CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212479Orig1s000
212479Orig2s000
212479Orig3s000
212479Orig4s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	November 1, 2022
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 212479
Product Name and Strength:	Jylamvo (methotrexate) oral solution, 2mg/mL
Applicant/Sponsor Name:	Therakind Limited
TTT ID #:	2022-1695
DMEPA 1 Safety Evaluator:	Teresa McMillan, PharmD
DMEPA 1 Team Leader:	Idalia Rychlik, PharmD

1 PURPOSE OF MEMORANDUM

NDA 212479 received a complete response on December 22, 2021. Thus, the Applicant resubmitted the Prescribing Information, carton labeling and container label for Jylamvo. The Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the labels and labeling for Jylamvo (Appendix A) to determine if it is acceptable from a medication error perspective.

2 CONCLUSION

The Applicant previously implemented all of our container label and carton labeling recommendations and we have no additional recommendations at this time. [a]

However, the Prescribing Information is unacceptable from a medication error perspective and we provide recommendations in Section 3 below.

[a] McMillan, T. Label and Labeling Review for Jylamvo (NDA 212479). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2021 DEC 01. RCM No.: 2021-466-1.

3 RECOMMENDATIONS FOR DIVISION OF RHEUMATOLOGY AND TRANSPLANT MEDICINE (DRTM)

A. Consider adding the following Section within the PI: Section 2.6 Administration for healthcare practitioners to align with the Instructions for Use placed in the Patient Information.

2.6 Administration

Put on disposable gloves before handling.

Shake the bottle.

Train patients or caregivers on proper handling, storage, administration, disposal and clean-up of accidental spillage prior to initiation of JYLAMVO and during each visit to the clinic.

Provide instructions regarding how to administer the specified dose, since instructions for use for JYLAMVO are suppled in the Patient Information and JYLAMVO is supplied with an oral dosing syringe (supplied in mL).

Advise patients that the oral dosing syringe is intended for multiple uses and provide the following instructions (See Patient Information for detailed instructions):

After use, wash the oral dosing syringe with warm 'soapy' water and rinse well.

- Hold the oral dosing syringe under water and move the plunger up and down several times to make sure the inside of the oral dosing syringe is clean.
- Separate the plunder and barrel and wash both thoroughly with warm 'soapy' water.
- Ensure the oral dosing syringe is completely dry before use of the oral dosing syringe again; and
- Store the oral dosing syringe in a hygienic place with JYLAMVO.

APPENDIX A. IMAGES OF CONTAINER LABEL AND CARTON LABELING RECEIVED ON NOVEMBER 18, 2021

Container label

Carton labeling

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/s/

TERESA S MCMILLAN
11/01/2022 04:09:52 PM

IDALIA E RYCHLIK
11/01/2022 04:23:00 PM

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

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

Memorandum

Date: November 1, 2022

To: Cindy Chee, Regulatory Project Manager
Division of Rheumatology and Transplant Medicine (DRTM)

From: Kyle Snyder, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Adewale Adeleye, Team Leader, OPDP

David Foss, Regulatory Review Officer, OPDP

Valerie Guerrier, Regulatory Review Officer, OPDP

Subject: OPDP Labeling Comments for JYLAMVO (methotrexate) oral solution (Jylamvo)

NDA: 212479

In response to DRTM's consult request dated June 3, 2022, OPDP has reviewed the proposed Prescribing Information (PI), Patient Package Insert (PPI), and carton and container labeling for the original NDA submission for Jylamvo.

Labeling: OPDP's comments on the proposed PI are based on the draft labeling received by electronic mail from DRTM on October 20, 2022, and are provided below.

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 October 31, 2022.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling received by electronic mail from DRTM on October 31, 2022, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Kyle Snyder at (240) 402-8792 or kyle.snyder@fda.hhs.gov.

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/s/

KYLE SNYDER
11/01/2022 09:08:52 AM

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

PATIENT LABELING REVIEW

Date:	October 31, 2022
To:	Cindy Chee, PharmD Regulatory Project Manager **Division of Rheumatology and Transplant Medicine (DRTM)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Nyedra W. Booker, PharmD, MPH Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Kyle Snyder, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	JYLAMVO (methotrexate)
Dosage Form and Route:	oral solution
Application Type/Number and Supplement Number:	NDA 212479
Applicant:	Therakind Limited

1 INTRODUCTION

On May 31, 2022, Therakind Limited submitted for the Agency's review a Resubmission of Response to FDA Complete Response (CR) Action Letter (dated December 22, 2021), to original New Drug Application (NDA) 212497 for JYLAMVO (methotrexate) oral solution.

