CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217514Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA OPQ Review and Evaluation

NDA 217514
Review # 01

OPQ RECOMMENDATION: APPROVAL

Drug Substance Retest Period: Proposed retest period (b) (4) months for (b) (4) dabrafenib mesylate drug substance when stored (b) (4)
FDA Assessment: Retest date of (b) (4) months may be granted when stored at the proposed storage conditions

Drug Product Expiration Dating Period: Proposed shelf life 24 months.
Climate zones I and II storage conditions: (b) (4)
Climate zones III and IV storage conditions: Do not store above 30°C.

FDA Assessment: An expiration dating period of 24 months may be granted when stored at USP controlled room temperature conditions: "Store at 20ºC to 25 ºC (68 ºF to 77 ºF); excursions permitted between 15 ºC and 30 CC (59ºF and 86ºF) [see USP Controlled Room Temperature].". Note that the carton, container, and package insert comply with current ONDP practice.

[Applicant will complete this section.]

Drug Name/Dosage Form	Dabrafenib mesylate/tablet for oral suspension
Strength	10 mg
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Indication	Dabrafenib 10 mg tablet for oral suspension (dispersible tablet) in combination with trametinib 4.7 mg powder for oral solution for the treatment of BRAF V600E mutation-positive low-grade glioma in pediatric patients 1 year of age and older
Applicant	Novartis Pharmaceutical Corporation
US agent, if applicable	Not applicable

[FDA will complete these sections.]

Submit Date(s)	August 17, 2022
Received Date(s)	August 17, 2022
PDUFA Goal Date	February 17, 2023

FDA assessment is indicated in colored fonts

Division/Office	Division of Oncology 2/Office of Oncologic Diseases
Review Completion Date	January 31, 2023
Established Name	Dabrafenib
(Proposed) Trade Name	TAFINLAR
Pharmacologic Class	Kinase inhibitor
Recommendation on Regulatory Action	Approval

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
SD 2	08/07/2022	All
SD 7	09/12/2022	OPMA
SD 8	09/16/2022	OPMA
SD 16	10/26/2022	Biopharm
SD 21	11/15/2022	DP
SD 26	12/12/2022	OPMA
SD 29	12/28/2022	OPMA
SD 30	01/06/2023	OPMA

Quality Review Team

DISCIPLINE	PRIMARY REVIEWER	SECONDARY REVIEWER
Drug Substance	Rajan Pragani	Haripada Sarker
Drug Product	Olen Stephens	Xing Wang
Process and Facility	Md Abdullah A Mahmud	Zhaoyang Meng
Microbiology	Julie Nemecek	Bryan Riley
Biopharmaceutics	Mei Ou	Mei Ou
Regulatory Business Process Manager	Janell Artis	
Application Technical Lead	Xing Wang	
ORA Lead	N/A	
Environmental	Olen Stephens	Xing Wang

ORBIS Partner Agency Quality Review Team (To be redacted for FOIA)

Agency	PRIMARY REVIEWER	SECONDARY REVIEWER
Anvisa	No reviewers assigned	No reviewers assigned
Israel Ministry of Health	(b) (4)	
Swissmedic Switzerland		

RELATED/SUPPORTING DOCUMENTS

DMFs:

[Applicant will complete]				[FDA will complete]	
DMF #	**Type**	**Holder**	**Item Referenced**	**Status**	**Comments**
(b) (4)	-	(b) (4)		Adequate	Open, Active, reviewed for this specific item
	III			Adequate	Open, Active, supports several approved A/NDAs
	III			Adequate	Open, Active, supports several approved A/NDAs
	-		r	Adequate	Open, Active, supports several approved A/NDAs
	-			Adequate	Open, Active, supports several approved A/NDAs
	-			Adequate	Open, Active, reviewed for this product including E/L study by the NDA holder

Other Documents: *IND, RLD, or sister applications*
[Applicant will complete this section.]

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	217514	Dabrafenib 10 mg tablet for oral suspension

CONSULTS

[FDA will complete this section.]

