CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217514Orig1s000

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:	March 10, 2023
Application Type and Number:	NDA 217514
Product Name and Strength:	Tafinlar (dabrafenib) tablets for oral suspension, 10 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Novartis Pharmaceuticals Corporation (Novartis)
PNR ID #:	2023-1044725013
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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Tafinlar, 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. Novartis did not submit an external name study for this proposed proprietary name.

1.1 BACKGROUND

Tafinlar (dabrafenib) was originally approved on May 29, 2013 under NDA 202806 and is currently available as 50 mg and 75 mg capsules.

Novartis submitted NDA 217514 for a new tablet for oral suspension formulation of Tafinlar for a new indication in combination with trametinib for the treatment of pediatric patients 1 year of age and older with low-grade glioma with a BRAF V600E mutation who require systemic therapy.

On February 24, 2023, Novartis submitted for our review the name, Tafinlar, under NDA 217514 for the newly proposed tablet for oral suspension formulation.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 24, 2023.

- Intended Pronunciation: TAFF-in-lar
- Active Ingredient: dabrafenib
- Indication of Use: Treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.
- Route of Administration: Oral
- Dosage Form: tablets for oral suspension
- Strength: 10 mg
- Dose and Frequency:

	Recommended dose	
Body weight	Total Daily Dose	(b) (4)
8 to 9 kg	20 mg twice daily	
10 to 13 kg	30 mg twice daily	
14 to 17 kg	40 mg twice daily	
18 to 21 kg	50 mg twice daily	
22 to 25 kg	60 mg twice daily	

26 to 29 kg	70 mg twice daily	(b) (4)
30 to 33 kg	80 mg twice daily	
34 to 37 kg	90 mg twice daily	
38 to 41 kg	100 mg twice daily	
42 to 45 kg	110 mg twice daily	
46 to 50 kg	130 mg twice daily	
≥ 51 kg	150 mg twice daily	

- How Supplied: 10 mg tablets for oral suspension: white to slightly yellow, round biconvex 6 mm tablet debossed with "D" on one side and "NVR" on the other side. Available in bottles of 210 with child resistant closures (NDC 0078-1154-21). Each bottle contains 2 silica gel desiccants.
- 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].

2 METHODS AND DISCUSSION

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Tafinlar 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 Tafinlar. The Division of Oncology 2 (DO2) concurred with the findings of OPDP's assessment for Tafinlar.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

[a] USAN stem search conducted on March 1, 2023.link above does not

2.2.2 Components of the Proposed Proprietary Name

Novartis did not provide a derivation or intended meaning for the proposed proprietary name, Tafinlar, in their submission. This proprietary name is comprised of a single word. We note that the proposed proprietary name contains the following medical abbreviations:

- AF = augmented formula, atrial fibrillation/atrial flutter
- IN = Intranasal
- LA = long acting
- LAR = long-acting release

Although we typically discourage the inclusion of medical abbreviations in the proprietary names, 'af', 'in', 'la', and 'lar' are common letter strings in proprietary names (e.g. Fintepla, Enbivinc, Sular) and we are unaware of any post-market reports of name confusion medication error associated with these specific abbreviations. We determined that the location for most of these abbreviations in the infix of the name is unlikely to be separated from the surrounding letters or be misunderstood within the context of a prescription that could lead to confusion. Therefore, in this case we do not object to the letter strings 'af', 'in', and 'la', in the proposed proprietary name. Additionally for the abbreviation "lar" at the suffix position, we evaluated the possibility of interpreting the name as "[drug name similar to Tafin] LAR." and did not identify any names that would pose a risk for confusion.[b] Therefore, in this case we also do not object to the letter string 'lar' in the proposed proprietary name.

