CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210563Orig1s000
210563Orig2s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	February 15, 2018
Requesting Office or Division:	Division of Hematology Products (DHP)
Application Type and Number:	NDA 210563
Product Name and Strength:	Imbruvica (ibrutinib) tablets, 140 mg, 280 mg, 420 mg, and 560 mg
Applicant/Sponsor Name:	Pharmacyclics LLC
FDA Received Date:	February 14, 2018
OSE RCM #:	2017-1815-2
DMEPA Safety Evaluator:	Nicole Garrison, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMO

The Division of Hematology Products (DHP) requested that we review the revised carton labeling and blister pack labeling for Imbruvica tablets (Appendix A) to determine if it is 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

The revised carton labeling and blister pack labeling for Imbruvica tablets is acceptable from a medication error perspective. We have no further recommendations at this time.

8 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Garrison N. Label and Labeling Review Memo for IMBRUVICA (NDA 210563). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 FEB 07. RCM No.: 2017-1815-1.

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/s/

NICOLE B GARRISON
02/15/2018

HINA S MEHTA
02/15/2018

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	February 7, 2018
Requesting Office or Division:	Division of Hematology Products (DHP)
Application Type and Number:	NDA 210563
Product Name and Strength:	Imbruvica (ibrutinib) tablets, 140 mg, 280 mg, 420 mg, and 560 mg
Applicant/Sponsor Name:	Pharmacyclics LLC
FDA Received Date:	January 22, 2018
OSE RCM #:	2017-1815-1
DMEPA Safety Evaluator:	Nicole Garrison, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMO

The Division of Hematology Products (DHP) requested that we review the revised carton labeling and blister pack labeling for Imbruvica tablets (Appendix A) to determine if it is 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

The revised carton labeling and blister pack labeling is unacceptable from a medication error perspective. For the carton labeling, there is inadequate differentiation between the 140 mg capsule strength (b) (4) and the 420 mg tablet strength (b) (4).

In our previous label and labeling review for Imbruvica tablets, we recommended deletion of (b) (4) on the blister pack labeling (b) (4) (b) (4). The Sponsor acknowledged our concern, however; based upon several market research studies they conducted with patients, nurses, pharmacists, and distributors, (b) (4) labeling was

[a] Garrison N. Label and Labeling Review for Imbruvica (NDA 210563). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JAN 11. RCM No.: 2017-1815.

the preferred package configuration (b) (4) (b) (4). We acknowledge the Sponsor's response to our information request, but provide additional revisions to the blister pack labeling. As currently presented, the blister pack labeling may potentially confuse the intended users and differs from other available dose packs.

3 RECOMMENDATIONS FOR PHARMACYCLICS LLC

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

A. Carton labeling

There is inadequate differentiation between the 140 mg capsule strength (b) (4) (b) (4) and the 420 mg tablet strength (b) (4)). Revise the color scheme of the 420 mg tablet strength (b) (4), so that it appears in its own unique color and the color does not overlap with any other colors utilized in highlighting the strengths. The use of the same (b) (4) scheme for the product's 140 mg capsule and 420 mg tablet strengths minimizes the difference between the strengths, which may lead to wrong strength selection errors.

B. Blister pack labeling

1. We recommend deleting (b) (4) (b) (4) in the blister pack as this may confuse the intended user.
2. For increased clarity, we recommend (b) (4) (b) (4)
3. We also recommend deleting (b) (4) (b) (4).
4. Add the proprietary name, established name, and product strength from the back of the blister pack labeling to the front of the blister pack labeling. In addition, revise the product strength to display the strength per tablet (e.g. 560 mg per tablet).

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[b] Response to Information Request received on January 22, 2018.

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/s/

NICOLE B GARRISON
02/07/2018

HINA S MEHTA
02/07/2018

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:	January 19, 2018
To:	Ann Farrell, MD Director **Division of Hematology Products (DHP)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Susan Redwood, MPH, BSN, RN Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Nisha Patel, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	IMBRUVICA (ibrutinib)
Dosage Form and Route:	tablets, for oral use
Application Type/Number:	NDA 210563
Applicant:	Pharmacyclics LLC

1 INTRODUCTION

On August 31, 2017, Pharmacyclics LLC., submitted for the Agency's review a 505 (b) (1) New Drug Application (NDA) 210563 for IMBRUVICA (ibrutinib) tablets, for oral use. IMBRUVICA (ibrutinib) capsules, for oral use, 140 mg was approved by the Agency in November 2013. To reduce the patient pill burden, and improve patient's compliance, a new tablet formulation of ibrutinib in four strengths was developed by Pharmacyclics. The purpose of this submission is to seek the approval of IMBRUVICA (ibrutinib) tablets for the same approved indications as the approved capsule formulation (NDA 205552), for the treatment of adult patients with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy
- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion
- Waldenström's macroglobulinemia (WM)
- Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
- Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

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 Hematology Products (DHP) on November 1, 2017 for DMPP to review the Applicant's proposed Patient Package Insert (PPI) for IMBRUVICA (ibrutinib) capsules, for oral use and IMBRUVICA (ibrutinib) tablets, for oral use.

