Drug Policy:

Rozlytrek™ (entrectinib)

POLICY NUMBER UM ONC_1367	**SUBJECT** Rozlytrek™ (entrectinib)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 3**
DATES COMMITTEE REVIEWED 09/11/19, 12/11/19, 04/08/20, 03/10/21, 11/15/21, 03/09/22	**APPROVAL DATE** March 9, 2022	**EFFECTIVE DATE** March 25, 2022	**COMMITTEE APPROVAL DATES** 09/11/19, 12/11/19, 04/08/20, 3/10/21, 11/15/21, 03/09/22	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1	**NCQA STANDARDS** UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. 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.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR
2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When applicable, generic alternatives are preferred over brand-name drugs.

B. NTRK-Fusion Positive Metastatic Solid Tumors

1. The member has recurrent/metastatic/unresectable solid tumor (e.g., NSCLC) with a positive NTRK fusion in the tumor tissue (test confirmation required) AND Rozlytrek (entrectinib) will be used as a single agent as initial or subsequent therapy, if not previously used as initial treatment.
2. NOTE: The preferred agent, per NCH Policy & NCH Pathway, for NTRK gene fusion positive recurrent, advanced, or metastatic solid tumors is Rozlytrek (entrectinib) over Vitrakvi (larotrectinib). This recommendation is based on the lack of Level 1 evidence (randomized clinical trial and/or meta-analyses) to show the superiority of Vitrakvi (larotrectinib) over Rozlytrek (entrectinib).

C. Non-small cell lung cancer (NSCLC)

1. The member has recurrent, advanced, or metastatic NSCLC and Rozlytrek (entrectinib) may be used as a single agent in members with ROS-1 rearrangement-positive tumors with CNS metastases as first-line therapy, or with ROS-1 rearrangement with/without CNS metastases for subsequent line therapy following prior therapy with Xalkori (crizotinib) or Zykadia (ceritinib).
2. NOTE: The preferred agent, per NCH Policy and NCH Pathway, for first line therapy of ROS1 positive NSCLC with CNS metastases is Rozlytrek (entrectinib); for members without CNS metastases, the preferred agent is Zalkori (crizotinib). This recommendation is based on the lack of Level 1 evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes on rate of CNS progression with Zalkori (crizotinib) compared with Rozlytrek (entrectinib).

III. EXCLUSION CRITERIA

A. Rozlytrek (entrectinib) use after disease progression with the same regimen or other NTRK-targeted therapy [e.g.,Vitrakvi (larotrectinib)] .

B. Concurrent use with other ROS-1/ALK inhibitor (e.g., crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib) or NTRK inhibitor (e.g., larotrectinib).

C. Dosing exceeds single dose limit of Rozlytrek (entrectinib) 600 mg.

D. Treatment exceeds the maximum limit of 90 (100 mg) and 90 (200 mg) tablets/month.

E. 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:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.

3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of 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).
5. 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.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. 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.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Drilon A, et al. Entrectinib in ROS1 fusion-positive non-small-cell lung cancer: integrated analysis of three phase 1-2 trials. Lancet Oncol. 2020 Feb;21(2):261-270.

B. Doebele RC, et al. Entrectinib in patients with advanced or metastatic NTRK fusion-positive solid tumours: integrated analysis of three phase 1-2 trials. Lancet Oncol. 2020 Feb;21(2):271-282.

C. Rozlytrek prescribing information. Genentech Inc South San Francisco, CA 2021.

D. Clinical Pharmacology Elsevier Gold Standard 2022.

E. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2022.

F. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2022.

G. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2022.

H. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

I. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.