None

TABLE OF CONTENTS

Evaluation of the Quality Information

DIFFERENCES IN M3 MODULE IN SUBMISSIONS TO DIFFERENT AGENCIES

#	FDA (US)	Israel	Singapore	Switzerland	Brazil
Drug Substance					
Description	White to slightly colored solid	(b) (4)			
Drug Product					
Specification P51, P52, P53, P56	(b) (4)				
Stability P81	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 package (b) (4)	(b) (4)			

1. EXECUTIVE SUMMARY

[FDA ATL will complete this section.]

a. Summary of Rationale for Recommendation:

The applicant provided sufficient information to assure the identity, strength, purity, and quality of the proposed drug product. All associated manufacturing, testing, packaging facilities were deemed acceptable. Based on the OPQ review team's evaluation of the information provided in the submission, OPQ recommends APPROVAL of NDA 217514 for TAFINLAR® (dabrafenib) tablets for oral suspension.

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:
Drug Substance - Adequate
Drug Product - Adequate
Quality Labeling - Adequate
Manufacturing - Adequate
Biopharmaceutics - Adequate
Microbiology – Adequate

Life Cycle Considerations:
[FDA (b) (4) to include any life-cycle considerations here]
None

2. APPLICATION BACKGROUND

The purpose of this NDA submission is to seek approval for dabrafenib in combination with trametinib for the treatment of pediatric patients 1 year of age and older with low-grade glioma who require systemic therapy. Dabrafenib and trametinib have been investigated in multiple clinical studies, mostly in adult patients, as both single agents and in combination (hereafter referred to as "D+T") to treat patients with BRAF V600 mutation-positive cancers since 2007. Following the initial approval of dabrafenib and trametinib in 2013, the combination therapy with D+T has been approved in over 80 countries worldwide for the treatment of advanced BRAF V600 mutation-positive solid tumors in adults including melanoma, non-small cell lung cancer, and anaplastic thyroid cancer (locally approved indications may vary), and has demonstrated a well-established benefit-risk profile in adult patients.
This application also seeks approval for novel age-appropriate pharmaceutical forms for dabrafenib (10 mg tablet for oral suspension/dispersible tablet) and trametinib (0.05 mg/mL oral solution after reconstitution) that can be conveniently dosed and administered in patients 1 year of age and older who are unable to swallow the solid dosage forms.
On March 28, 2022, FDA granted Breakthrough Therapy designation for dabrafenib in combination with trametinib for the treatment of pediatric patients one year of age and older with LGG with a BRAF V600E mutation who require systemic therapy.
On Feb 8, 2016, FDA granted Orphan Drug Designation for dabrafenib for the treatment of malignant glioma with BRAF V600 mutation.

3. SUMMARY OF CMC SPECIFIC PRESUBMISSION AGREEMENTS

The Applicant's Position:

The drug substance is cross-referenced to NDA202806 for Tafinlar® 50 mg and 75 mg capsule, hard. (b) (4) Updated modules have been submitted to NDA 202806 as agreed. Batch analyses and stability modules (b) (4) are included in the submission to NDA 217514.

The FDA's Assessment: ***Consistent with FDA's records***

[FDA will complete this section.]

4. ENVIRONMENTAL ASSESSMENT

The Applicant's Position:

As set forth in 21 CFR Part 25.31(b), action on a New Drug Application (NDA) is categorically excluded from the requirement to prepare an Environmental Assessment (EA) or an Environmental Impact Statement (EIS) if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be less than 1 part per billion (ppb). "Increased use", as defined in 21 CFR Part 25.5(a), will occur if the drug is "administered at higher dosage levels, for longer duration or for different indications than were previously in effect, or if the drug is a new molecular entity."
Novartis Pharmaceuticals Corporation is filing a New Drug Application for Tafinlar (dabrafenib) tablet for oral suspension and Mekinist® (trametinib) powder for oral solution. Dabrafenib is an orally bioavailable inhibitor of B-Raf (BRAF) protein with potential antineoplastic activity. Trametinib is an orally bioavailable, reversible, highly selective, allosteric inhibitor of mitogen-activated extracellular signal regulated kinase 1 (MEK1) and MEK2. In the current NDA, Novartis is seeking approval for the combination of dabrafenib and trametinib in the following indication:
"TAFINLAR in combination with trametinib, for 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."
"MEKINIST in combination with dabrafenib, for 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."
Novartis certifies that this submission for Tafinlar and Mekinist qualifies for a categorical exclusion in accordance with 21 CFR Part 25.31(b) as the estimated environmental intake concentration of the active moieties, dabrafenib and trametinib, will be significantly less than 1 ppb, based on the peak production estimates within the next five years.
Further, Novartis states that, to the best of its knowledge, no extraordinary circumstances exist which may significantly affect the quality of the human environment and would thus require the preparation of at least an Environmental Assessment.

