UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2026 P 1297-9
Program	Prior Authorization/Notification
Medication	Rozlytrek™ (entrectinib)
P&T Approval Date	10/2019, 10/2020, 10/2021, 10/2022, 1/2023, 1/2024, 1/2025, 1/2026, 5/2026
Effective Date	8/1/2026

1. Background:

Rozlytrek (entrectinib) is a kinase inhibitor indicated for the treatment of:

- Adult patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC).
- Adult and pediatric patients 1 month 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 the confirmatory trials.

The National Comprehensive Cancer Network (NCCN) also recommends the use of Rozlytrek in solid tumors that are (NTRK) gene fusion positive with differing clinical circumstances.

Coverage Information:
Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. <u>Patients less than 19 years of age</u>

1. **Rozlytrek** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

Authorization will be issued for 12 months.

B. <u>Ampullary Adenocarcinoma</u>

1. **<u>Initial Authorization</u>**

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a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of ampullary adenocarcinoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) **One** of the following:

(a) Used for metastatic disease
(b) Used for disease progression

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

C. Appendiceal Neoplasms and Cancers

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of **one** of the following appendiceal neoplasms and cancers:

(a) Appendiceal adenocarcinoma
(b) Goblet cell adenocarcinoma
(c) Undifferentiated carcinoma not otherwise specified

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Used as second-line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

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a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

D. Biliary Tract Cancer

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of biliary tract cancer (e.g., gallbladder, cholangiocarcinoma)

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is **one** of the following:

(a) Gross Residual (R2)
(b) Metastatic
(c) Resectable locoregionally advanced
(d) Unresectable

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

E. Breast Cancer

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of breast cancer

-AND-

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(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is without a known acquired resistance mutation [e.g., TRKA G595R substitution, TRKA G667C substitution, or other recurrent kinase domain (solvent front and xDFG) mutations]

-AND-

(4) Disease is **one** of the following:

(a) Metastatic
(b) Recurrent unresectable
(c) Unresponsive to preoperative systemic therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

F. Central Nervous System Cancers

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of **one** of the following:

(a) Circumscribed glioma
(b) Glioblastoma
(c) High-grade glioma
(d) Brain metastases

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is **one** of the following:

(a) Metastatic

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(b) Recurrent or progressive

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

G. Cervical Cancer

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of cervical cancer

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Used as second-line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

H. Colorectal Cancers

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of colon or rectal cancer

-AND-

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(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Used as second-line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

I. Esophageal, Esophagogastric Junction, and Gastric Cancers

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of esophageal, esophagogastric junction, or gastric cancer

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is **one** of the following:

(a) Metastatic
(b) Recurrent
(c) Unresectable locally advanced

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

J. Gastrointestinal Stromal Tumors

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1. **Initial Authorization**

   a. **Rozlytrek** will be approved based on **all** of the following criteria:

      (1) Diagnosis of gastrointestinal stromal tumor

      -AND-

      (2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

      -AND-

      (3) Used in **one** of the following settings:

         (a) Neoadjuvant therapy to decrease surgical morbidity
         (b) Gross residual disease (R2 resection)
         (c) Unresectable primary disease
         (d) Preoperative/intraoperative tumor rupture
         (e) Recurrent/metastatic disease

   Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Rozlytrek** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

   Authorization will be issued for 12 months.

K. Head and Neck Cancers

1. **Initial Authorization**

   a. **Rozlytrek** will be approved based on **all** of the following criteria:

      (1) Diagnosis of salivary gland tumor

      -AND-

      (2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

      -AND-

      (3) Used as second-line or subsequent therapy

   Authorization will be issued for 12 months.

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2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

L. Hepatocellular Carcinoma

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of hepatocellular carcinoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is recurrent or metastatic

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

M. Histiocytic Neoplasms

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of histiocytic neoplasm

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

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(3) Disease is **one** of the following:

(a) Metastatic
(b) Relapsed/refractory
(c) Symptomatic unresectable or multifocal

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

N. Melanoma

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of cutaneous melanoma

-AND-

(2) Disease is positive for **one** of the following gene fusions:

(a) ROS1-gene fusion
(b) NTRK-gene fusion

-AND-

(3) Disease is metastatic or unresectable

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months

O. Neuroendocrine and Adrenal Tumors

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

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(1) Diagnosis of neuroendocrine tumor

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is without a known acquired resistance mutation [e.g., TRKA G595R substitution, TRKA G667C substitution, or other recurrent kinase domain (solvent front and xDFG) mutations]

-AND-

(4) Disease is **one** of the following:

(a) Locoregional unresectable
(b) Metastatic

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

P. Non-Small Cell Lung Cancer (NSCLC)

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of non-small cell lung cancer (NSCLC)

-AND-

(2) Disease is positive for **one** of the following gene fusions:

(a) ROS1-gene fusion
(b) NTRK-gene fusion

-AND-

(3) Disease is **one** of the following:

(a) Advanced

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(b) Metastatic
(c) Recurrent

Authorization will be issued for 12 months.

