Effective Date: 10/01/2019
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Policy Number: C17881-A

Rozlytrek (entrectinib)

PRODUCTS AFFECTED

Rozlytrek (entrectinib)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
non-small cell lung cancer, solid tumors

REQUIRED MEDICAL INFORMATION:
A. NON-SMALL CELL LUNG CANCER (NSCLC):
1. Documentation the member has recurrent, advanced, or metastatic non-small cell lung cancer [DOCUMENTATION REQUIRED]
AND
2. Prescriber attests member will be using as monotherapy
AND
3. Documentation that patient’s tumors are ROS1 rearrangement-positive using either a fluorescence in situ hybridization (FISH) or next-generation sequencing (NGS) laboratory-developed test [DOCUMENTATION REQUIRED]
AND
4. Prescriber attests that an assessment of left ventricular ejection fraction, liver enzyme testing,serum uric acid levels, QT interval and electrolytes, and ophthalmological exam will

be completed as necessary prior to initiation of therapy * per FDA product label (WARNINGSAND PRECAUTIONS)

B. SOLID TUMOR WITH NEUROTROPHIC RECEPTOR TYROSINE KINASE (NTRK) GENEFUSION:
   1. Documentation of diagnostically confirmed solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation – Lab resultconfirming a positive test for NTRK gene fusion using RT-PCR, FISH, or NGS testing methodology must be submitted (reviewed through MCP-051) [DOCUMENTATION REQUIRED]
      AND
   2. Documentation of presences of metastatic disease or where surgical resection is likely toresult in severe morbidity [DOCUMENTATION REQUIRED]
      AND
   3. Documentation of member's prior therapies with start and stop dates and that there are no satisfactory alternative treatments, or the member has progressed following treatment. [DOCUMENTATION REQUIRED]
      AND
   4. Documentation of radiographically measurable disease [DOCUMENTATIONREQUIRED]
      AND
   5. Prescriber attests that member has fully recovered from toxic effects of prior chemotherapy
      AND
   6. The member has NOT previously used a neurotrophic receptor tyrosine kinase (NTRK) targetedtherapy

CONTINUATION OF THERAPY:

A. ALL INDICAITONS:
   1. Documentation within chart notes of patient's clinical benefit since starting Rozlytrek (entrectinib)
      AND
   2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
      AND
   3. Member has not experienced any intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 3 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with an oncologist. [If prescribed in consultation, consultation notes must besubmitted within initial request and reauthorization requests]

AGE RESTRICTIONS:

NON-SMALL CELL LUNG CANCER (NSCLC): 18 years of age and older
SOLID TUMORS: 12 years of age and older

QUANTITY:

Adults: 600 mg (#3 200 mg capsules) once daily for both NSCLC and solid tumors Pediatrics >12 years: dosage based on body surface area:

- BSA N> 1.50 m2: 600 mg once daily
- BSA 1.11 to 1.50 m2: 500 mg once daily
- BSA 0.91 to 1.10 m2: 400 mg once daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Antirheumatic-Janus Kinase Inhibitors

FDA-APPROVED USES:
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 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 theconfirmatory trials

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
NTRK fusion-positive cancer is not limited to certain types of cells or tissues and can occur in any part of the body. NTRK gene fusions occur in various adult and pediatric solid tumors with varying prevalence, including appendiceal cancer, breast cancer, cholangiocarcinoma, colorectal cancer, gastrointestinal stromal tumor (GIST), infantile fibrosarcoma, lung cancer, mammary analogue secretory carcinoma of the salivary gland, melanoma, pancreatic cancer, thyroid cancer, and varioussarcomas. It may affect > 60% of both adult and pediatric patients with certain rare tumor types, such as secretory breast, secretory salivary gland and infantile fibrosarcoma.

The efficacy of Rozlytrek in patients with NTRK gene fusion-positive tumors was evaluated in a pooled subgroup of 54 adult patients who were enrolled in one of the multicenter, single-arm, open-label clinical trials and who had unresectable or metastatic solid tumors with an NTRK gene fusion.To be included in this pooled subgroup, patients were required to have progressed following systemic therapy for their disease, if available, or would have required surgery causing significant morbidity for locally advanced

disease. In addition, the member had to have measurable disease,undergo at least 6 months of follow-up after the first dose of Rozlytrek, and not have prior therapywith a TRK inhibitor.

NSCLC is the most common type of lung cancer and accounts for 85% of all lung cancer diagnoses.The ROS1 gene fusions account for 1–2% of all NSCLC. While the ROS1 gene fusion can be foundin any member with NSCLC, young never smokers with NSCLC have the highest incidence of ROS1 gene fusions. The efficacy of Rozlytrek with ROS1-positive NSCLC was evaluated in a pooled subgroup of 51 patients with ROS1- positive metastatic NSCLC who received Rozlytrek at various doses and schedules (90% received Rozlytrek 600 mg orally once daily) and who were enrolled in one of three multicenter, single-arm, open-label clinical trials. To be included in this pooled subgroup, patients were required to have histologically confirmed, recurrent or metastatic, ROS1- positive NSCLC, no prior ROS1 therapy, an ECOG performance status ≤ 2, and measurabledisease.

Rozlytrek is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-smallcell lung cancer (NSCLC) whose tumors are ROS1-positive; adult and pediatric patients 12 years ofage 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 progressed following treatment or have no satisfactoryalternative therapy. This indication was approved under accelerated approval based on tumor response rate and durability of response

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Rozlytrek (entrectinib) that are not an FDA-approved indication or not included in this policy are considered experimental/investigational or not a covered benefit of this policy. This subject tochange based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS:

Tumor Testing

Biomarker testing for ROS1 in NSCLC and NTRK gene fusions across all solid tumors is the only way to identify people who are eligible for treatment with Rozlytrek. Roche is developing personalized medicines and advanced diagnostics, in conjunction with Foundation Medicine, to help identify people with ROS1 and NTRK gene fusions. Foundation Medicine will submit Foundation One CDx to the FDA for approval as a companion diagnostic for Rozlytrek. An approvedcompanion diagnostic for Rozlytrek is not available at this time.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

Rozlytrek CAPS 100MG, Rozlytrek CAPS 200MG

100 mg hard capsules bottles of 30: NDC 50242-0091-30

200 mg hard capsules bottles of 90: NDC 50242-0094-90

REFERENCES

1. Rozlytrek [prescribing information]. South San Francisco, CA; Genentech. November 2021
2. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network Inc. Available at: http://www.nccn.org.
3. Gatalica, Z et al. Molecular characterization of cancers with NTRK gene fusions. Mod Pathol 2019; 32:147-153. doi: 10. 1038/s41379-018-0118-3
4. Study of oral RXDX-101 in adult patients with locally advanced or metastatic cancer TargetingNTRK1, NTRK2, NTRK3, ROS1, or ALK Molecular Alterations. - Full Text View - ClinicalTrials.gov. (2019). Retrieved 10 October 2019, from https://clinicaltrials.gov/ct2/show/NCT02097810
5. Basket Study of Entrectinib (RXDX-101) for the Treatment of Patients With Solid Tumors Harboring NTRK 1/2/3 (Trk A/B/C), ROS1, or ALK Gene Rearrangements (Fusions) - FullText View - ClinicalTrials.gov. (2019). Retrieved 10 October 2019, from https://clinicaltrials.gov/ct2/show/NCT02568267