The FDA's Assessment: ***Adequate***

In Module 1.12.14, the applicant provided estimated calculations for the amount of the active moiety entering the aquatic environment over the next five years. The calculations show that the expected introduction concentration remains well below the 1 ppb limit.

5. FACILITIES

Drug substance manufacturing, quality control and stability storage and testing facilities are listed on the following page:

---------- [Applicant to fill] ----------

Site/address	FEI/DUNS	Responsibility	[FDA to fill] Recommendation
[redacted]	[redacted]	(b) (4)	*Not applicable for N217514*
			Not applicable for N217514
			Not applicable for N217514
			Approve
			Approve
			Approve
			Not applicable for N217514
			Not applicable for N217514

Site/address	FEI/DUNS	Responsibility	Recommendation
(b) (4)			*Not applicable for N217514*
(b) (4) No longer active			

In the above table, (b) (4) is introduced in NDA 202806 as an alternative drug substance manufacturing, quality control and stability testing site (b) (4)

Drug product manufacturing, packaging and testing facilities are listed below:

---------- [Applicant to fill] ----------			[FDA to fill]
Site/address	**FEI/DUNS**	**Responsibility**	**Recommendation**
Novartis Pharma Stein AG Schaffhauserstrasse 4332 Stein Switzerland	3002653483/ 488152505	Manufacture/ (b) (4)	*Approve*
(b) (4)			*Approve*
			No Evaluation Necessary

(b) (4)

No Evaluation Necessary

The FDA's Assessment: ***Adequate***

(b) (4)

(b) (4)

[redacted]

Response (Adequate): (b) (4)

[redacted] Applicant updated the Form FDA 356 h with the manufacturing sites intended to be used for commercial manufacturing of NDA 217514. The response is deemed adequate.

6. DRUG SUBSTANCE

A cross reference is made to dabrafenib mesylate drug substance sections of approved NDA 202806.

(b) (4)

[redacted]

49 Page(s) have been Withheld in Full as B4 (CCI/TS) immediately following this page

8. BIOPHARMACEUTICS

a. BCS Classification

Applicant to fill:

BCS Classification: BCS II

FDA assessment (FDA to fill): Note the formal BCS designation is not requested. Acceptable

b. Dissolution Test

[Applicant to fill]

USP Apparatus	Paddle Rotation Speed	Medium Volume	Temperature	Medium	Acceptance Criterion
II	75 rpm	500 mL	37°C	Hydrochloric acid 0.075 M	Not less than (b) (4)% (Q value) of the declared content in 15 minutes

Biopharmaceutics Figure 1: Dissolution Profiles as a function of:

(b) (4)

3 Page(s) have been Withheld in Full as B4 (CCI/TS) immediately following this page

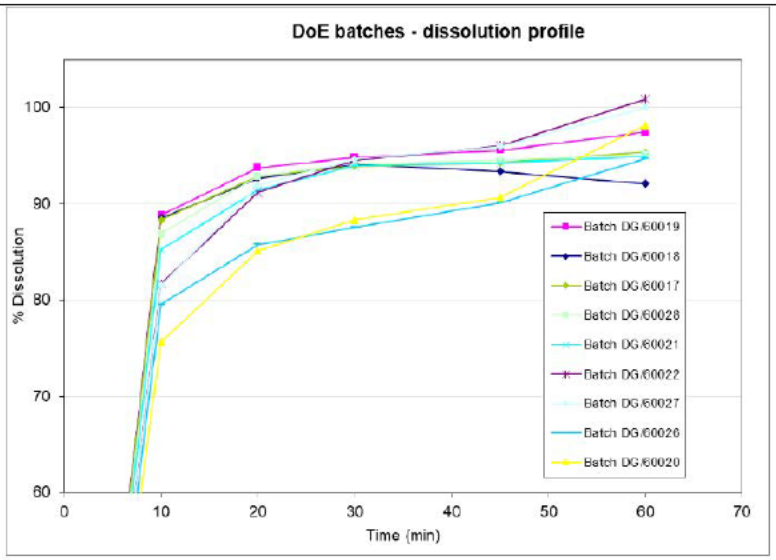
(b) (4)

[redacted]

