CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218466Orig1s000

OTHER REVIEW(S)

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

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)

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Date of This Review:	April 17, 2024
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	NDA 218466 and NDA 215039/S-002
Product Name, Dosage Form, and Strength:	Vijoice (alpelisib) oral granules, 50 mg per packet, and tablets, 50 mg, 125 mg, and 200 mg
Applicant Name:	Novartis Pharmaceuticals Corp.
FDA Received Date:	March 18, 2024 and April 10, 2024
TTT ID #:	2023-5335-2
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD

1 PURPOSE OF MEMORANDUM

Novartis Pharmaceuticals Corp. submitted a revised carton labeling received on March 28, 2024 and a revised container label received on April 10, 2024 for Vijoice. The Division of Oncology 2 (DO2) requested that we review the revised container label and carton labeling for Vijoice (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

Novartis Pharmaceuticals Corp. implemented all of our recommendations and we have no additional recommendations at this time.

APPENDIX A. IMAGES OF LABELS AND LABELING RECEIVED ON MARCH 28,2024 AND APRIL 10, 2024.

Container Label(s)

[a] Stewart, J. Label and Labeling Review for Vijoice (NDA 218466 and NDA 215039/S-002). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2024 Mar 29. TTT ID: 2023-5335-1.

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MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

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)

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Date of This Review:	March 29, 2024
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	NDA 218466 and NDA 215039/S-002
Product Name, Dosage Form, and Strength:	Vijoice (alpelisib) oral granules, 50 mg per packet, and tablets, 50 mg, 125 mg, and 200 mg
Applicant Name:	Novartis Pharmaceuticals Corp.
FDA Received Date:	March 12, 2024 and March 28, 2024
TTT ID #:	2023-5335-1
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD

1 PURPOSE OF MEMORANDUM

Novartis Pharmaceuticals Corp. submitted a revised container label received on March 12, 2024 and revised carton labeling received on March 28, 2024 for Vijoice. The Division of Oncology 2 (DO2) requested that we review the revised container label and carton labeling for Vijoice (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

Novartis Pharmaceuticals Corp. implemented all of our recommendations; however, have identified an area for improvement on the container label (packet label) to support the safe and effective use of Vijoice granules. We provide a recommendation in Section 3 below.

Of note, Novartis proposes that the packaging configuration consisting of the originally submitted container label (packet label) accompanied by the approved carton and USPI/PPI be supplied until Sep-2024, at which point Vijoice 50 mg granules packaged in the revised container labeling (packet) will become available[b]. We find Novartis' proposal acceptable.

3 RECOMMENDATIONS FOR NOVARTIS PHARMACEUTICALS CORP.

A. Container Label- Granules (NDA 218466)

1. Given administration instructions for the Vijoice granules are available on the carton labeling as well as in the Patient Information labeling, revise the statement on the packet that reads [redacted] (b) (4) to read "Directions: See the Carton or Patient Information for administration instructions."

[a] Stewart, J. Label and Labeling Review for Vijoice (NDA 218466 and NDA 215039/S-002). Silver Spring (MD): FDA, CDER, OSE, DMEPA2 (US); 2024 FEB 15. TTT ID: 2023-5335.

[b] Response to FDA Labeling Comments (NDA 218466 Vijoice Oral Granules). East Hanover (NJ): Novartis Pharmaceuticals Corp; 2024 MAR 12. Available from: \\CDSESUB1\EVSPROD\nda218466\0008\m1\us\cover.pdf

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****Pre-decisional Agency Information****

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

Memorandum

Date: 2/28/2024

To: Maritsa Stephenson, Regulatory Project Manager, Division of Oncology 2 (DO2)

From: Courtney Leach, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Rachael Conklin, Team Leader, OPDP

Subject: OPDP Labeling Comments for VIJOICE® (alpelisib) tablets, for oral use and VIJOICE® (alpelisib) granules, for oral use

NDA/BLA: 218466; 215039, S-002

Background:
In response to DO2's consult request dated August 24, 2023, OPDP has reviewed the proposed Prescribing Information (PI), Patient Package Insert (PPI) and carton and container labeling for the original NDA submission for VIJOICE® (alpelisib) granules, for oral use and for supplement 002 for VIJOICE® (alpelisib) tablets, for oral use. NDA 215039-S002 is a labeling supplement to update the parent NDA 215039 for VIJOICE tablets with the new VIJOICE granules formulation under NDA 218466.

