**
         ii. There is CNS metastases; **AND**
            a. Treatment with entrectinib (Rozlytrek) has been ineffective, contraindicated, or not tolerated

II. Repotrectinib (Agutyro) is considered <u>investigational</u> when used for all other conditions, including but <u>not limited to</u>:
   A. Advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC)
   B. NSCLC with other mutations (e.g. ALK, RET, BRAF, etc.)
   C. Solid tumors with ROS1 rearrangement
   D. Repotrectinib (Augtyro) used in combination with another oncology therapy

E. KRAS-mutant solid tumors

## 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 is not used in combination with any other oncology therapy

## Supporting Evidence

I. Repotrectinib (Augtyro) is a 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). Repotrectinib (Augtyro) is an oral capsule administered once daily for 14 days, then increased to twice daily thereafter.
**II.** Lung cancer is the second most common cancer diagnosed in the United States and the leading cause of cancer-related death. Non-small cell lung cancer represents up to 85% of lung cancer diagnoses. ROS1 fusions are rare and occur in about 1-2% of patients with NSCLC. The median age of diagnosis is 50 years old and ROS1 rearrangement is more common in females. ROS1 rearrangement tends to be more aggressive and there is an increased risk of G2032R mutations, which result in TKI resistance, and ultimately, fewer treatment options. Central nervous system metastases are the most common site of disease progression after development of TKI resistance. Given the complexity of management of mCRC, the treatment of mCRC must be initiated by, in or consultation with, an oncologist.
III. Repotrectinib (Augtyro) is the third FDA-approved TKI and joins entrectinib (Rozlytrek) and crizotinib (Xalkori) for treatment of ROS1-positive NSCLC. Repotrectinib (Augtyro) is the first TKI approval that includes patients with ROS1-positive non-small cell lung cancer who have previously received a ROS1 tyrosine kinase inhibitor, in addition to patients who are tyrosine kinase inhibitor naïve. Repotrectinib (Augtyro) will compete against entrectinib (Rozlytrek) and crizotinib (Xalkori) in the first- and second-line setting.
IV. Repotrectinib (Augtyro) was studied in a Phase 1/2, international, multicenter, single arm, open label, multi cohort study which included 71 TKI-naïve participants who received up to one prior line of platinum-based chemotherapy and 56 participants who received 1 prior ROS1 TKI with no prior platinum-based chemotherapy. Participants received repotrectinib (Augtyro) 160mg once daily for 12 days, then 160mg twice daily. Baseline characteristics were similar between both cohorts: median age 57 years old, mostly female (>60%), of those ROS1 TKI-naïve, 72% of participants were also chemotherapy naïve, there was 24% brain metastases in the TKI-naïve group and 46% in the prior TKI group, and of those that had prior TKI therapy, 82% had received

crizotinib. The primary endpoint, overall response rate (ORR), was 78% (n=56, 95% CI, 68-88) for the TKI-naïve cohort and 38% (n=56, 95% CI, 25-52) for the cohort with prior TKI. The median progression free survival (PFS) was 35.7 months (95% CI, 27.4-non-estimable) and 9.0 months (95%, 17.8-non-estimable) for the TKI-naïve and prior TKI cohorts, respectively. The median time to response was 1.8 months.

V. The safety analysis was completed in all 426 participants of the Phase 2 pooled population, which included other genetic mutations (e.g. ALK, NTRK1-3, etc.). The most common adverse events included dizziness (58%), dysgeusia (50%), paresthesia (30%), constipation (26%), anemia (26%), and ataxia (20%). Adverse events led to dose reduction in 163 participants (38%), dose interruption in 213 participants (50%), and treatment discontinuation in 31 participants (7%).

**VI.** There is moderate confidence that repotrectinib (Augtyro) provides an objective and meaningful difference in patients with NSCLC. Although there is low confidence in the single arm, open label study design, the trial has a similar study design and comparable efficacy endpoints to similar treatment options. Repotrectinib's (Augtyro) efficacy endpoints are promising as the duration of response and progression free survival are non-estimable and quality of life measures demonstrate an increase of ≥ 10 points at cycle 6 and stable scores throughout treatment.

VII. The National Comprehensive Cancer Network (NCCN) guidelines have been updated to recommend entrectinib (Rozlytrek), crizotinib (Xalkori), and repotrectinib (Augtyro) as first and second line therapy (category 2A, all preferred). After progression on therapy, if there is brain metastases, guidelines recommend entrectinib (Rozlytrek), repotrectinib (Augtyro), or lorlatinib (Lobrena) (category 2A). The TRIDENT-1 trial permitted participants to receive prior entrectinib (Rozlytrek) (N= 9, 16%) or crizotinib (Xalkori) (N= 46, 82%) and requiring step through these agents for metastatic disease is both clinically appropriate and cost-effective.

## Investigational or Not Medically Necessary Uses

I. There are ongoing clinical studies to assess efficacy and safety of repotrectinib (Augtyro) in other settings. Notably, clinical trials in the settings of NSCLC with other mutations are underway. Repotrectinib (Augtyro) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. NSCLC with other mutations (e.g. ALK, RET, BRAF, etc.)
   B. Solid tumors with ROS1 rearrangement
   C. Repotrectinib (Augtyro) used in combination with another oncology therapy
   D. KRAS-mutant solid tumors

## References

1. Augtyro (repotrectinib) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; November 2023.
2. Drilon A, Camidge DR, Lin JJ, et al. Repotrectinib in ROS1 Fusion-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2024;390(2):118-131.

3. Food and Drug Administration. FDA approves repotrectinib for ROS1-positive non-small cell lung cancer. Updated November 11, 2023. Accessed January 30, 2024. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-repotrectinib-ros1-positive-non-small-cell-lung-cancer.
4. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Versions 2.2024 – February 9, 2024). 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 17, 2024.

## 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 |
|---|---|
| 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 |
| encorafenib (Braftovi®), binimetinib (Mektovi®) | Malignant melanoma, unresectable or metastatic, with BRAF V600E or V600K mutation, combination therap |
| | Metastatic colorectal cancer, with BRAF V600E mutation, combination therapy |
| pralsetinib (Gavreto®) | RET Fusion-Positive Non-Small Cell Lung Cancer |
| sotorasib (Lumakras®) | Non-Small Cell Lung Cancer (NSCLC), advanced or metastatic with a KRAS G12C mutation |

## Policy Implementation/Update:

| Action and Summary of Changes | Date |
|---|---|
| Policy created | 05/2024 |