CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218550Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	September 22, 2023
Application Type and Number:	NDA 218550
Product Name and Strength:	Rozlytrek (entrectinib) Oral Pellets, 50 mg per packet
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Genentech, Inc. (Genentech)
PNR ID #:	2023-1044725317
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD
DMEPA 2 Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD, BCPS

Contents

1 INTRODUCTION 1
1.1 Regulatory History 1
1.2 Product Information 1
2 RESULTS 1
2.1 Misbranding Assessment 1
2.2 Safety Assessment 2
3 CONCLUSION 5
3.1 Comments to the Applicant/Sponsor 5
4 REFERENCES 6
APPENDICES 7

1 INTRODUCTION

This review evaluates the proposed proprietary name, Rozlytrek, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Genentech did not submit an external name study for this proposed proprietary name.

1.1 BACKGROUND

Rozlytrek (entrectinib) was originally approved on August 15, 2019 under NDA 212725 and is currently available as 100 mg and 200 mg capsules.

Genentech submitted NDA 218550 for a proposed new oral pellet formulation of Rozlytrek. The proposed product is supplied in packets; the contents of which is to be sprinkled directly onto one or more spoonsful of soft food and taken by mouth and followed by water. This proposed formulation would expand the dose range for the treatment of younger pediatric patients with solid tumors and provide an option for adult and pediatric patients who have difficulty or are unable to swallow whole capsules.

On August 28, 2023, Genentech submitted the name, Rozlytrek, for our review under NDA 218550 for the newly proposed oral pellet formulation.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 28, 2023.

- Intended Pronunciation: roz lye' trek
- Active Ingredient: entrectinib
- Indication of Use: For the treatment of (b) (4) adult patients with solid tumors that:
    - have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, as detected by an FDA-approved test without a known acquired resistance mutation.
    - are metastatic or where surgical resection is likely to result in severe morbidity.
    - have progressed following treatment or have no satisfactory alternative therapy.
- Route of Administration: Oral
- Dosage Form: Oral Pellets
- Strength: 50 mg per packet
- Dose and Frequency:
    - Recommended Dosage for *NTRK* Gene Fusion-Positive Solid Tumors:
        - Adults: 600 mg orally once daily.
        - Pediatric Patients: Recommended dosage is based on age and body surface area (BSA) as shown below.

Reference ID: 5249596

Age	Recommended Daily Dosage
>6 months	BSA ≥1.51 m^2: 600 mg once daily BSA 1.11 to 1.50 m^2: 400 mg once daily BSA 0.81 to 1.10 m^2: 300 mg once daily BSA 0.51 to 0.80 m^2: 200 mg once daily (b) (4)
>1 month to ≤6 months	250 mg/m^2 once daily
(b) (4)	

- How Supplied: individual packets in a 42-count carton
- Storage: Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F) *[see USP Controlled Room Temperature]* . Store in the original container to protect from moisture.

2 METHODS AND DISCUSSION

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Rozlytrek.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Rozlytrek would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Rozlytrek. The Division of Oncology 2 (DO2) concurred with the findings of OPDP's assessment for Rozlytrek.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Rozlytrek.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[a].

2.2.2 Components of the Proposed Proprietary Name

Genentech indicated in their submission that the proposed proprietary name, Rozlytrek, is derived from the mechanism of action. This proprietary name is comprised of a single word that

[a] USAN stem search conducted on March 1, 2023.

does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On September 7, 2023, the Division of Oncology 2 (DO2) did not forward any comments or concerns relating to Rozlytrek at the initial phase of the review.

2.2.4 Multiple Dosage Forms Under a Single Proprietary Name

The applicant has proposed to market two dosage forms, capsules and oral pellets, under the same proprietary name using a single Prescribing Information to cover (b) (4) and adult indications. We contacted Clinical Pharmacology via email on September 18, 2023 for their assessment of the data to determine whether the proposed Rozlytrek (entrectinib) oral pellet formulation is equivalent to the existing Rozlytrek capsule formulation on a milligram for milligram basis. Clinical Pharmacology informed us that there was a relative bioavailability study comparing Rozlytrek capsules and pellets, which showed comparability. Further, patients were switched between formulations during clinical studies.