PI:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on February 15, 2024, and our comments are provided below.

PPI:
A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed for the proposed PPI, and comments were sent under separate cover on February 26, 2024.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling accessed from SharePoint on February 20, 2024, and our comments are provided below.

Thank you for your consult. If you have any questions, please contact Courtney Leach at (301) 796-1044 or Courtney.Leach@fda.hhs.gov.

PI:

Section	Statement from Draft (if applicable)	OPDP Comments
2.X VIJOICE Dosage Form Overview	"VIJOICE is available in two dosage forms: tablets and oral granules." (underline emphasis added)	The PI contains both "granules" and "oral granules" when referencing the formulation. We recommend being consistent throughout the PI when referencing the formulation. We defer to DO2 on the use of "granules" vs. "oral granules".
2.X VIJOICE Preparation and Administration Instructions; VIJOICE Tablets and VIJOICE Granules	"Place VIJOICE tablets in a (b) (4) containing 2 to 4 ounces of water…" (b) (4) "Add 1 to 3 teaspoons of a beverage…" (b) (4) (underline emphasis added)	Is there concern for potential medication errors when using two different units of measurement for the administration instructions? Would adding the quantity in mL help mitigate the potential for errors? For example, (b) (4) and (b) (4) We defer to DMPP/DMEPA/DO2 on whether this is necessary.
2.X VIJOICE Preparation and Administration Instructions; VIJOICE Granules	"Pour the contents of one VIJOICE granules packet into a (b) (4) cup. Add 1 to 3 teaspoons of a beverage (water, milk, or apple juice) or soft food (applesauce or yogurt) and administer the mixture immediately."	We recommend clarifying if the mixture needs to be mixed or stirred after adding a beverage or soft food to the granules.

Carton and Container Labeling:

Section	Statement from Draft (if applicable)	OPDP Comments

Back panel of the carton labeling	Administration options for Vijoice oral granules on the back panel of the carton labeling	Once the PI is finalized, we recommend updating the carton and container labeling to be consistent with the **"VIJOICE Preparation and Administration Instructions"** section of the PI.
Principal display panel on the carton and packet labeling	"Vijoice (alpelisib) 50 mg Oral granules" (underlined emphasis added.)	The PI contains both "granules" and "oral granules" when referencing the formulation. The carton and packet display "Oral granules". Once the PI is finalized, we recommend being consistent on the carton and packet labeling in accordance with the PI. We defer to DO2 on the use of "granules" vs. "oral granules".

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Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	February 26, 2024
To:	Maritsa Stephenson, PharmD, BCPS Regulatory Health Project Manager **Division of Oncology II (DO2)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
	Barbara Fuller, RN, MSN, WOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Jessica Chung, PharmD, MS Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
	Courtney Leach, PharmD, BCCCP, BCPS Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	VIJOICE (alpelisib)
Dosage Form and Route:	granules, for oral use
Application Type/Number:	NDA 218466
Applicant:	Novartis Pharmaceuticals Corporation

1 INTRODUCTION

On June 29, 2023, Novartis Pharmaceuticals Corporation submitted for the Agency's review an original New Drug Application (NDA) 218466 for VIJOICE (alpelisib) granules, for oral use. VIJOICE (alpelisib) tablets, for oral use are currently approved under NDA 215039. With this submission the Applicant seeks approval for a new granules dosage form intended to provide an alternative dosage form for patients prescribed VIJOICE (alpelisib) 50 mg.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Oncology II (DO2) on August 24, 2023, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for VIJOICE (alpelisib) granules, for oral use.

2 MATERIAL REVIEWED

- Draft VIJOICE **(**alpelisib**)** tablets and VIJOICE (alpelisib) granules PPI received on June 29, 2023, and received by DMPP and OPDP on February 16, 2024.
- Draft VIJOICE **(**alpelisib**)** tablets and VIJOICE (alpelisib) granules Prescribing Information (PI) received on June 29, 2023, and received by DMPP and OPDP on February 16, 2024.
- Approved VIJOICE **(**alpelisib**)** tablets, for oral use labeling dated November 17, 2022.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level. In our review of the PPI the target reading level is at or below an 8th grade level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss.

In our collaborative review of the PPI we:

- simplified wording and clarified concepts where possible
- ensured that the PPI is consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI is free of promotional language or suggested revisions to ensure that it is free of promotional language

- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI is consistent with the approved labeling where applicable.

4 CONCLUSIONS

The PPI is acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI.

Please let us know if you have any questions.

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02/27/2024 02:47:20 PM

LABEL AND LABELING 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:	February 15, 2024
Requesting Office or Division:	Division of Oncology 2 (DO2)
Application Type and Number:	NDA 218466 and NDA 215039/S-002
Product Name, Dosage Form, and Strength:	Vijoice (alpelisib) oral granules, 50 mg per packet, and tablets, 50 mg, 125 mg, and 200 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Novartis Pharmaceuticals Corp.
FDA Received Date:	June 29, 2023, September 15, 2023, and November 22, 2023
TTT ID #:	2023-5335
DMEPA 2 Safety Evaluator:	Janine Stewart, PharmD
DMEPA 2 Team Leader:	Ashleigh Lowery, PharmD

1 REASON FOR REVIEW

NDA 218466

As part of the approval process for Vijoice (alpelisib) oral granules, an alternative dosage form of alpelisib for pediatric and adult patients, the Division of Oncology 2 (DO2) requested that we review the proposed Vijoice prescribing information (PI), patient information, container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

NDA 215039/S-002

Novartis Pharmaceuticals Corp. submitted an Efficacy Supplement under NDA 215039 for Vijoice (alpelisib) tablets, which cross references NDA 218466 submitted in support of the proposed Vijoice granule dosage form. The supplement includes cross-over study data to support the bioequivalence of both dosage forms when administered in the fed state. Novartis seeks to approval to co-label both dosage forms under a single Vijoice labeling.

2 BACKGROUND

Vijoice (alpelisib) was originally approved on April 5, 2022 under NDA 215039 and is currently available as 50 mg, 125 mg, and 200 mg tablets.

Novartis submitted NDA 218466 for a proposed new oral granule formulation of Vijoice. The proposed product is supplied in packets; the contents of which is to be sprinkled directly onto the tongue and swallowed with water or mixed with a beverage or soft food before administration. This proposed dosage form is intended to provide an alternative and to optimize treatment delivery only for adult and pediatric patients who are prescribed Vijoice 50 mg.

We contacted Clinical Pharmacology via email on November 9, 2023 for their assessment of the data to determine whether the proposed Vijoice (alpelisib) oral granule formulation is equivalent to the existing Vijoice tablet formulation on a milligram for milligram basis. Clinical Pharmacology informed us the applicant submitted clinical bioequivalence study data which demonstrated that the proposed 50 mg granule formulation is equivalent to and interchangeable with the approved 50 mg tablet formulation.

3 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Other	E – N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

4 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We reviewed the proposed PI changes to Section 2 Dosage and Administration, Section 3 Dosage Forms and Strengths, Section 16 How Supplied/Storage and Handling, and Section 17 Patient Counseling Information, and Patient Information, all involving the addition of the newly proposed granule formulation. We determined that the PI and Patient Information may be improved for clarity.

We reviewed the Vijoice oral granules container label, and carton labeling and determined that they could be improved to ensure safe medication use.

5 CONCLUSION & RECOMMENDATIONS

The proposed Vijoice PI and Patient Information may be improved for clarity. The proposed Vijoice granules container label and carton labeling could be improved to ensure safe medication use. We provide specific recommendations in Section 5.1 below.

