PHARMACY COVERAGE GUIDELINE

AUGTYRO™ (repotrectinib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Augtyro (repotrectinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Individual is 18 years of age or older with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC)

    b. Individual is 12 years of age or older with solid tumors with **ALL** of the following:
        i. Has a neurotrophic tyrosine receptor kinase (NTRK) gene fusion

ii. Is locally advanced or metastatic or where surgical resection is likely to result in severe morbidity
iii. Has progressed following treatment or have no satisfactory alternative therapy

c. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

3. Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **ONE** of the following:
   a. Xalkori (crizotinib)
   b. Rozlytrek (entrectinib)

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. **For non-small cell lung cancer (NSCLC):** There is documentation of ROS1 rearrangement(s) in tumor specimens
   b. **For solid tumors:** There is documentation of neurotrophic tyrosine receptor kinase (NTRK) gene fusion
   c. Eastern Co-operative Oncology Group (ECOG) status of 0-1
   d. Liver function tests including bilirubin
   e. Uric acid level
   f. Negative pregnancy test in a woman of childbearing potential

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual is not currently taking any other drugs that may result in a significant drug interaction requiring discontinuation such as use with:
   a. Moderate and strong CYP3A inhibitors (e.g., fluconazole, erythromycin, ketoconazole, itraconazole, nelfinavir, telaprevir, boceprevir, others)
   b. P-gp inhibitors (e.g., amiodarone, clarithromycin, cyclosporine, diltiazem, propafenone, quinidine, others)
   c. Moderate and strong CYP3A inducers (e.g., armodafinil, bexarotene, nafcillin, rifampin, rifabutin, phenobarbital, carbamazepine, others)
   d. Hormonal contraceptives

7. Individual does not have symptomatic brain metastases

8. Individual does not have severe renal impairment or kidney failure (eGFR-MDRD <30 mL/min) and is not on dialysis

9. Individual does not have moderate (total bilirubin >1.5-3 times upper limit of normal [ULN] with any aspartate aminotransferase (AST)) or severe (total bilirubin >3 times ULN with any AST) hepatic impairment

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Augtyro (repotrectinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as the following:
    a. There is no documentation of disease progression
    b. There is no documentation of unacceptable drug toxicity

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Life-threatening consequences: urgent intervention indicated for dizziness, ataxia, and cognitive impairment
    b. Interstitial Lung Disease (ILD)/Pneumonitis
    c. Life-threatening hepatotoxicity that does not resolve in 4-weeks or if it recurs
    d. Hyperuricemia
    e. Other adverse reaction that does not resolve in 4-weeks or if it recurs

6. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

7. Individual is not currently taking any other drugs that may result in a significant drug interaction requiring discontinuation such as use with:
    a. Moderate and strong CYP3A inhibitors (e.g., fluconazole, erythromycin, ketoconazole, itraconazole, nelfinavir, telaprevir, boceprevir, others)
    b. P-gp inhibitors (e.g., amiodarone, clarithromycin, cyclosporine, diltiazem, propafenone, quinidine, others)
    c. Moderate and strong CYP3A inducers (e.g., armodafinil, bexarotene, nafcillin, rifampin, rifabutin, phenobarbital, carbamazepine, others)
    d. Hormonal contraceptives

8. Individual does not have symptomatic brain metastases

9. Individual does not have severe renal impairment or kidney failure (eGFR-MDRD <30 mL/min) and is not on dialysis

10. Individual does not have moderate (total bilirubin >1.5-3 times upper limit of normal [ULN] with any aspartate aminotransferase (AST)) or severe (total bilirubin >3 times ULN with any AST) hepatic impairment

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Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**
  2. **Off-Label Use of Cancer Medications**

Description:

Augtyro (repotrectinib) is a kinase inhibitor indicated for the treatment of adult individuals with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC). Augtyro (repotrectinib) is also indicated for the treatment of adult and pediatric individuals 12 years of age and older with solid tumors that: have a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion; are locally advanced or metastatic or where surgical resection is likely to result in severe morbidity; and have progressed following treatment or have no satisfactory alternative therapy. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Augtyro (repotrectinib) product information, revised by E.R. Squibb & Sons, L.L.C. 06-2024. Available at label (fda.gov). Accessed December 10, 2024.

Neal JW. Personalized, genotype-directed therapy for advanced non-small cell lung cancer. In: UpToDate, Lilenbaum RC, Vora SR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated January 22, 2025. Accessed January 28, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer Version 5.2025 –Updated January 14, 2025. Available at https://www.nccn.org. Accessed January 28, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03093116: A Phase 1/2, Open-Label, Multi-Center, First-in-Human Study of the Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity of TPX-0005 in Patients With Advanced Solid Tumors Harboring ALK, ROS1, or NTRK1-3 Rearrangements (TRIDENT-1). Available from: http://clinicaltrials.gov. Last update posted November 09, 2023. Last verified November 2023. Accessed December 06, 2023. Re-evaluated January 28, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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