PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral – Neurotrophic Tyrosine Receptor Kinase Gene Fusion) – Rozlytrek Prior Authorization Policy
- Rozlytrek® (entrectinib capsules and oral pellets – Genentech)

REVIEW DATE: 10/01/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Rozlytrek, a kinase inhibitor, is indicated for the following uses:[1]

- **Non-small cell lung cancer (NSCLC)**, with *ROS1*-positive metastatic disease, as detected by an FDA-approved test, in adults.
- **Solid tumors**, in adults and pediatric patients ≥ 1 month of age that:
  - Have a neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion, as detected by an FDA-approved test without a known acquired resistance mutation; AND
  - Are metastatic or surgical resection of the tumor is likely to result in severe morbidity; AND
  - Have either progressed following treatment or there are no satisfactory alternative therapies.

The solid tumors 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.

Guidelines

Rozlytrek is addressed in guidelines by the National Comprehensive Cancer Network (NCCN):[2,3]

- **NSCLC.** Guidelines (version 8.2025 – August 15, 2025) recommend Rozlytrek as one of the "Preferred" first-line treatment options for patients with *ROS1* rearrangement-positive NSCLC (category 2A).[2] Rozlytrek is also recommended as a "Preferred" first-line treatment option for patients with *NTRK* gene fusion-positive NSCLC (category 2A).
- **Solid tumors.** The NCCN Drugs and Biologics Compendium notes the use of Rozlytrek for *NTRK* gene fusion-positive tumors associated with the following cancers: ampullary adenocarcinoma, biliary tract cancer, breast cancer, central nervous system cancers (e.g., glioma, glioblastoma, brain metastases), cervical cancer, colon cancer, esophageal and esophagogastric junction cancers, gastric cancer, gastrointestinal stromal tumors, head and neck cancers (e.g., salivary gland tumors), hepatobiliary cancers, histiocytic neoplasms, melanoma (cutaneous), neuroendocrine tumor, non-small cell lung cancer, occult primary, ovarian cancer/fallopian tube cancer/primary peritoneal cancer, pancreatic cancer, rectal cancer, small bowel adenocarcinoma, soft tissue sarcomas, thyroid carcinoma, uterine neoplasms, vaginal, and vulvar cancer.[3] Rozlytrek is a category 2A recommendation for most of these cancers. Rozlytrek is recommended for use as a first-line and/or second-line treatment option for these cancers.
- **Pediatric Central Nervous System Cancers.** Guidelines (version 1.2024 – February 26, 2024) recommend Rozlytrek as adjuvant therapy and for recurrent or progressive disease (category 2A for both), for tyrosine receptor kinase (*TRK)* fusion-positive pediatric diffuse high-grade gliomas.[4]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Rozlytrek. All approvals are provided for the duration noted below.

- **Rozlytrek® (entrectinib capsules and oral pellets – Genentech)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Non-Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

Note: If the patient has non-small cell lung cancer with neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion, see **Solid Tumors** indication.
A) Patient is ≥ 18 years of age; AND
B) Patient has metastatic disease; AND
C) Patient has *ROS1*-positive disease; AND
D) The mutation was detected by an approved test.

2. Solid Tumors. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: Examples of solid tumors include breast cancer, colorectal cancer, head/neck cancer, hepatocellular carcinoma, biliary cancer, histiocytic neoplasm, non-small cell lung cancer (*NTRK* gene fusion-positive), ovarian cancer, pancreatic cancer, salivary gland tumors, sarcoma, thyroid cancer, adult glioma.
A) Patient is ≥ 1 month of age; AND
B) The tumor is positive for neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion; AND
C) Patient meets ONE of the following (i or ii):
i. The tumor is metastatic; OR
ii. Surgical resection of tumor will likely result in severe morbidity.

Other Uses with Supportive Evidence

3. Pediatric Diffuse High-Grade Gliomas. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is < 18 years of age; AND
B) The tumor is positive for neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion; AND
C) Patient meets ONE of the following (i or ii):
i. The medication is used as adjuvant therapy; OR
ii. The medication is used for recurrent or progressive disease.

CONDITIONS NOT COVERED

- **Rozlytrek® (entrectinib capsules and oral pellets – Genentech)**

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Rozlytrek® capsules and oral pellets [prescribing information]. South San Francisco, CA: Genentech; January 2024.
2. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 8.2025 – August 15, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 24, 2025.
3. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 23, 2025. Search term: entrectinib.

4. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 3.2025 – September 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 24, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Non-Small Cell Lung Cancer:** Added Note to refer to Solid Tumors indication if the patient has non-small cell lung cancer with neurotrophic receptor tyrosine kinase (NTRK) gene fusion. **Solid Tumors:** In the list of examples of solid tumors, separated hepatobiliary cancers into hepatocellular carcinoma and biliary cancer. Specified lung cancer to state "non-small cell lung cancer (*NTRK* gene fusion-positive)". Also added "adult glioma" due to the addition of the new indication (see below). **Pediatric Diffuse High-Grade Gliomas:** Added new approval condition and criteria under "Other Uses with Supportive Evidence" based on NCCN Compendium recommendation for NTRK gene fusion pediatric gliomas.	09/27/2023
Selected Revision	Added oral pellets dosage form to the policy. **Solid Tumors:** Rozlytrek received expanded age indication for use in patients ≥ 1 month of age. Previously it was indicated in patients ≥ 12 years of age.	11/22/2023
Annual Revision	No criteria changes	10/16/2024
Update	04/20/2025: The policy name was changed from "Oncology – Rozlytrek PA Policy" to "Oncology (Oral – Neurotrophic Tyrosine Receptor Kinase Gene Fusion) – Rozlytrek PA Policy".	N/A
Annual Revision	No criteria changes.	10/01/2025

N/A – Not applicable.