5.1 RECOMMENDATIONS FOR DIVISION OF ONCOLOGY 2 (DO2)

A. Prescribing Information

1. Dosage and Administration Section

a. In Section 2, consider adding a section header after *Recommended Dosage* titled "Dosage Form Overview" to provide an introduction of the available dosage forms as follows:

2.X VIJOICE Dosage Form Overview

VIJOICE is available in two dosage forms: tablets and oral granules.

The physician should prescribe the most appropriate dosage form of VIJOICE according to the required dose and patient needs.

VIJOICE Tablets (50 mg, 125 mg, and 200 mg) may be administered as:

- Whole tablets: For patients who can swallow whole tablets.
- Tablets prepared as an oral suspension: For patients who have difficulty swallowing whole tablets.

VIJOICE Oral Granules (50 mg per packet):

- For patients who are prescribed a 50 mg daily dose only. [see Dosage and Administration (2.X)]
- Do not use multiple 50 mg packets or a partial packet of granules for patients prescribed a 125 mg or 250 mg dose *[see Clinical Pharmacology (12.3)]*.

VIJOICE tablets and VIJOICE granules should not be combined to achieve the prescribed dose.

b. Consider revising the title of Section *2.2 Administration* to read "2.X *VIJOICE Administration Overview"* since the information provided is a general overview.
c. Consider adding a section header at the end of the VIJOICE Administration Overview section that reads "*2.X VIJOICE Preparation and Administration Instructions*".

2. How Supplied/Storage and Handling Section

a. Consider removing the (b) (4) after the "Tablets:" and "Granules:" sub headers to remove redundancy given the strengths are listed in each section.

b. Consider revising the VIJOICE Granules preparation and administration instructions by combining the 2nd and 3rd administration options into one set of instructions. Further, we recommend simplifying the measurements expressed in the instructions to include teaspoons and ounces. Revise as follows:

VIJOICE Granules

Each packet is for single use only.
No packet should be used if the packet seal is broken.

Do not attempt to use partial quantities of (b) (4) from 50 mg (b) (4) packets to prepare a dose. Multiple packets of granules should not be combined to achieve a VIJOICE dose of 125 mg or 250 mg.

- For patients for whom a daily dose of 50 mg is prescribed, administer VIJOICE granules *[see Clinical Pharmacology (12.3)]* in one of the following ways:
    - Pour the contents of one VIJOICE granules packet directly onto the tongue and swallow with approximately 2 to 4 ounces of water. If needed, rinse the mouth with additional water and swallow to ensure no particles remain in the mouth.
    - Pour the contents of one VIJOICE granules packet into a (b) (4) cup.

      Add 1 to 3 teaspoons of a beverage (water, milk, or apple juice) OR soft food (applesauce or yogurt) and administer the mixture immediately.

Rinse the (b) (4) cup with up to 2 ounces of water, milk or apple juice and administer the mixture immediately to ensure the entire dose is administered. If particles remain, repeat until the full dose is administered.

- Discard the granules mixed with water, milk, apple juice, applesauce, or yogurt if they are not administered within 2 hours after preparation.

(b) (4).

5.2 RECOMMENDATIONS FOR NOVARTIS PHARMACEUTICALS CORP.

We recommend the following be implemented prior to approval of this NDA:

A. General Comments (Container labels & Carton Labeling)

1. To clearly indicate the proposed 50 mg granule packets are for patients who are prescribed Vijoice 50 mg only, revise the strength statement to facilitate provider and patient comprehension regarding the daily dosage and the number packets required to achieve the stated dosage.

50 mg daily dose
Take one 50 mg packet once daily.

2. To reduce clutter on the principal display panel, relocate the statement that reads "Oral Granules" to appear after the established name as follows:

(apelisib) oral granules

B. Carton Labeling

1. For consistency with the PI, revise the statement on the side panel, (b) (4) to read: Recommended Dosage: See Prescribing Information.
2. Revise the preparation and administration information on the back panel for improved clarity and brevity as follows:
   a. Revise the header on the back panel to read "Take Vijoice in one of the following ways:"
   b. Before or next to the first administration option, add an image to depict a packet pouring granules onto the tongue and a partially full (b) (4).
   c. Revise the administration steps as follows:

      1. Pour the contents of one packet directly on tongue.
      2. Swallow granules with 2 to 4 ounces of water.

3. Rinse mouth with more water and swallow to make sure the entire dose is taken.

d. Before or next to the second administration option, add an image of a packet of granules pouring into a [redacted] cup with a spoon next to it.

e. Revise the 2nd [redacted] to improve readability and to provide space for the added images by revising the preparation and administration steps as follows:

1. Pour the contents of one packet into a [redacted] cup.

2. Add 1 to 3 teaspoons of a beverage (water, milk, or apple juice) OR soft food (applesauce or yogurt) and mix.

3. Administer the mixture by mouth right away.

4. Rinse the [redacted] cup with up to 2 ounces of water, milk or apple juice and drink the mixture right away to ensure the entire dose is taken.

5. If any granule or mixture remains, repeat Step 4

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Vijoice received on June 29, 2023 from Novartis Pharmaceuticals Corp..

Table 2. Relevant Product Information for Vijoice		
Initial Approval Date	NDA 218466 N/A	NDA 215039 Approved April 5,2022
Active Ingredient	alpelisib	
Indication	For the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy.	
Route of Administration	Oral	
Dosage Form	oral granules	Tablets
Strength	50 mg per packet	50 mg, 125 mg, 200 mg
Dose and Frequency	Pediatric/adult patients prescribed Vijoice 50 mg only: 50 mg once daily with food.	Maximum daily dose in adult patients: 250 mg once daily. • (b) (4) • (b) (4) dose reduction: 125 mg once daily • (b) (4) dose reduction: 50 mg once daily

Table 2. Relevant Product Information for Vijoice		
How Supplied	Packets: 28-count carton (each packet contains 50 mg alpelisib)	250 mg daily dose: Each carton contains 2 blister packs (56 tablets total). Each blister pack contains a 14-day supply of 28 tablets (14 tablets, 200 mg alpelisib per tablet and 14 tablets, 50 mg alpelisib per tablet) 125 mg daily dose: Each carton contains 1 blister pack . Each blister pack contains a 28-day supply of 28 tablets (28 tablets, 125 mg alpelisib per tablet) 50 mg daily dose: Each carton contains 1 blister pack. Each blister pack contains a 28-day supply of 28 tablets (28 tablets, 50 mg alpelisib per tablet)
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]*.	
Container Closure	Alpelisib 50 mg granules are packaged in (b) (4) sachets contained in a cardboard-based box (secondary packaging).	Foil blister packs packaged in paperboard wallets packaged in paperboard cartons.

APPENDIX B. PREVIOUS DMEPA REVIEWS

On November 9, 2023, we searched for previous DMEPA reviews relevant to this current review using the terms, Vijoice. Our search identified 2 previous reviews[a,b] since the date of our last search on April 4, 2022, and we considered our previous recommendations to see if they are applicable for this current review.

[a] Stewart, J. Label and Labeling Review for Vijoice (NDA 215039). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 APR 04. RCM No.: 2021-1509-1.

[b] Stewart, J. Label and Labeling Review for Vijoice (NDA 215039). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 MAR 04. RCM No.: 2021-1509.

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error data, we reviewed the following Vijoice labels and labeling submitted by Novartis Pharmaceuticals Corp..

- Container label received on September 15, 2023
- Carton labeling received on September 15, 2023
- Prescribing Information and Patient Information (Image not shown) received on June 29, 2023, available from \\CDSESUB1\EVSPROD\nda218466\0000\m1\us\proposed-clean.docx

F.2 Label and Labeling Images

Container label(s)

(b) (4)

[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: December 6, 2023

TO: Dr. Harpreet Singh, MD
Director
Division of Oncology II (DO2)
Office of Oncologic Diseases (OOD)
Office of New Drug (OND)

Partha Roy, Ph.D.
Director
Office of Bioequivalence (OB)
Office of Generic Drugs (OGD)