The proposed indications for JYLAMVO (methotrexate) oral solution are for the:

- Treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen
- Treatment of adults with mycosis fungoides
- Treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen
- Treatment of adults with rheumatoid arthritis
- Treatment of adults with severe psoriasis

This 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 Rheumatology and Transplant Medicine (DRTM) on June 2, 2022, and June 3, 2022, respectively, for DMPP and OPDP to review the Applicant's Patient Package Insert (PPI) for JYLAMVO (methotrexate) oral solution.

2 MATERIAL REVIEWED

- Draft JYLAMVO (methotrexate) oral solution PPI received on May 31, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 20, 2022.
- Draft JYLAMVO (methotrexate) oral solution Prescribing Information (PI) received on May 31, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 20, 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. J

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. We have reformatted the PPI document using the Arial font, size 10.

In our review of the PPI, we have:

- 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)

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 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/

NYEDRA W BOOKER
10/31/2022 10:47:08 AM

KYLE SNYDER
10/31/2022 02:07:16 PM

LASHAWN M GRIFFITHS
10/31/2022 02:25:35 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drugs
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Division of Pediatric and Maternal Health
Silver Spring, MD 20993
Telephone 301-796-2200
FAX 301-796-9855

MEMORANDUM TO FILE

Date of Consult Request:	6/23/2022
From:	Division of Pediatrics and Maternal Health (DPMH)
To:	Division of Rheumatology and Transplant Medicine (DRTM)
NDA:	212479
Drug Product:	Jylamvo (Methotrexate 2mg/mL oral solution)
Applicant:	Therakind
Proposed Indication(s):	Treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen Treatment of adults with mycosis fungoides Treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen Treatment of adults with rheumatoid arthritis Treatment of adults with severe psoriasis

DRTM submitted a consult request to DPMH on June 23, 2022, requesting input on the labeling for this resubmission. Specifically, the Division requested DPMH to determine if there was outstanding protected exclusivities or patents that would require disclaimer

language to be added in place of the carved-out information. During the review, DPMH consulted with OCC to discuss the appropriateness for a carveout. DPMH recommended to not include a carveout as the Sponsor was not proposing to label for any pediatric indication and there is no information that would be protected under the currently proposed label. As such, the label does not have the same regulatory requirements as the label requiring a carve out for protected information and therefore a disclaimer is not appropriate. OCC concurred with DPMH's recommendation that disclaimer language is not needed in the labeling. This recommendation was relayed to the Division during labeling meetings.

DPMH participated in several internal meetings with the Division, OTBB and OCC throughout the review. DPMH has no further comments at this time, thus, this memorandum will close out the consult request.

DPMH RPM – Jacquline Yancy
DPMH CPMS- George Greeley
DPMH Pediatrics MO Reviewer – Dina Zand
DPMH Pediatrics Team Leader – Mona Khurana
DPMH Deputy Division Director – John J. Alexander

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/s/

JACQULINE A YANCY
10/26/2022 10:54:24 AM

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

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

Memorandum

Date: December 17, 2021

To: Cindy Chee, PharmD, Regulatory Project Manager
Division of Rheumatology and Transplant Medicine (DRTM)

From: Lynn Panholzer, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Aline Moukhtara, RN, MPH, Team Leader, OPDP

Subject: OPDP Labeling Consult Request for JYLAMVO (methotrexate) oral solution

NDA: 212479

This memo is in response to DRTM's labeling consult request dated March 24, 2021. DRTM has communicated that a Complete Response (CR) Action is planned for this application. Therefore, OPDP defers comment on the proposed labeling at this time, and requests that DRTM submit a new consult request during the subsequent review cycle. If you have any questions, please contact Lynn Panholzer at (301) 796-0616 or lynn.panholzer@fda.hhs.gov.

