

## Clinical Policy: Entrectinib (Rozlytrek)

Reference Number: ERX.SPA.356

Effective Date: 12.01.19

Last Review Date: 11.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

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

### Description

Entrectinib (Rozlytrek<sup>™</sup>) is a kinase inhibitor.

### FDA Approved Indication(s)

Rozlytrek is indicated for the treatment of:

- Adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive.
- Adult and pediatric patients 12 years of age and older with solid tumors that:
  - have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation,
  - are metastatic or where surgical resection is likely to result in severe morbidity, and
  - have either progressed following treatment or have no satisfactory alternative therapy.

*This indication is approved under accelerated approval based on tumor response rate and durability 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.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions<sup>™</sup> that Rozlytrek 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, advanced, or metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is ROS1 positive;
5. Member has not received prior ROS1 targeted therapy (e.g., Xalkori<sup>®</sup>, Zykadia<sup>®</sup>, Lorbrena<sup>®</sup>);
6. For brand Rozlytrek requests, member must use generic entrectinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 600 mg (3 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:

**Medicaid** – 6 months

**Commercial** – Length of Benefit

##### B. NTRK Fusion-Positive Solid Tumor (must meet all):

1. Diagnosis of a solid tumor (*see Appendix D for examples*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;

4. Meets one of the following (a or b):
  - a. Disease is metastatic;
  - b. Member has failed or is not a candidate for primary therapy (e.g., surgery, chemotherapy, radiation);
5. Tumor is positive for an NTRK gene fusion (e.g., ETV6-NTRK3, TPM3-NTRK1) without a known resistance mutation;
6. Member has not received prior NTRK targeted therapy (e.g., Vitrakvi®);
7. For brand Rozlytrek requests, member must use generic entrectinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a, b, or c):\*
  - a. Adults: Dose does not exceed 600 mg (3 capsules) per day;
  - b. Pediatrics: Dose does not exceed any of the following (i, ii, or iii):
    - i. Body surface area (BSA) > 1.50 m<sup>2</sup>: 600 mg PO QD;
    - ii. BSA 1.11 to 1.50 m<sup>2</sup>: 500 mg PO QD;
    - iii. BSA 0.91 to 1.10 m<sup>2</sup>: 400 mg PO QD;
  - c. 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:**

**Medicaid** – 6 months

**Commercial** – Length of Benefit

**C. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Rozlytrek for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):\*
  - a. Adults: New dose does not exceed 600 mg (3 capsules) per day;
  - b. Pediatrics: New dose does not exceed any of the following (i, ii, or iii):
    - i. BSA > 1.50 m<sup>2</sup>: 600 mg PO QD;
    - ii. BSA 1.11 to 1.50 m<sup>2</sup>: 500 mg PO QD;
    - iii. BSA 0.91 to 1.10 m<sup>2</sup>: 400 mg PO QD;
  - c. 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:**

**Medicaid** – 12 months

**Commercial** – Length of Benefit

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less);** or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 policy – ERX.PA.01 or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

BSA: body surface area  
FDA: Food and Drug Administration  
NCCN: National Comprehensive Cancer Network

NSCLC: non-small cell lung cancer  
NTRK: neurotrophic tyrosine receptor kinase

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

None reported

*Appendix D: Examples of Solid Tumors*

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

- Breast cancer
- Central nervous system cancers
- Cholangiocarcinoma
- Colorectal cancer
- Esophageal and esophagogastric junction cancers
- Gastric cancers
- Gynecological cancers (e.g., epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer, uterine cancers, vulvar cancers (squamous cell), cervical cancers)
- Hepatobiliary cancers
- Lung cancer
- Neuroendocrine cancers
- Pancreatic cancer
- Salivary gland tumor
- Soft tissue sarcoma (e.g., retroperitoneal/intraabdominal, angiosarcoma, rhabdosarcoma, sarcoma of the extremity, solitary fibrous tumor, superficial trunk, undifferentiated pleomorphic sarcoma, extremity/body wall, or head/neck)
- Thyroid cancer (papillary, Hurthle cell, anaplastic, or follicular carcinoma)

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
ROS1-positive NSCLC	Adults: 600 mg PO QD	600 mg/day
NTRK fusion-positive solid tumor	Adults: 600 mg PO QD Pediatrics (≥ 12 years of age) by BSA: <ul style="list-style-type: none"> <li>• BSA &gt; 1.50 m<sup>2</sup>: 600 mg PO QD</li> <li>• BSA 1.11 to 1.50 m<sup>2</sup>: 500 mg PO QD</li> <li>• BSA 0.91 to 1.10 m<sup>2</sup>: 400 mg PO QD</li> </ul>	600 mg/day

**VI. Product Availability**

Capsules: 100 mg, 200 mg

**VII. References**

1. Rozlytrek Prescribing Information. South San Francisco, CA: Genentech USA, Inc.; August 2019. Available at: [https://www.gene.com/download/pdf/rozlytrek\\_prescribing.pdf](https://www.gene.com/download/pdf/rozlytrek_prescribing.pdf). Accessed June 23, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed June 23, 2021.

3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 5.2021. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/nscl.pdf](https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf). Accessed June 23, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	10.01.19	11.19
Ad hoc change: NTRK fusion tumors: no known resistance mutation added for clarity, pediatric dosing details added.	11.19.19	
4Q 2020 annual review: no significant changes; updated Appendix D with additional examples of solid tumors per NCCN Compendium; references reviewed and updated.	07.14.20	11.20
4Q 2021 annual review: no significant changes; added redirection to generic product once available; references reviewed and updated.	06.23.21	11.21

**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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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