2 MATERIAL REVIEWED

- Draft IMBRUVICA (ibrutinib) capsules and IMBRUVICA (ibrutinib) tablets PPI received on August 31, 2017, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on January 16, 2018 and January 18, 2018.
- Draft IMBRUVICA (ibrutinib) capsules and IMBRUVICA (ibrutinib) tablets Prescribing Information (PI) received on August 31, 2017, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on January 16, 2018 and January 18, 2018.
- Approved IMBRUVICA (ibrutinib) capsules NDA 205552 labeling dated December 20, 2017.

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.

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 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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/s/

SUSAN W REDWOOD
01/19/2018

NISHA PATEL
01/19/2018

BARBARA A FULLER
01/19/2018

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

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

Memorandum

Date: January 19, 2018

To: Kelly Miller, Regulatory Project Manager
Division of Hematology Products (DHP)

Virginia Kwitkowski, Associate Director for Labeling, DHP

From: Nisha Patel, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Mathilda Fienkeng, Team Leader, OPDP

Subject: OPDP Labeling Comments for IMBRUVICA® (ibrutinib) capsules, for oral use, IMBRUVICA® (ibrutinib) tablets, for oral use

NDA: 210563

In response to DHP's consult request dated September 15, 2017, OPDP has reviewed the proposed product labeling (PI) and patient package insert (PPI) for the original NDA submission for IMBRUVICA® (ibrutinib) capsules, for oral use and IMBRUVICA® (ibrutinib) tablets, for oral use (Imbruvica).

PI and PPI: OPDP's comments on the proposed labeling are based on the draft PI emailed to OPDP on January 16, 2018, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed, and comments on the proposed PPI were sent under separate cover on January 19, 2018.

Thank you for your consult. If you have any questions, please contact Nisha Patel at (301) 796-3715 or nisha.patel@fda.hhs.gov.

Package Insert

Section	Statement from draft	Comment
17 Patient Counseling Information	Inform patients to take IMBRUVICA orally once daily according to their physician's instructions and that the oral dosage **(capsules or tablets)** should be swallowed whole with a glass of water **without** (b) (4) (b) (4) approximately the same time each day (emphasis added).	We note that the Dosage and Administration section of the full PI states, "Do not open, break, or chew the capsules. **Do not cut, crush, or chew the tablets** (emphasis added)." OPDP recommends revising the Patient Counseling Information section of the full PI to include the information above regarding tablets.

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/s/

NISHA PATEL
01/19/2018

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
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:	January 12, 2018
Requesting Office or Division:	Division of Hematology Products (DHP)
Application Type and Number:	NDA 210563
Product Name and Strength:	Imbruvica (ibrutinib) tablets, 140 mg, 280 mg, 420 mg, and 560 mg
Product Type:	Single-Ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Pharmacyclics LLC
Submission Date:	August 31, 2017, September 21, 2017 and December 28, 2017
OSE RCM #:	2017-1815
DMEPA Safety Evaluator:	Nicole Garrison, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD

1 REASON FOR REVIEW

This review evaluates the proposed container label, carton labeling, and Prescribing Information (PI) for Imbruvica (ibrutinib) tablets, 140 mg, 280 mg, 420 mg, and 560 mg (NDA 210563) for areas of vulnerability that could lead to medication errors. The Division of Hematology Products (DHP) requested this review as a part of their evaluation to the 505(b)(1) NDA submission for Imbruvica (ibrutinib) tablets.

1.1 BACKGROUND INFORMATION

Imbruvica (ibrutinib) capsules NDA 205552 was approved on November 13, 2013 for the treatment of patients with Mantle Cell Lymphoma (MCL). Since its original approval, Imbruvica has received additional indications for the treatment of patients with Chronic Lymphocytic Leukemia (CLL), Waldenstrom's Macroglobulinemia (WM), CLL/Small lymphocytic lymphoma (SLL), CLL/SLL with 17p deletion, Marginal Zone Lymphoma (MZL), and Chronic graft versus host disease (cGVHD).