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/s/

LYNN M PANHOLZER
12/17/2021 09:26:15 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drugs
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Division of Pediatric and Maternal Health
Silver Spring, MD 20993
Telephone 301-796-2200
FAX 301-796-9855

MEMORANDUM TO FILE

Date of Consult Request:	11/01/2021
From:	Division of Pediatrics and Maternal Health (DPMH)
To:	Division of Rheumatology and Transplant Medicine (DRTM)
NDA/BLA Number:	212479
Drug Product:	Jylamvo (Methotrexate 2mg/mL oral solution)
Applicant:	Therakind
Proposed Indication(s):	Treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen Treatment of adults with mycosis fungoides Treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen Treatment of adults with rheumatoid arthritis Treatment of adults with severe psoriasis

DRTM submitted a consult request to DPMH on November 1, 2021 asking for assistance in evaluating and proposing pediatric labeling language in section 8.4 for a 505(b)(2) application for Jylamvo with Methotrexate tablets (NDA 008085) as the Listed Drug.

DRTM sought assistance with the labeling for Jylamvo due to another liquid dosage form of Methotrexate (Xatmep: NDA 208400) which currently holds Orphan Drug Exclusivity for the indications of treatment of acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen and management of active polyarticular juvenile idiopathic arthritis in pediatric patients only.

DPMH participated in an internal team meeting with the Office of Regulatory Policy, Office of Orphan Products Development, and DRTM on November 16, 2021 to discuss the potential pediatric labeling and Pediatric Research Equity Act implications for Jylamvo due to the current Orphan Drug Exclusivity for Xatmep. In addition, DPMH participated in an internal NDA Wrap-up meeting with DRTM on November 17, 2021. During this meeting, it was communicated that the plan for the current application was a Complete Response Action due to issues surrounding facility inspections (CMC). Due to this planned action, DPMH was notified during the meeting that labeling discussions will not take place.

DPMH- Pediatrics has no further comments at this time, thus, this memorandum will close out the consult request. If labeling discussions resume, DPMH may be re-consulted.

DPMH Pediatrics MO Reviewer – Shamir Tuchman
DPMH Pediatrics Team Leader – Mona Khurana
DPMH Deputy Division Director – John J. Alexander
DPMH RPM – Jacquline Yancy/Denise Johnson-Lyles
DPMH CPMS- George Greeley

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/s/

JACQULINE A YANCY
12/15/2021 02:13:58 PM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	December 1, 2021
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 212479
Product Name and Strength:	Jylamvo (methotrexate) oral solution, 2 mg/ mL
Applicant/Sponsor Name:	Therakind Limited
OSE RCM #:	2021-466-1
DMEPA 1 Safety Evaluator:	Teresa McMillan, PharmD
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on November 18, 2021 for Jylamvo. Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the revised Prescribing Information, container labels and carton labeling for Jylamvo (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 Applicant implemented all of our container label and carton labeling recommendations and we have no additional recommendations at this time. We defer to the Division of Rheumatology and Transplant Medicine (DRTM) for the acceptability of the Prescribing Information.

[a] McMillan, T. Label and Labeling Review for Jylamvo (NDA 212479). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2021-OCT 27. RCM No.: 2021-466.

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON NOVEMBER 18, 2021

Container Labels

Carton Labeling

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/s/

TERESA S MCMILLAN
12/01/2021 03:09:01 PM

IDALIA E RYCHLIK
12/01/2021 03:11:26 PM

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

REVIEW DEFERRAL MEMORANDUM

Date:	November 29, 2021
To:	Cindy Chee, PharmD Regulatory Project Manager **Division of Rheumatology and Transplant Medicine (DRTM)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Marcia Williams, PhD Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Lonice Carter, MS, RN, CNL Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
Subject:	Review Deferred: Patient Package Insert (PPI)
Drug Name (established name):	JYLAMVO (methotrexate)
Dosage Form and Route:	oral solution
Application Type/Number:	NDA 212479
Applicant:	Therakind Limited

1 INTRODUCTION

On March 1, 2021, Therakind Limited submitted for the Agency's review an original New Drug Application (NDA) 212479 for JYLAMVO (methotrexate) oral solution. Therakind Limited seeks approval of this 505(b)(2) application with reference to NDA # 008085 Methotrexate Tablets. Therakind Limited has developed a new oral liquid formulation of methotrexate [JYLAMVO (methotrexate) 2 mg/ml Oral Solution] as an alternative oral presentation to the authorized tablet form, for the proposed treatment of neoplastic diseases, rheumatoid arthritis and psoriasis.