FDA Comment: (b) (4)

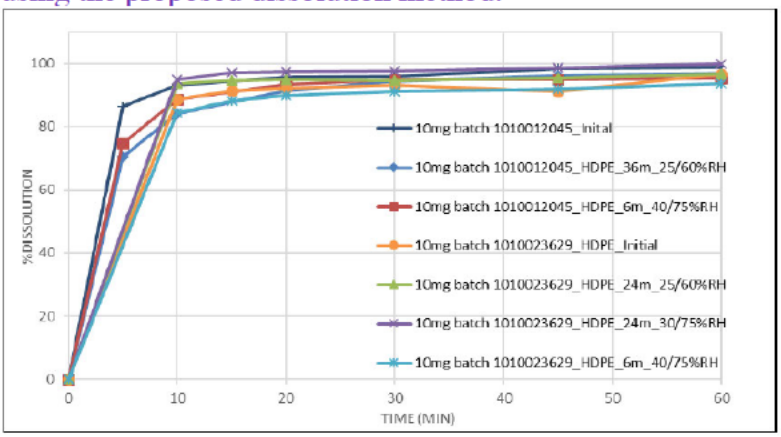
[redacted]

In addition, FDA reviewed the provided data support the discriminating ability with regards to drug product composition. Different DoE batches with different compositions showed different dissolution by using the proposed dissolution method (*figure below*), so that the proposed dissolution method has acceptable discriminating ability with regards to composition.



Dissolution profiles of DoE batches with different compositions (from Figure 6-4 in M.3.2.P.2 Dissolution Method Development)

FDA reviewed the data to support the discriminating ability of the proposed dissolution method with regards to storage condition. As figure showed below, pivotal clinical batch 1010012045 (from study G2101) and clinical batch 1010023629 (from study G2201) showed complete and stable dissolution under long-term stability conditions 25°C/60% RH and 30°C/75% RH up to 36 months with no trends being observed by using the proposed dissolution method.



Dissolution profiles of pivotal clinical batches (1010012045 and 1010023629) under long-term and accelerated stability conditions (from Figure 6-8 in M.3.2.P.2 Dissolution Method Development)

(b) (4)

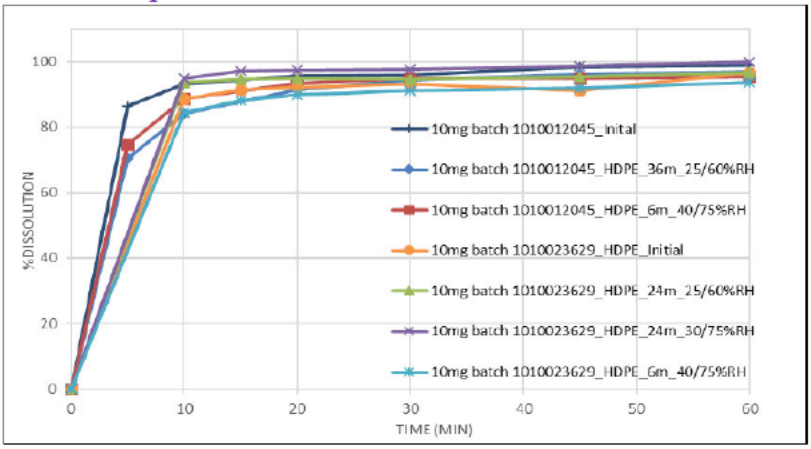
(b) (4)

[redacted]

f. Justification for selection of the acceptance criteria (or criterion)

(b) (4)	Applicant's comments: Dissolution profile of registration stability batches in the proposed dissolution method is provided.

FDA Comment: Note the *figure f* above provided by the Applicant was not pivotal or registration batches dissolution data profiles. The dissolution data profiles of the pivotal clinical batch 1010012045 (from study G2101) and clinical batch 1010023629 (from study G2201) under long-term and accelerated stability conditions up to 36 months are presented below.



Dissolution profiles of pivotal clinical batches (1010012045 and 1010023629) under long-term and accelerated stability conditions (from Figure 6-8 in M.3.2.P.2 Dissolution Method Development)

Dissolution data of three registration batches (1010029776, 1010029777, and 1010029778) were collected at 15 minutes under various stability conditions by using the proposed dissolution method. The data showed that all three registration batches pass the proposed dissolution acceptance criterion of "Q(b) (4)% in 15 minutes" either at Stage 1 or Stage 2 testing from release to 12 months. Combined with the dissolution data from clinical batches (*figure above*), the proposed dissolution acceptance criterion of "Q=(b) (4)% in 15 minutes" is acceptable.