Imbruvica capsule 140 mg is currently marketed in the United States. On December 20, 2017, the 70 mg capsule was approved to allow for dose reductions in patients with moderate hepatic impairment. Depending on the treatment indication, patients may be required to take 3 capsules (420 mg) or 4 capsules (560 mg) per dose. To reduce the patient pill burden, and improve patient's compliance, the Applicant has proposed a new tablet formulation of Imbruvica in four strengths (140 mg, 280 mg, 420 mg, and 560 mg). The tablet formulation is intended for the treatment of the same approved indications and the same dose as the approved capsule formulation (NDA 205552).

2 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 Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
Human Factors Study	C- N/A
ISMP Newsletters	D- N/A
FDA Adverse Event Reporting System (FAERS)*	E- N/A
Other	F- N/A
Labels and Labeling	G

N/A=not applicable for this review

Table 1. Materials Considered for this Label and Labeling Review	
Material Reviewed	**Appendix Section (for Methods and Results)**

*We do not typically search FAERS for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Pharmcyclics submitted a 505 (b)(1) application to obtain marketing approval of Imbruvica tablets to reduce patient pill burden and increase patient compliance with therapy. Imbruvica tablets will have the same indication and dosing as the currently marketed Imbruvica capsules. Imbruvica tablets will be supplied in cartons with blister cards containing 28 tablets.

We performed a risk assessment of the proposed container labels, carton labeling, and PI for Imbruvica (ibrutinib) tablets to determine whether there are significant concerns in terms of safety, related to preventable medication errors. We identified areas of the proposed labels and labeling that could be revised to improve clarity and readability of important information. For the proposed labels and labeling, we recommend revising the color scheme of the 280 mg, 420 mg, and 560 mg strengths, including the package type on the principal display panel (PDP), revising the usual dose statement and the product strength statement. For the blister pack labeling we recommend deleting (b) (4) and revising the cautionary statement. For the proposed PI, we recommend revising statements in Section 2 Dosage and Administration to provide clarity on administration of the dose.

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes that the proposed PI, labels and labeling can be improved to increase clarity of important information on the labels to promote the safe use of the product. We provide recommendations in Section 4.1 and Section 4.2 below and advise that they are implemented prior to the approval of this NDA.

4.1 RECOMMENDATIONS FOR THE DIVISION

A. Highlights of Prescribing Information
    1. Dosage and Administration
        a. Revise the statement, (b) (4) (b) (4) To "Dose should be taken orally with a glass of water."
        b. Revise the statement, (b) (4) To "Do not cut, crush, or chew the tablets."
B. Full Prescribing Information
    1. Dosage and Administration
        a. Section 2.1, *Dosing Guidelines*

i. Revise the statement, [redacted] to "The dose should be taken orally with a glass of water."
ii. See A.1.b and revise the full prescribing information accordingly.

4.2 RECOMMENDATIONS FOR PHARMCYCLICS

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

A. Carton labeling
1. There is inadequate differentiation between the font color of the proprietary name [redacted] and the color scheme of the 280 mg and 560 mg strengths [redacted]. Revise the color scheme of the 280 mg and 560 mg strengths [redacted], so that either strength appears in its own unique color and the color does not overlap with any other colors utilized in highlighting the strengths. The use of the same [redacted] color font for the proprietary name and one for the product's strength minimizes the difference between the strengths, which may lead to wrong strength selection errors.
2. There is inadequate differentiation between the 140 mg capsule strength [redacted] and the 420 mg tablet strength [redacted]). Revise the color scheme of the 420 mg tablet strength [redacted] so that it appears in its own unique color and the color does not overlap with any other colors utilized in highlighting the strengths. The use of the same [redacted] color scheme for the product's 140 mg capsule and 420 mg tablet strengths minimizes the difference between the strengths, which may lead to wrong strength selection errors.
3. The package type (wallet card) is omitted from Principal Display Panel (PDP). Revise the PDP to include the net quantity with the package type as follows:

   "Wallet card contains 28 tablets"

4. Revise the usual dose statement from [redacted] to "Dosage: See prescribing information" in accordance with 21 CFR 201.55.
5. Revise the product strength on the PDP to state the total product strength (e.g. 560 mg per tablet).
6. Revise the statement, [redacted] To "Do not cut, crush, or chew the tablets." to prevent confusion.

A. Blister pack labeling
1. We recommend deleting [redacted]. We recommend this revision to prevent delays in dosing.
2. For each strength of Imbruvica tablets, revise the cautionary statement, [redacted] to

"Every tablet is identical and contains (include the total amount [e.g. 560 mg]) of Imbruvica per tablet"

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Imbruvica that Pharmacyclics submitted on August 31, 2017 and December 28, 2017.

