

Rozlytrek™ (entrectinib) (Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Rozlytrek 100 mg capsule: 5 capsules per day
- Rozlytrek 200 mg capsules: 3 capsules per day

B. Max Units (per dose and over time) [Medical Benefit]:

- 600 mg daily

III. Initial Approval Criteria

- Patient does not have a history of prolonged QTc interval (i.e., QTc interval > 450 milliseconds); **AND**
- Patient will not use therapy in combination with drugs which prolong QT-interval (e.g., amiodarone, sotalol, levofloxacin, venlafaxine, quetiapine, sumatriptan, etc.); **AND**
- Patients with symptoms of or known risk factors for congestive heart failure (CHF) have had left ventricular ejection fraction (LVEF) assessed prior to therapy; **AND**
- Patient will not use therapy with other *NTRK*-inhibitor (i.e., larotrectinib) or ROS1-directed (e.g., crizotinib, etc.) therapy; **AND**
- Patient does not have signs and symptoms of hyperuricemia as evidenced by a baseline serum acid level as tested prior to initiation of therapy; **AND**
- Patient will avoid concomitant use with moderate or strong CYP3A Inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
- Patient will avoid concomitant use with moderate or strong CYP3A Inhibitors (e.g., erythromycin, itraconazole, indinavir, grape fruit juice, etc.); **AND**

Solid Tumors with *NTRK* gene fusion †

- Patient is 12 years or older; **AND**
- Patient has one of the following solid tumors§: soft tissue sarcoma, salivary gland (mammary analogue secretory carcinoma), non-small cell lung cancer, or breast cancer; **AND**
- Tumor has a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion or fusion partner in ETV6-NTRK3 or TPM3-NTRK1 or TPR-NTRK1* without a known acquired resistance mutation; **AND**
- Patient has metastatic disease or locally advanced disease and is not a candidate for surgery due to the potential of causing severe morbidity; **AND**
- Patient has no satisfactory alternative treatments or disease has progressed following treatment; **AND**
- Patient has not received an NTRK-inhibitor in a previous line of therapy

Non-Small Cell Lung Cancer †

- Patient is 18 years or older; **AND**
- Patient has metastatic disease; **AND**
- Patient's tumor is *ROS1*-positive‡; **AND**
- Patient has not been previously treated with *ROS1*-inhibitor therapy (i.e., crizotinib, ceritinib, etc.)

*An FDA-approved test for the detection of *NTRK* gene fusion is not currently available. *NTRK* gene fusions can be identified by means of the following testing methodologies: next-generation sequencing (NGS), fluorescence in situ hybridization (FISH), or reverse transcription-polymerase chain reactions (RT-PCR), etc.

‡An FDA-approved test for the detection of *ROS1* gene fusions is not currently available. *ROS1* gene fusions can be identified by means of the following testing methodologies: NGS, FISH, etc.

§ Note: Requests for other *NTRK* fusion partners (e.g., *LMNA-NTRK1*, *SQSTM1-NTRK1*, *PEAR1-NTRK1*, *EML4-NTRK3*, *CD74-NTRK1*, *PLEKHA6-NTRK1*, *CDC42BPA-NTRK1*, *EPS15L1-NTRK1*, *RBPM5-NTRK3*, *ERC1-NTRK1*, *PDIA3-NTRK1*, *TRIM33-TRK1*, *AKAP13-NTRK3*, *KIF7-NTRK3*, *FAM19A2-NTRK3*, *CGN-NTRK1*, *SQSTM1-NTRK2* etc.) and/or solid tumors (e.g., thyroid, colorectal, neuroendocrine, pancreas, gynecological, or cholangiocarcinoma, etc.), other than those specified, will be evaluated on a case-by-case basis.

† FDA approved indication(s); ‡ Compendia recommended indication(s)

IV. Renewal Criteria

Coverage can be renewed based on the following criteria:

- Patient continues to meet the criteria identified in Section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: congestive heart failure, hepatotoxicity, CNS effects (e.g., cognitive

impairment, mood disorders, dizziness, and sleep disturbances), skeletal fractures, hyperuricemia, QT-interval prolongation, visual disturbances, etc.

V. Dosage/Administration

Indication	Dose
<i>NTRK</i> Gene Fusion-Positive Solid Tumors	<p>Adult Patients 600 mg orally once daily</p> <p>Pediatric Patients ≥ 12 years</p> <ul style="list-style-type: none"> – BSA > 1.50 m²: 600 mg orally once daily – BSA 1.11 to 1.50 m²: 500 mg orally once daily – BSA 0.91 to 1.10 m²: 400 mg orally once daily
<i>ROS1</i> -Positive NSCLC	The recommended dosage of Rozlytrek is 600 mg orally once daily.
Rozlytrek is taken with or without food until disease progression or unacceptable toxicity	

VI. Billing Code/Availability Information

HCPCS code:

- J8999 – prescription drug, oral, chemotherapeutic, nos

NDC:

- Rozlytrek 100 mg capsules: 50242-0091-xx
- Rozlytrek 200 mg capsules: 50242-0094-xx

VII. References

1. Rozlytrek [package insert]. San Francisco, CA; Genentech, Inc.; August 2019. Accessed August 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) entrectinib. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed August 2019.
3. Amatu A, Sartore-Bianchi A, Siena S. *NTRK* gene fusions as novel targets of cancer therapy across multiple tumour types. *ESMO Open*. 2016 Mar 18;1(2):e000023.
4. Lartigue J. TRK inhibitors advance rapidly in “tumor agnostic” paradigm. August 4, 2017. <http://www.onclive.com/publications/oncology-live/2017/vol-18-no-15/trk-inhibitors-advance-rapidly-in-tumoragnostic-paradigm>. Accessed January 29, 2018.
5. Meldolesi J. Neurotrophin Trk receptors: new targets for cancer therapy. *Rev Physiol Biochem Pharmacol*. 2017 Sep 8. doi: 10.1007/112_2017_6.

6. Stransky N, Cerami E, Schalm S, Kim JL, Lengauer C. The landscape of kinase fusions in cancer. *Nat Commun.* 2014 Sep 10;5:4846.
7. Cocco E. *et al* NTRK fusion- positive cancers and TRK inhibitor therapy; Nature Reviews *Nature Reviews Clinical Oncology* volume 15, pages731–747 (2018)

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C07	Malignant neoplasm of parotid gland
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.10	Malignant neoplasm of peripheral nerves of unspecified upper limb, including shoulder
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.20	Malignant neoplasm of peripheral nerves of unspecified lower limb, including hip
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder

ROZLYTREK™ (entrectinib) Prior Auth Criteria

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ICD-10	ICD-10 Description
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right female breast
C50.022	Malignant neoplasm of nipple and areola, left female breast
C50.029	Malignant neoplasm of nipple and areola, unspecified female breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast

ICD-10	ICD-10 Description
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung

ICD-10	ICD-10 Description
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.3	Personal history of malignant neoplasm of breast
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC