



# Evolut Clinical Guideline 3219 for Rozlytrek™ (entrectinib)

<b>Guideline Number:</b> Evolut_CG_3219	<b><u>Applicable Codes</u></b>	
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<b>Original Date:</b> September 2019	<b>Last Revised Date:</b> November 2025	<b>Implementation Date:</b> November 2025

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## STATEMENT

### Purpose

To define and describe the accepted indications for Rozlytrek (entrectinib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

## INDICATIONS

**Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided**

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

### Non-Small Cell Lung Cancer

- The member has recurrent, advanced, or metastatic NSCLC and Rozlytrek (entrectinib) may be used as a single agent in adult members with ROS-1 rearrangement-positive NSCLC as first-line or subsequent therapy.

### NTRK-Fusion Positive Metastatic Solid Tumors

- Rozlytrek (entrectinib) may be used as a single agent as initial or subsequent therapy in adult and pediatric members older than 1 month of age with recurrent/metastatic/unresectable solid tumors (e.g., NSCLC) with a positive NTRK fusion in the tumor tissue (test confirmation required).

## CONTRAINDICATIONS/WARNINGS

- None

## EXCLUSION CRITERIA

- Rozlytrek (entrectinib) is used after disease progression with the same regimen or other NTRK-targeted therapy [e.g., Vitrakvi (larotrectinib)], unless the member has

progressed on first line Rozlytrek (entrectinib) for ROS-1 rearrangement positive NSCLC. In this setting, Rozlytrek (entrectinib) may be continued as subsequent therapy if the member is asymptomatic or has disease that is limited to lung cancer with CNS progression as the exception.

- Concurrent use with other anti-cancer therapies.
- Dosing exceeds single dose limit of Rozlytrek (entrectinib) 600 mg in Non-Small Cell Lung Cancer.
- Refer to Tables 1 and 2 below for dosing limits for NTRK-Fusion-Positive Metastatic Solid Tumors.

**Table 1. Recommended dosage for Adults and Pediatric patients for the Treatment of NTRK Gene Fusion-Positive Solid Tumors**

Patient Population	Recommended Dosage of ROZLYTREK	Duration of Treatment
Adults	600 mg orally once daily	Until disease progression or unacceptable toxicity.
Pediatric patients with BSA $\geq 1.51 \text{ m}^2$ :		
Pediatric patients > 6 months:	see Table 2	
Pediatric patients > 1 month to $\leq 6$ months:	250 mg/m <sup>2</sup> orally once daily*	

**Table 2. Recommended dosage for Pediatric Patients Older than 6 Months for the Treatment of NTRK Gene Fusion-Positive Solid Tumors**

Body Surface Area (BSA)*	Recommended Dosage Orally Once Daily
$\leq 0.50 \text{ m}^2$	300 mg/m <sup>2</sup> **
0.51 to 0.80 m <sup>2</sup>	200 mg
0.81 to 1.10 m <sup>2</sup>	300 mg
1.11 to 1.50 m <sup>2</sup>	400 mg
$\geq 1.51 \text{ m}^2$	600 mg

- Treatment exceeds the maximum limit of:
  - 90 (100 mg) and 90 (200 mg) capsules/month
  - 84 (50 mg) oral pellets/month
- Investigational use of Rozlytrek (entrectinib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately

represented in the published evidence.

- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
- Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

## CODING AND STANDARDS

### Codes

- J8999 - entrectinib

### Applicable Lines of Business

<input type="checkbox"/>	CHIP (Children’s Health Insurance Program)
<input checked="" type="checkbox"/>	Commercial
<input checked="" type="checkbox"/>	Exchange/Marketplace
<input checked="" type="checkbox"/>	Medicaid
<input type="checkbox"/>	Medicare Advantage

## POLICY HISTORY

Date	Summary
November 2025	<ul style="list-style-type: none"> <li>● Converted to new Evolent guideline template</li> <li>● This guideline replaces UM ONC_1367 Rozlytrek (entrectinib)</li> <li>● Updated maximum dosage form quantities in exclusion criteria</li> <li>● Updated references</li> </ul>
November 2024	<ul style="list-style-type: none"> <li>● Updated dosage forms, and added oral pellet strengths to exclusion criteria</li> <li>● Updated maximum dosage form quantities in exclusion criteria</li> <li>● Updated references</li> </ul>

## LEGAL AND COMPLIANCE

### Guideline Approval

#### Committee

**Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee**

### Disclaimer

*Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.*

## REFERENCES

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