Beyond these noted abbreviations, we note that Tafinlar does not contain any additional 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 March 10, 2023, the Division of Oncology 2 (DO2) did not forward any comments or concerns relating to Tafinlar 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 tablets for oral suspension, under the same proprietary name to cover both pediatric and adult patients for treatment of the approved indications. We contacted Clinical Pharmacology via email on March 1, 2023 for their assessment of the data to determine whether the proposed Tafinlar (dabrafenib) tablet for oral suspension is equivalent to the existing Tafinlar capsule on a milligram for milligram basis. Clinical Pharmacology informed us that similar steady state exposure was observed for dabrafenib for oral suspension and dabrafenib capsule formulations with AUCtau and Cmax ratios of 1.0 and 1.0, respectively. These results support comparable PK of dabrafenib between liquid and solid formulations.

Table 1 below compares the currently marketed capsule formulation (to be swallowed whole) and the proposed pediatric tablets for oral suspension (to be dispersed in water before ingestion).

[b] POCA search conducted on March 9, 2023 in version 5.2.

Table 1. Product Characteristics of Tafinlar (capsules) and Tafinlar (tablets for oral suspension)		
	Tafinlar[c]	**Tafinlar (proposed)**
Application Number	NDA 202806	NDA 217514
Active Ingredient	dabrafenib	
Indication	Tafinlar is a kinase inhibitor indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. Tafinlar is indicated, in combination with trametinib, for: • the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. • the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.	Tafinlar is a kinase inhibitor indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. Tafinlar is indicated, in combination with trametinib, for: • *(proposed) the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy* • the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or

[c] Tafinlar. DailyMed. National Library of Medicine; February 2023. Available from https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=fee1e6b1-e1a5-4254-9f2e-a70e0f8dbdea&type=pdf

	• the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test. • the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options. • the treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options.	V600K mutations as detected by an FDA-approved test. • the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection. • the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test. • the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options. • the treatment of adult and pediatric patients 6 years of age and older with locally advanced or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment or have no satisfactory alternative treatment options
Route of Administration	Oral	
Strength	50 mg and 75 mg	10 mg
Dose and Frequency	Approved Capsule: See Full Prescribing Information[1] ***Proposed Tablet for Oral Suspension (weight-based):***	

<table>
<tr><td></td><td colspan="2">
Table 2. Recommended Dosage for TAFINLAR Tablets for Oral Suspension (Weight-based Dose)
<table>
<tr><td></td><td colspan="2">Recommended dose</td></tr>
<tr><td>Body weight</td><td>Total Daily Dose</td><td>(b) (4)</td></tr>
<tr><td>8 to 9 kg</td><td>20 mg twice daily</td><td rowspan="14"></td></tr>
<tr><td>10 to 13 kg</td><td>30 mg twice daily</td></tr>
<tr><td>14 to 17 kg</td><td>40 mg twice daily</td></tr>
<tr><td>18 to 21 kg</td><td>50 mg twice daily</td></tr>
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<tr><td>46 to 50 kg</td><td>130 mg twice daily</td></tr>
<tr><td>≥ 51 kg</td><td>150 mg twice daily</td></tr>
</table>
</td></tr>
<tr><td>Dosage Form</td><td>Capsule</td><td>Tablet for Oral Suspension</td></tr>
<tr><td>How Supplied</td><td>Bottles of 120 Capsules</td><td>Bottles of 210 tablets with child resistant closures. Each bottle contains 2 silica gel desiccants.</td></tr>
<tr><td>Storage:</td><td colspan="2">Store at room temperature 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Store in original bottle with the desiccants.</td></tr>
</table>

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 Tafinlar. We further acknowledge that, when marketing under the same proprietary name, the differences between the two dosage forms such as the different strengths and the different the method of oral administration (Disperse tablets in water, then drink vs. swallow capsule whole) 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, Tafinlar.

2.2.5 Communication of DMEPA's Determination

On March 10, 2023, DMEPA 2 communicated our determination to the Division of Oncology 2 (DO2).

3 CONCLUSION

The proposed proprietary name, Tafinlar, 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 NOVARTIS PHARMACEUTICALS CORPORATION

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

If any of the proposed product characteristics as stated in your submission, received on February 24, 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. [d]

[d] 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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03/10/2023 03:10:27 PM

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