2. Reauthorization

a. Rozlytrek will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months

Q. Occult Primary [Cancer of Unknown Primary (CUP)] Cancer

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of **one** of the following occult primary cancers:

(a) Adenocarcinoma
(b) Carcinoma not otherwise specified
(c) Squamous cell carcinoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is without a known acquired resistance mutation [e.g., TRKA G595R substitution, TRKA G667C substitution, or other recurrent kinase domain (solvent front and xDFG) mutations]

-AND-

(4) Used in **one** of the following settings:

(a) Asymptomatic patients with PS 0 and aggressive disease
(b) Symptomatic patients with performance status (PS) 1-2

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

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Authorization will be issued for 12 months.

R. Ovarian/Fallopian Tube/Primary Peritoneal Cancers

1. **Initial Authorization**

   a. **Rozlytrek** will be approved based on **all** of the following criteria:

      (1) Diagnosis of **one** of the following:

         (a) Fallopian tube cancer
         (b) Ovarian cancer
         (c) Primary peritoneal cancer

-AND-

      (2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

      (3) **One** of the following histologies:

         (a) Endometrioid
         (b) Carcinosarcoma (Malignant Mixed Müllerian Tumors)
         (c) Clear cell carcinoma of the ovary
         (d) Mucinous carcinoma
         (e) Serous carcinoma

-AND-

      (4) Disease is persistent or recurrent

   Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Rozlytrek** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

   Authorization will be issued for 12 months.

S. Pancreatic Adenocarcinoma

1. **Initial Authorization**

   a. **Rozlytrek** will be approved based on **all** of the following criteria:

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(1) Diagnosis of pancreatic adenocarcinoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is **one** of the following:

(a) Locally advanced
(b) Metastatic

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

T. Small Bowel Cancer

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of small bowel adenocarcinoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Used as second-line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

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U. Soft Tissue Sarcoma

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of soft tissue sarcoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is **one** of the following:

(a) Advanced
(b) Metastatic

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

V. Thyroid Carcinoma

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of **one** of the following thyroid cancers:

(a) Papillary carcinoma
(b) Follicular carcinoma
(c) Oncocytic carcinoma
(d) Anaplastic carcinoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

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(3) Disease is **one** of the following:

(a) Metastatic
(b) Persistent
(c) Unresectable locoregional recurrent

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

Authorization will be issued for 12 months.

W. Uterine Neoplasm

1. **Initial Authorization**

a. **Rozlytrek** will be approved based on **all** of the following criteria:

(1) Diagnosis of **one** of the following uterine neoplasms:

(a) Endometrial carcinoma
(b) Uterine Sarcoma

-AND-

(2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

-AND-

(3) Disease is **one** of the following:

(a) Advanced
(b) Inoperable
(c) Recurrent
(d) Metastatic

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Rozlytrek** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

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Authorization will be issued for 12 months.

X. Vaginal/Vulvar Cancer

1. **Initial Authorization**

   a. **Rozlytrek** will be approved based on **all** of the following criteria:

      (1) Diagnosis of vaginal or vulvar cancer

      -AND-

      (2) Disease is positive for neurotrophic tyrosine receptor kinase (NTRK) gene fusion (e.g., *ETV6-NTRK3*, *TPM3-NTRK1*, *LMNA-NTRK1*, etc.)

      -AND-

      (3) Used as second-line or subsequent therapy

   Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Rozlytrek** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Rozlytrek therapy

   Authorization will be issued for 12 months.

Y. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B.

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

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4. References:

1. Rozlytrek [package insert]. Genentech USA, Inc.: South San Francisco, CA; January 2024.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed November 18, 2025.

Program	Prior Authorization/Notification - Rozlytrek (entrectinib)
Change Control	
10/2019	New program.
10/2020	Annual review. No changes to clinical criteria.
10/2021	Annual review with no changes to clinical criteria. Updated references.
10/2022	Annual review with no changes to clinical criteria. Added state mandate footnote. Updated references.
1/2023	Removed criteria requiring previous treatment progression or no alternative therapy based on first line recommendations per NCCN for certain cancers. Updated reference.
1/2024	Annual review with update to background. No changes to clinical criteria. Updated references.
1/2025	Annual review with no changes to clinical criteria. Updated references.
1/2026	Annual review. Expanded section on solid tumors to specify each type with their own criteria based on FDA label and NCCN guidance.
5/2026	Removed “metastatic” from non-small cell lung cancer for the diagnostic criterion.

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