Table 2. Relevant Product Information for Imbruvica

Product Name	**Imbruvica capsules**	**Imbruvica tablets**
Initial Approval Date	November 13, 2013	N/A
Active Ingredient	Ibrutinib	
Indication	Imbruvica is indicated for the treatment of patients with: • Mantle cell lymphoma (MCL) who have received at least one prior therapy • Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) • Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion • Waldenstrom's macroglobulinemia (WM) • Marginal zone lymphoma (MZL) for patients who require systemic therapy and have received at least one prior anti-CD20-based therapy. • Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.	
Route of Administration	Oral	
Dosage Form	Capsules	Tablets
Strength	Capsules: 70 mg and 140 mg	Tablets: 140 mg, 280 mg, 420 mg, and 560 mg
Dose and Frequency	MCL and LZL: 560 mg taken orally once daily CLL/SLL, WM, and cGVHD: 420 mg taken orally once daily	
How Supplied	• 70 mg capsules (28 capsules per bottle) • 140 mg capsules (90 and 120 capsules per bottle)	• 140 mg tablets (28 tablets per carton) • 280 mg tablets (28 tablets per carton) • 420 mg tablets (28 tablets per carton) • 560 mg tablets (28 tablets per carton)
Storage	• Store bottles at room temperature 20°C to 25°C (68°F to 77°F).	• Store tablets in original packaging at room temperature 20°C to

	Excursions are permitted between 15°C and 30°C (59°F to 86°F). Retain in original package until dispensing.	25°C (68°F to 77°F). Excursions are permitted between 15°C and 30°C (59°F to 86°F).
Container Closure	• White HDPE bottles with a child-resistant closure	• Carton of one folded blister card containing two 14-count blister strips for a total of 28 tablets

APPENDIX B. PREVIOUS DMEPA REVIEWS

On December 29, 2017, we searched DMEPA's previous reviews using the terms, Imbruvica. Our search identified four labeling reviews[a,b,c,d] and one post marketing review[e], and we confirmed that our previous recommendations were implemented.

[a] Rahimi, L. Label and Labeling Review for Imbruvica NDA 205552/S-002. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 JAN 12. RCM No.: 2014-2236.

[b] Garrison, N. Label and Labeling Review for Imbruvica NDA 205552/S-016. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 NOV 02. RCM No.: 2016-2187.

[c] Garrison, N. Label and Labeling Review for Imbruvica NDA 205552/S-20. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 NOV 08. RCM No.: 2017-1565.

[d] Garrison, N. Label and Labeling Review Memorandum for Imbruvica NDA 205552/S-20. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2017 DEC 01. RCM No.: 2017-1565-1.

[e] Ayres, E. Postmarket Signal Work for Imbruvica NDA 205552. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 22015 DEC 18. RCM No.: 2015-2548.

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[f] along with postmarket medication error data, we reviewed the following Imbruvica labels and labeling submitted by Pharmacyclics on August 31, 2017, September 21, 2017 and December 28, 2017.

- Container labels and Carton labeling
- Prescribing Information

G.2 Label and Labeling Images

Container labels and Carton labeling

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

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/s/

NICOLE B GARRISON
01/12/2018

HINA S MEHTA
01/12/2018

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: 12/1/2017

TO: Division of Hematology Products
Office of Hermatology and Oncology Products

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Recommendation to accept data without an on-site inspection**

RE: NDA 210563

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without an on-site inspection. The rationale for this decision is noted below.

Rationale

OSIS recently inspected the sites listed below. The inspectional outcomes of the inspections were classified as No Action Indicated (NAI). Although the bioanalytical study reports were not provided (b) (4), the clinical portions of the current studies concluded between January and November 2016. Therefore, OSIS infers that the bioanalytical portions of the current studies were conducted around that time (Jan – Nov 2016) and that the previously inspected studies were conducted within approximately one to two years of the bioanalytical portion of the current studies.

Inspection Sites

Facility Type	Facility Name	Facility Address
Analytical	(b) (4)	
Clinical	Celerion	2420 West Baseline Road, Tempe, AZ

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: 11/29/2017

TO: Division of Hematology Products
Office of Hermatology and Oncology Products

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to Inspect Mamo**

RE: NDA 210563

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without an on-site inspection. The rationale for this decision is noted below.

Rationale

OSIS has no inspection history for Janssen-Cilag International, however, an inspection of the site can not be conducted because the requested review goal date of February 28, 2018 provides insufficient time for the inspection to be completed to meet that goal date.

Inspection Site

Facility Type	Facility Name	Facility Address
Clinical	Janssen-Cilag International N.V.	Janssen Research and Development Pharmacology Unit, Merksem, Lange Bremstraat 70, B-2170 Antwerpen, Belgium.

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/s/

SHILA S NKAH
12/01/2017