Overall, FDA considered that the proposed dissolution method parameters have been evaluated. The proposed dissolution method showed acceptable discriminating ability with regards to composition and (b) (4)/storage condition. The overall dissolution data support the proposed dissolution acceptance criterion. Therefore, the proposed dissolution method and acceptance criterion are acceptable as a QC test for batch release and stability testing, as: USP Apparatus II (Paddle), 75 rpm, 500 mL of 0.075 N HCl, pH 1.2, 37°C; Q=(b) (4)% in 15 minutes.

	Applicant to fill:	FDA assessment: see FDA comments above
The dissolution method is discriminating for:		
i) Particle size distribution (PSD) Link[1]: [3.2.P.2.2], page 13	Not discrimitating	Agree Page#:
ii) Polymorph/solid state form Link[1]: [3.2.P.2.2], page 13	Not applicable	Agree Page#:
iii) Formulation variations Link[1]: [3.2.P.2.2], page 13	Discriminating	Agree Page#:
iv) Manufacturing process variations Link[1]: [3.2.P.2.2], page 13	Not discrimitating	Agree Page#:
v) Other (specify): Storage conditions Link[1]: [3.2.P.2.2], page 13	Discriminating	Agree Page#:

[1]The applicant to provide link to the appropriate section in the submission. FDA reviewer may update the link as needed.

c. Bridging Throughout Drug Product Development (Formulation, Process, or Site Change)

[To the Applicant: Include a schematic representation of the development of your proposed drug product from initial IND-product to the to-be-marketed product. Include all the formulation/manufacturing/process/etc. changes that occurred throughout development, the studies (in vitro or in vivo) bridging those products, and the PK, clinical, stability-registration studies in which those products were used.
Applicant provide supporting data/Figure(s) here:]

The composition of the proposed commercial formulation is the same as the one used for the pivotal pediatric clinical study CDRB436G2201 and in registration stability studies. Initial clinical batches for the pivotal study were manufactured at (b) (4) The manufacturing process was then transferred to Novartis Pharma Stein AG, Switzerland, which has been the site for the manufacture of further clinical batches and the samples for the registration stability studies and is the proposed commercial manufacturing site.
The manufacturing process has been the same in terms of unit operations and their sequence throughout development with a few minor changes implemented as a consequence of process improvements. A comparison of the process parameters and ranges used during the various stages of development is provided in section 3.2.P.2.3. None of these minor changes required bioavailability bridging. The absence of potential impact of manufacturing process changes has been monitored through testing of the CQAs of the tablet for oral suspension/dispersible tablet both at release and during stability.

[To the Applicant: Insert text here]

The FDA's Assessment: ***Adequate***

Different formulations were developed and used from the initial clinical studies to the commercial products, (b) (4) (iii) tablets for oral suspension, 10 mg. These formulations have been used in all Phase I/II and pivotal studies, i.e., DRB436A2102, CTMT212X2101, DRB436G2101, and DRB436G2201. The pharmacokinetics (PK) and relative bioavailability data information of these formulations and different dose have been evaluated and is under purview of Office of Clinical Pharmacology (OCP).

During pharmaceutical development, (b) (4) The same proposed dissolution method was used from Phase 1/2 pivotal clinical batches to registration/stability batches.

From the response to the Biopharmaceutics Information Request dated 10/27/2022, the Applicant clarified that (i) clinical batches manufactured at (b) (4) (b) (4) kg scale) were debossed with "8" on one side and no deboss on the other; (ii) commercial batches manufactured at Novartis Stein (b) (4) kg scale) are debossed with "D" on one side and "NVR" on the other. The comparative dissolution testing showed that the clinical batch (e.g., 1010021609 manufactured at (b) (4) and commercial batches (e.g., clinical batch, 1010023629, registration batches 1010029776, 1010029777 and 1010029778, manufactured at Novartis Stein) with minor change in debossing, minor change in manufacturing process parameters, and from different manufacturing sites, had comparable and consistent dissolution behavior (*table and figure below*).

