Rozlytrek (entrectinib)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Rozlytrek
- **Generic name:** Entrectinib
- **Pharmacological class:** Kinase inhibitor
- **Strength and Formulation:** 100mg, 200mg; capsules
- **Manufacturer:** Genentech
- **How supplied:** Bottle—30-count (100mg), 90-count (200mg)
- **Legal Classification:** Rx

Rozlytrek


NDC 50242-094-90
Rozlytrek™
(entrectinib)
capsules
200 mg
90 capsules
℞only
Genentech
EXP
Lot
NDC 50242-091-30
Rozlytrek™
(entrectinib)
capsules
100 mg
30 capsules
℞only
Genentech
EXP
Lot

Indication

- Treatment of adult patients with metastatic **non-small cell lung cancer** (NSCLC) whose tumors are *ROS1*-positive
- Treatment of 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 either progressed following treatment or have no satisfactory alternative therapy

Dosage & Administration

Adults

- Confirm presence of *ROS1* rearrangement(s) or a *NTRK* gene fusion
- Swallow whole
- **NSCLC or solid tumors**: 600mg once daily. Both: give until disease progression or unacceptable toxicity
- **Avoid moderate or strong CYP3A inhibitors**; if unavoidable, reduce to 200mg once daily (moderate CYP3A inhibitors); or 100mg once daily (strong CYP3A inhibitors)
- Dose modifications for adverse reactions (CHF, CNS effects, hepatotoxicity, hyperuricemia, QT interval prolongation, vision disorders, anemia or neutropenia, others): see full labeling

Dosage & Administration

Children

- NSCLC: not established
- **Solid tumors**: <12yrs: not established
- Confirm presence of a *NTRK* gene fusion
- Swallow whole
- ≥12yrs: body surface area (BSA) >1.50m^2: 600mg once daily; BSA 1.11–1.50m^2: 500mg once daily; BSA 0.91–1.10m^2: 400mg once daily
- Give until disease progression or unacceptable toxicity
- **Avoid moderate or strong CYP3A inhibitors**; if unavoidable and ≥12yrs (w. BSA >1.50m^2), reduce to 200mg once daily (moderate CYP3A inhibitors); or 100mg once daily (strong CYP3A inhibitors)
- Dose modifications for adverse reactions: see full labeling

Considerations for Special Populations

- **Pregnancy:** may cause fetal harm; verify pregnancy status prior to initiating
- **Nursing mothers**: discontinue breastfeeding during treatment and for 7 days after the final dose
- **Pediatric**: <12 years old, safety, efficacy not established for solid tumors; safety, efficacy not established in NSCLC
- **Geriatric:** trials did not include sufficient numbers to determine response difference
- **Renal impairment**: not studied in severe impairment
- **Hepatic impairment**: not studied in moderate or severe impairment

Warnings/Precautions

- **Assess LVEF** prior to initiation in those with risk factors for CHF
- Withhold, reduce dose or permanently discontinue based on severity if **CHF or CNS effects** occur
- Increased risk for **fractures**
- **Monitor LFTs** (including AST/ALT) every 2 weeks during the 1st month, then monthly thereafter, and as clinically indicated; withhold or permanently discontinue based on severity; if withheld, resume at same or reduced dose

Warnings/Precautions

- Known long QT syndrome
- Bradyarrhythmias
- Uncontrolled heart failure
- Electrolyte abnormalities
- **Assess** QT interval, electrolytes, and serum uric acid levels prior to initiation then periodically; withhold and resume (at same or reduced dose) based on severity; monitor

Warnings/Precautions

- Withhold dose if **vision disorders** or new changes occur until improvement or stabilization; conduct an ophthalmological exam as clinically appropriate
- Advise use of **effective contraception** during and for 5 weeks (females of reproductive potential) or for 3 months (males w. female partners) after the last dose

Interactions

- **Potentiated by** moderate or strong CYP3A inhibitors; avoid; if unavoidable, reduce dose (see Dosing)
- Avoid **grapefruit** products
- **Antagonized by** moderate or strong CYP3A inducers; avoid use
- Avoid concomitant drugs known to **prolong QTc interval**

Adverse Reactions

- **Most common (≥20%)**: fatigue, constipation, dysgeusia, edema, dizziness, diarrhea, nausea, dysesthesia, dyspnea, myalgia, cognitive impairment, increased weight, cough, vomiting, pyrexia, arthralgia, vision disorders

- **Others:** CHF, CNS effects, skeletal fractures, hepatotoxicity, hyperuricemia, QT prolongation

Mechanism of Action

- Entrectinib is an inhibitor of the tropomyosin receptor tyrosine kinases (TRK) TRKA, TRKB, and TRKC (encoded by the neurotrophic tyrosine receptor kinase [*NTRK*] genes *NTRK1*, *NTRK2*, and *NTRK3*, respectively), proto-oncogene tyrosine-protein kinase ROS1 (ROS1), and anaplastic lymphoma kinase (ALK)
- The major active metabolite of entrectinib, M5, showed similar *in vitro* activity against TRK, ROS1, and ALK
- Entrectinib demonstrated *in vitro* and *in vivo* inhibition of cancer cell lines derived from multiple tumor types harboring *NTRK*, *ROS1*, and *ALK* fusion genes

Clinical Trials

- Efficacy of Rozlytrek was evaluated in a pooled subgroup of patients with ***ROS1*-positive metastatic NSCLC**
- Study patients were required to have histologically confirmed, recurrent or metastatic, *ROS1*-positive NSCLC, ECOG performance status ≤2, measurable disease per RECIST v 1.1, ≥12 months of follow-up from first posttreatment tumor assessment, and no prior therapy with a ROS1 inhibitor

Clinical Trials

- Efficacy outcome measures included overall response rate (ORR) and duration of response (DoR) according to RECIST v1.1 as assessed by blinded independent central review (BICR)
- Efficacy was assessed in 51 patients with *ROS1*-positive NSCLC

Clinical Trials

Results

- ORR: 78% ([95% CI, 65–89]; N=51)
- Complete response: 6%
- Partial response: 73%
- DoR: ranged from 1.8 to 36.8+ months (n=40 out of 51)
- Tumor shrinkage persisted for at least 12 months in 55% of the 40 patients

Clinical Trials

- Efficacy of Rozlytrek was evaluated in a pooled subgroup of patients with **unresectable or metastatic solid tumors with a *NTRK* gene fusion**
- Study 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; measurable disease per RECIST v1.1; at least 6 months of follow-up after the first dose of Rozlytrek; and no prior therapy with a TRK inhibitor

Clinical Trials

- Efficacy outcome measures were ORR and DoR, as determined by a BICR according to RECIST v1.1
- Efficacy was assessed in the first 54 patients with solid tumors with an *NTRK* gene fusion
- Most common cancers were sarcoma, lung cancer, salivary gland tumors, breast cancer, thyroid cancer, and colorectal cancer

Clinical Trials

Results

- ORR: 57% ([95% CI, 43–71]; N=54)
- Complete response: 7.4%
- Partial response: 50%
- DoR: ranged from 2.8 to 26.0+ months (n=31 out of 54)
- Tumor shrinkage persisted for at least 9 months in 61% of the 31 patients
- See full labeling for efficacy by tumor type and by *NTRK* gene fusion partner

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/rozlytrek/