Table 1 below compares the currently marketed capsule formulation and the proposed oral pellet formulation.

Table 1. Product Characteristics of Rozlytrek Capsules and Rozlytrek Oral Pellets

	Rozlytrek[b]	**Rozlytrek (proposed)**
Application Number	NDA 212725	NDA 218550
Active Ingredient	entrectinib	entrectinib
Indication	• For the treatment of adult patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC), as detected by an FDA-approved test. • For the treatment of adult (b) (4) with solid tumors that: - have a neurotrophic tyrosine receptor kinase *(NTRK)* gene fusion, as detected by an FDA-approved test without a known acquired resistance mutation,	

[b] Rozlytrek. DailyMed. National Library of Medicine; September 2023. Available from https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=c7c71b0c-2549-4495-86b6-c2807fa54908&type=pdf

<table>
<tr><td></td><td colspan="2">- are metastatic or where surgical resection is likely to result in severe morbidity, and
- have progressed following treatment or have no satisfactory alternative therapy.</td></tr>
<tr><td>Route of Administration</td><td>Oral</td><td>Oral</td></tr>
<tr><td>Strength</td><td>100 mg and 200 mg</td><td>50 mg per packet</td></tr>
<tr><td>Dose and Frequency</td><td colspan="2">Adults: 600 mg orally once daily with or without food until disease progression or unacceptable toxicity.
Pediatric (older than 6 months):
<table>
<tr><th>Body Surface Area (BSA)*</th><th>Recommended Dosage
Orally, once daily (b) (4)</th></tr>
<tr><td>≥ 1.51 m^2</td><td>600 mg (b) (4)</td></tr>
<tr><td>1.11 to 1.50 m^2</td><td>400 mg (b) (4)</td></tr>
<tr><td>0.81 to 1.10 m^2</td><td>300 mg</td></tr>
<tr><td>0.51 to 0.80 m^2</td><td>200 mg</td></tr>
</table>
(b) (4)

Pediatric (> 1 Month to ≤ 6 Months): 250 mg/m^2 orally once daily, (b) (4)
(b) (4)</td></tr>
<tr><td>Dosage Form</td><td>Capsules</td><td>Oral Pellets (proposed)</td></tr>
</table>

How Supplied	30-count 100 mg capsules 90-count 200 mg capsules	42-count carton (each packet contains 50 mg entrectinib)
Storage:	Store (b) (4) in the original container to protect from moisture.	Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F) *[see USP Controlled Room Temperature]*. Store in the original container to protect from moisture.

We note that the proposed dosage forms share the same active ingredient, route of administration, and frequency of administration. It is a common and accepted practice to have multiple dosage forms of an active ingredient managed under one proprietary name. Additionally, our routine postmarketing surveillance has not identified any signals attributed to name confusion involving Rozlytrek. We further acknowledge that, when marketing under the same proprietary name, the differences between the two dosage forms such as the different method of oral administration can be communicated and differentiated by labels and labeling.

Therefore, given the aforementioned considerations, we do not object to the Applicant's proposal to market the proposed product with the proprietary name, Rozlytrek.

2.2.5 Communication of DMEPA's Determination

On September 22, 2023, DMEPA 2 communicated our determination to the Division of Oncology 2 (DO2).

3 CONCLUSION

The proposed proprietary name, Rozlytrek, is conditionally acceptable.

If you have any questions or need clarifications, please contact Latonia Ford, OSE project manager, at 301-796-4901.

3.1 COMMENTS TO GENENTECH, INC.

We have completed our review of the proposed proprietary name, Rozlytrek, and have concluded that this name is conditionally acceptable.

If any of the proposed product characteristics as stated in your submission, received on August 28, 2023 are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [c]

[c] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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