Clinical Policy: Repotrectinib (Augtyro)

Reference Number: CP.PHAR.667
Effective Date: 03.01.24
Last Review Date: 02.25
Line of Business: Commercial, HIM*, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Repotrectinib (Augtyro™) is a kinase inhibitor.

**For Health Insurance Marketplace (HIM),* *if request is through pharmacy benefit, Augtyro is non-formulary and should not be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Augtyro is indicated for the treatment of:

- Adult patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC).
- Adult and pediatric patients 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 the confirmatory trials.*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Augtyro is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of recurrent, locally advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is ROS1 positive;*
   **See criteria set I.B for NTRK fusion-positive NSCLC*
5. For Augtyro requests, member must use repotrectinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):

i. 320 mg per day;
ii. 2 capsules per day;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. NTRK Fusion-Positive Cancer (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Solid tumor (*see Appendix D for examples)*;
   b. Histiocytic neoplasms (e.g., Erheim-Chester disease, Langerhans cell histiocytosis, Rosai-Dorfman disease) (*off-label*);
2. Prescribed by or in consultation with one of the following (a or b):
   a. Oncologist;
   b. For histiocytic neoplasm, a hematologist;
3. Age ≥ 12 years;
4. Disease is positive for an NTRK-gene fusion (e.g., ETV6-NTRK3, IL1RL2-NTRK2, TPM3-NTRK1);
5. Disease meets one of the following (a, b, or c):
   a. Disease is recurrent, advanced, or metastatic;
   b. Surgical resection is likely to result in severe morbidity;
   c. Disease is histiocytic neoplasms;
6. One of the following (a, b, or c):
   a. Disease has progressed following treatment;
   b. There is no satisfactory alternative therapy;
   c. One of the following NCCN compendium recommended indications (i-ix):
      i. Biliary tract cancer (e.g., extrahepatic/intrahepatic cholangiocarcinoma, gallbladder cancer);
      ii. Gastrointestinal stromal tumors;
      iii. Salivary gland tumors;
      iv. Hepatocellular carcinoma;
      v. Histiocytic neoplasms;
      vi. NSCLC;
      vii. Pancreatic adenocarcinoma;
      viii. Soft tissue sarcoma;
      ix. Anaplastic thyroid carcinoma;
7. For Augtyro requests, member must use repotrectinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 320 mg per day;
      ii. 2 capsules per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Augtyro for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Augtyro requests, member must use repotrectinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 320 mg per day;
      ii. 2 capsules per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer
NTRK: neurotrophic tyrosine receptor kinase
ROS1: ROS proto-oncogene 1

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: Examples of Solid Tumors

(Examples are drawn from the Augtyro pivotal trial, as described in the FDA prescribing information, as well as the National Comprehensive Center Network (NCCN) Augtyro compendium.)

- Ampullary adenocarcinoma
- Breast cancer
- Biliary tract cancers (e.g., extrahepatic/intrahepatic cholangiocarcinoma, gallbladder cancer)
- Central nervous system cancers (e.g., circumscribed glioma, pleomorphic xanthoastrocytoma, glioblastoma, brain metastases)
- Colorectal cancer (including appendiceal adenocarcinoma)
- Esophageal and esophagogastric junction cancers
- Gastric cancer
- Gastrointestinal stromal tumors
- Head and neck cancer (e.g., salivary gland tumors)
- Hepatocellular carcinoma
- Neuroendocrine and adrenal tumors (extrapulmonary poorly differentiated)
- NSCLC
- Occult primary

- Ovarian cancer/fallopian tube cancer/primary peritoneal cancer (e.g., carcinosarcoma (malignant mixed mullerian tumors), clear cell carcinoma of the ovary, endometroid carcinoma, low-grade serious carcinoma, mucinous neoplasms of the ovary)
- Pancreatic adenocarcinoma
- Peripheral nerve sheath tumor
- Small bowel adenocarcinoma
- Soft tissue sarcoma (e.g., extremity/body wall, head/neck, retroperitoneal/intra-abdominal, rhabdomyosarcoma)
- Thyroid carcinoma (e.g., anaplastic, follicular, oncocytic, papillary)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ROS1-positive NSCLC, NTRK fusion-positive solid tumor	160 mg PO QD for 14 days, then increase to 160 mg PO BID until disease progression or unacceptable toxicity	320 mg/day

VI. Product Availability

Capsules: 40 mg, 160 mg

VII. References

1. Augtyro Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; June 2024. Available at: https://www.augtyro.com/. Accessed October 21, 2024.
2. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 11.2024. Available at www.nccn.org. Accessed October 29, 2024.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 29, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.12.23	02.24
Added HIM non-formulary status note with reference to review all HIM requests under formulary exception policy, HIM.PA.103.	04.17.24	05.24
RT4: added new solid tumor indication with criteria and new strength 160 mg capsule; template changes for HIM applied to other diagnoses/indications and diagnoses/indications for which coverage is NOT authorized sections.	07.15.24	
1Q 2025 annual review: for NSCLC, added recurrent NSCLC per NCCN compendium recommendation; revised NTRK fusion-positive solid tumor section to NTRK fusion-positive cancer to include off-label non-solid tumor indications; for NTRK fusion-positive cancer, added histiocytic neoplasm indication per NCCN 2A recommendation with allowance for hematology specialty, revised "prescribed as subsequent therapy" to "disease has progressed following treatment", added bypass for gastrointestinal stromal tumors, salivary gland tumors, histiocytic neoplasms,	10.30.24	02.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
pancreatic adenocarcinoma, soft tissue sarcoma, and anaplastic thyroid carcinoma per NCCN; in Appendix D, updated examples of solid tumors with listed indications from NCCN; references reviewed and updated.		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.