FROM: Yi-Ying Chen, MSc.
Division of New Drug Study Integrity (DNDSI)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Charles Bonapace, Pharm.D.
Director
DNDSI
OSIS

SUBJECT: Review of Analytical Remote Regulatory Assessment of (b) (4)

1. Remote Regulatory Assessment Summary

The Office of Study Integrity and Surveillance (OSIS) conducted an analytical RRA of studies CBYL719F12101 (NDA 218466, Alpelisib Granule), NON-RESPONSIVE conducted at (b) (4)

No objectionable conditions were observed and Form FDA 483 was not issued at the RRA close-out. Based on the RRA findings, there are no identified concerns for (b) (4), regarding reliability of the data for reviewed studies CBYL719F12101, NON-RESPONSIVE for the review division consideration.

2. Reviewed Studies:

NDA 218466 (Alpelisib, Granule)

Study Number: CBYL719F12101
Study Title: "A Single-Center, Randomized, Open-Label, Three-Period Crossover Study To Investigate The Bioequivalence Of Alpelisib Granule And Film-Coated Tablet Formulation, And The Food Effect Of Alpelisib Granule Formulation In Adult Healthy Volunteers"
Dates of Study Sample Analysis: August 8 – November 24, 2022

NON-RESPONSIVE

Analytical Site: (b) (4)

3. Scope of RRA

(b) (4)

OSIS scientist Yi-Ying Chen, MSc., reviewed the analytical portion of the above studies conducted at (b) (4).

3.1 Previous Inspections

This was the first RRA of (b) (4) under the BA/BE program.

The previous analytical inspection of both the (b) (4) was conducted by OSIS from (b) (4). A tour of the (b) (4) was conducted at the beginning of the inspection and the study documents generated at the (b) (4) were transferred to the (b) (4) for review during the inspection. At the conclusion of the inspection, Form FDA 483 was not issued. The final classification was No Action Indicated (NAI).

3.2 Current RRA

The current RRA included reviewing the relevant records of method validation, study sample analysis, standard operating procedures (SOPs), sample receipt/storage, facility of bioanalytical operations, calibration and maintenance records, audit trails of instruments used in the reviewed studies, and interviews with the firm's management and staff.

3.3 RRA Observations

At the conclusion of the RRA, I did not observe any objectionable conditions. No items were discussed with firm's management during the RRA close-out meeting.

Yi-Ying Chen, MSc.
Chemist

Draft: YEC 12/5/2023, 12/6/2023
Edit: GB 12/05/2023; CB 12/05/2023

ECMS:
https://ecmsweb.fda.gov/webtop/drl/objectId/0b0026f881b16f28

cc:
OTS/OSIS/Kassim/Folian/Mitchell/Fenty-Stewart/Haidar/Mirza/Pham
OTS/OSIS/DNDSI/Bonapace/Dasgupta/Ayala/Biswas/Chen
OTS/OSIS/DGDSI/Cho/Benson/Skelly/Au/Ou

OSIS File #: (b) (4) **(NDA 218466)**
NON-RESPONSIVE

eNSpect Assignment ID: (b) (4)
eNSpect OpID: (b) (4)

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/s/

YIYING E CHEN
12/06/2023 09:04:54 AM

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12/06/2023 10:24:47 AM

CHARLES R BONAPACE
12/06/2023 11:21:07 AM

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 9/28/2023

TO: Division of Oncology I (DO I)
Office of Oncologic Diseases (OOD)

FROM: Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct an on-site inspection**

RE: NDA 218466

The Office of Study Integrity and Surveillance (OSIS) determined that an inspection is not needed for the site listed below. The rationale for this decision is noted below.

Rationale

OSIS conducted a Remote Regulatory Assessment (RRA) for the site in (b) (4). The RRA was conducted under the following submissions: NON-RESPONSIVE.

OSIS concluded that data from the reviewed studies were reliable.

Site

Facility Type	Facility Name	Facility Address
Analytical	(b) (4)	

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/s/

JAMES J LUMALCURI
09/28/2023 11:47:07 AM