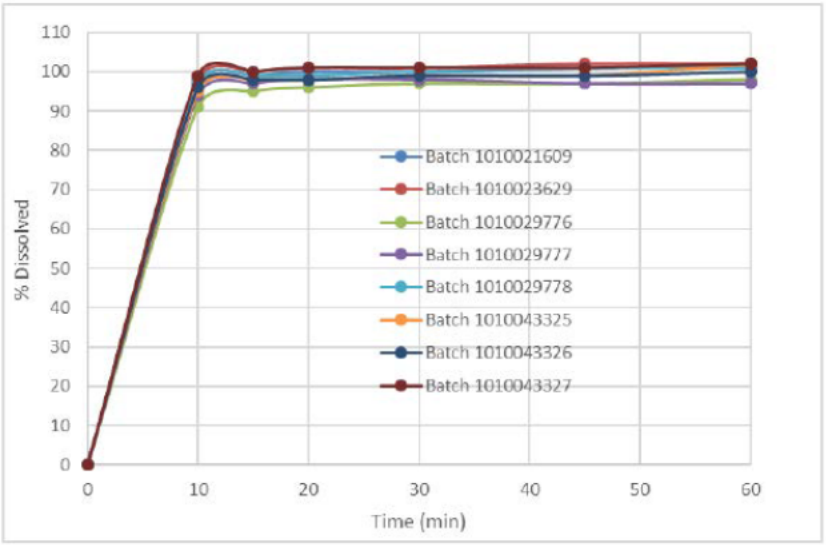
Summary of DRB436 10 mg dispersible tablets batch information and process parameters for (b) (4) (from Table 2-1 in 10/27/2022 IR response)

Table 2-1 Summary of DRB436 10 mg dispersible tablets batch information and process parameters (b) (4)

(b) (4)

(b) (4)

Dissolution profile comparison for DRB436 10 mg dispersible tablet clinical batch, registration stability batches and pre-validation batches by using the proposed dissolution method (n=12) (from Figure 3-1 in 10/27/2022 IR response)



Since from the pivotal clinical batches to the commercial batches: (i) there is no formulation/composition change; (ii) the minor change in imaging (debossing) and manufacturing process, and the changes in manufacturing site and scale up, do not impact dissolution. Overall, scientific bridging throughout the drug development appears to be established, also pending on the OCP's assessment of PK data information provided.

d. Biowaiver Request

The Applicant's Position:

The NDA does not contain a biowaiver request.

A biowaiver is not needed for dabrafenib 10 mg tablet for oral suspension/dispersible tablet for the following reasons:

- There is only one strength of the dosage form.
- The composition of the proposed commercial formulation is the same as the one used for the pivotal pediatric clinical study CDRB436G2201 and in registration stability studies.
- The manufacturing process has been the same in terms of unit operations and their sequence throughout development with a few minor changes implemented as a consequence of process improvements. None of these minor changes required bioavailability bridging.
- A comparison to the marketed solid dosage form (capsule, hard) has been evaluated by a human PK study CDRB436G2101 and popPK data evaluation of clinical study data, namely of the pivotal pediatric study CDRB436G2201.

The FDA's Assessment: ***Adequate***

Biowaiver request is not needed or required because only one strength product is proposed.

e. Data to Support IVIVC and/or PBBM Modeling, If Applicable.

Not applicable

The FDA's Assessment: ***Adequate***

There is no modeling being provided.

9. LABELING

The proposed package insert is a revision of the approved label for Tafinlar® (dabrafenib) capsules, for oral use to include Tafinlar® (dabrafenib) tablets for oral suspension.

USPI

Highlights: ***Adequate***

The label adds the new dosage form with appropriate representation of the dosage form and its strength.

Section 2 (if relevant): ***Adequate***

Section 2.3 includes administration instructions for the oral suspension following dispersing the tablet. The administration instructions are accurate with regards to time required for tablet disintegration and an in-use time that is related to maintaining the suspension (not chemical degradation concerns). The instructions for preparing the suspension is included in the 'Instructions for Use' addendum. CMC differs to DMEPA with regards to whether this information should also be included in Section 2.

Section 3 Dosage Forms and Strengths: ***Adequate***

The section includes the new dispersible tablet dosage form. The description of the tablets is accurate and consistent with the specification of the tablet.

Section 11 Description: ***Adequate***

If the following excipients used in the drug product, include warning/declaration in the USPI:

(b) (4)

This section was edited to include the tablet for oral suspension dosage form. An accurate description of the strength and mesylate salt content is included. The excipients are listed, but should be organized alphabetically.

