Reference number(s)
3165-A

Specialty Guideline Management
Rozlytrek

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Rozlytrek	entrectinib

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Solid Tumors

Rozlytrek is indicated for the treatment of adult and pediatric patients older than 1 month of age with solid tumors that:

- have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, as detected by an FDA-approved test without a known acquired resistance mutation,
- are metastatic or where surgical resection is likely to result in severe morbidity, and
- have progressed following treatment or have no satisfactory alternative therapy.

Non-Small Cell Lung Cancer

Rozlytrek is indicated for the treatment of adult patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC), as detected by an FDA-approved test.

Compendial Uses[2]

- Non-small cell lung cancer
- Cutaneous melanoma
- Histiocytic neoplasms with NTRK gene fusion:
    - Erdheim-Chester Disease (ECD)
    - Langerhans Cell Histiocytosis (LCH)
    - Rosai-Dorfman Disease

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review: NTRK gene fusion status or ROS1 status (where applicable).

Coverage Criteria

Solid Tumors[1,2]

Authorization of 12 months may be granted for treatment of solid tumors when the tumors have a NTRK gene fusion without a known acquired resistance mutation, as demonstrated by laboratory testing (e.g., next-generation sequencing [NGS] or fluorescence in situ hybridization [FISH]).

Non-Small Cell Lung Cancer (NSCLC)[1,2]

Authorization of 12 months may be granted for treatment of recurrent, advanced, or metastatic NTRK gene fusion-positive or ROS1-rearrangement positive NSCLC as a single agent.

Cutaneous Melanoma[2]

Authorization of 12 months may be granted for treatment of metastatic or unresectable NTRK gene fusion-positive or ROS1-gene fusion positive cutaneous melanoma as second-line or subsequent therapy as a single agent for disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy.

Histiocytic Neoplasms[2]

Authorization of 12 months may be granted for the treatment of any of the following NTRK gene fusion-positive histiocytic neoplasm subtypes as a single agent:

- Symptomatic or relapsed/refractory Erdheim-Chester Disease (ECD)
- Langerhans Cell Histiocytosis (LCH)
- Symptomatic or relapsed/refractory Rosai-Dorfman Disease

Continuation of Therapy

ROS1-Rearrangement Positive NSCLC and NTRK gene fusion-positive gastrointestinal stromal tumor (GIST)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for ROS1-rearrangement positive NSCLC or NTRK gene fusion-positive gastrointestinal stromal tumor (GIST) when there is no evidence of unacceptable toxicity while on the current regimen.

All Other Indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

References

1. Rozlytrek [package insert]. South San Francisco, CA: Genentech USA, Inc. January 2024.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed July 10, 2025.