Section 16 How Supplied/Storage and Handling: ***Adequate***

The description of the tablets for oral suspension is accurate. There is a placeholder for the NDC number, which is acceptable. The text should be revised to include instructions to 'Store and dispense in the original bottle with the desiccant.' The section should also include a description of the container closure as being 'Child Resistant'. The storage condition is consistent with current USP Controlled Room Temperature preferred language.

Manufacturer Information (Name and Address): ***Provided: Adequate***
The distributor's information is provided.

Carton/Container Label ***Adequate***

The carton and container labels contain all the required information including the accurate dosage form, expression of strength based on the salt free dabrafenib, expiration, storage conditions, and manufacturer. [redacted] (b) (4) instructions to dispense in the original container and to not remove the desiccant cannisters. The carton container includes a description of its contents, the tablet bottle plus two dosing cups. There are instructions to dispense the product with the medication guide.

Microbiology assessment:
The required amount of tablets for dosing are dissolved in water in a dosing cup (1-4 tablets in 5 mL of water or 5-15 tablets in 10 mL of water). Tablets may take up to 3 minutes to dissolve. After this solution is consumed, an additional 5 mL of water is added to the dosing cup to dissolve any remaining drug residue. This solution is also administered to the patient to ensure the full dosage is received.

The solution is administered no more than 30 minutes after the tablets have been dissolved. The solution should be discarded after 30 minutes. The risk of microbial proliferation is therefore low.

Final Risk Assessments

[FDA will complete this section.]
To the Review Team: *Keep the appropriate Table; delete the rest*

Initial Risk Identification			Review Assessment		
Attribute/ CQA	**Factors that can impact the CQA**	**Risk Ranking**	**Risk Mitigation Approach**	**Final Risk Evaluation**	**Lifecycle Considerations/ Comments**
Assay, stability	• Formulation • Container closure • Raw materials • Process parameters • Scale/equipment • Site	Low		Low	
Physical stability (solid state)	• Formulation • Raw materials • Process parameters • Scale/equipment • Site	Low		Low	
Content Uniformity	• Formulation • Container closure • Raw material • Process Parameters • Scale/equipment • Site	Low		Low	
Moisture content	• Formulation • Container closure • Process parameters • Scale/equipment • Site	High	(b) (4)	Medium	
Microbial Limits	• Formulation • Raw materials • Process parameters • Scale/equipment • Site	Low		Low	
Dissolution – BCS Class II & IV	• Formulation • Container Closure • Raw materials • Process parameters • Scale/equipment • Site	Medium		Low	The proposed dissolution method and acceptance criterion are acceptable as a QC test for batch release and stability testing.

Recommendation Page

[FDA will complete this section.]

Drug Substance: Approval

Primary Reviewer: Rajan Pragani Date: December 1, 2022
Secondary Reviewer: Haripada Sarker Date: December 5, 2022

Drug Product: Approval

Primary Reviewer: Olen Stephens Date: December 6, 2022
Secondary Reviewer: Xing Wang Date: January 31, 2023

Process and Facility: Approval

Primary Reviewer: Md Abdullah A Mahmud Date: January 6, 2023
Secondary Reviewer: Zhaoyang Meng Date: January 6, 2023

Biopharmaceutics: Approval

Primary Reviewer: Mei Ou Date: October 28, 2022
Secondary Reviewer: Mei Ou Date: October 28, 2022

Microbiology: Approval
Primary Reviewer: Julie Nemecek
Secondary Reviewer: Bryan Riley

Application Technical Lead: Approval

Xing Wang Date: January 31, 2023

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/

XING WANG
01/31/2023 03:48:23 PM

RAJAN PRAGANI
01/31/2023 03:59:47 PM

HARIPADA SARKER
01/31/2023 10:15:26 PM

OLEN M STEPHENS
02/01/2023 06:21:50 AM
Concur

MEI OU
02/01/2023 07:40:30 AM

MD ABDULLAH A MAHMUD
02/01/2023 08:47:30 AM

ZHAOYANG MENG
02/01/2023 08:51:11 AM

JULIE C NEMECEK
02/01/2023 08:52:46 AM

BRYAN S RILEY
02/01/2023 11:47:22 AM
I concur.