On March 24, 2021, the Division of Rheumatology and Transplant Medicine (DRTM) requested that the Division of Medical Policy Programs (DMPP) review the Applicant's proposed Patient Package Insert (PPI) for JYLAMVO (methotrexate) oral solution.

This memorandum documents the DMPP review deferral of the Applicant's proposed PPI for JYLAMVO (methotrexate).

2 CONCLUSIONS

Due to outstanding Chemistry, Manufacturing and Control (CMC) deficiencies, DRTM plans to issue a Complete Response (CR) letter. Therefore, DMPP defers comment on the Applicant's patient labeling at this time. A final review will be performed after the Applicant submits a complete response to the Complete Response (CR) letter. Please send us a new consult request at such time.

Please notify us if you have any questions.

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/s/

LONICE J CARTER
11/29/2021 11:00:28 AM

MARCIA B WILLIAMS
11/29/2021 11:49:40 AM

LASHAWN M GRIFFITHS
11/30/2021 06:57:24 AM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	October 27, 2021
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 212479
Product Name, Dosage Form, and Strength:	Jylamvo (methotrexate) oral solution , 2 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Therakind Limited (Therakind)
FDA Received Date:	Match 1, 2021
OSE RCM #:	2021-466
DMEPA 1 Safety Evaluator:	Teresa McMillan, PharmD
DMEPA 1 Team Leader:	Idalia Rychlik, PharmD

1 REASON FOR REVIEW

As part of the approval process for Jylamvo (methotrexate) oral solution , the Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the proposed Jylamvo prescribing information (PI), container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

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 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
*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

3 FINDINGS AND RECOMMENDATIONS

Table 2: Identified Issues and Recommendations for Division of Rheumatology and Transplant Medicine (DRTM)

Prescribing Information			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Full Prescribing Information			
1.	*The patient instructions for use (IFU) have been omitted from Section 2 Dosage and Administration.*	*Omission of the instructions for use may lead to administration errors. Additionally, the IFU have been embedded within the patient information and is not easily retrievable.*	*We recommend the development of a separate Instructions for Use (IFU). Ensure the patient instructions for use or administration are located in the Patient Information of the Prescribing Information and in*

			Section 2. Dosage and Administration to help mitigate administration errors. We defer to Patient Labeling for the accuracy of use of the patient friendly language.
2.	*We note that the Patient Information section has omitted disposal information.*	*Omission of this information may lead to unintended exposure or disposal errors.*	*We recommend adding the following section to the Patient Information:* *How should I dispose of JYLAMVO?* *This medicine should not be disposed of in wastewater or household waste. Ask your pharmacist how to dispose of (throw away) JYLAMVO that is no longer needed.* *We defer to Patient Labeling for the accuracy of use of the patient friendly language.*

Table 3: Identified Issues and Recommendations for Therakind Limited (Therakind) (entire table to be conveyed to Applicant)

Container Labels and Carton Labeling			
1.	*The lot and expiration numbers are undefined.*	*Undefined lot and expiration numbers may lead to identification issues and deteriorated drug product issues.*	*As currently presented, the format for the expiration date is not defined. To minimize confusion and reduce the risk for deteriorated drug medication errors, identify the format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only*

			numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a forward slash or a hyphen be used to separate the portions of the expiration date. Define the lot number as well.
2.	The terminology used to describe the recommended dosage are not consistently presented.	Lack of consistency of dosage terminology may contribute to dosing errors.	For consistency with the Prescribing Information (PI) consider revising the (b) (4) statement to the following: Recommended dosage: See Prescribing Information
3.	*The (b) (4) (b) (4) are on the principal display panel.*	*Overcrowding of the principal display panel can lead to prominent information being overlooked.*	*Delete the following statement:" (b) (4) Replace this statement with the following boxed statement: Attention Pharmacist: Dispense the accompanying Patient Information to each patient.*
4.	*Disposal information is omitted on the carton and container.* *Additionally, beyond use information is omitted on*	*Omission of this information may lead to adulterated product use, unintended exposure or disposal errors.*	*Include the statements "Date of first opening __/__/__. Discard unused portion 3 months after first opening. Ask your pharmacist how to*

	the carton and could be improved to increase comprehension on the container.		*throw away any unused medication." in bold font under the storage information on the container label and carton labeling. The "__/__/__" statement will alert the users to write a complete date (month, day, and year) on the container label and carton labeling. Additionally,* we recommend "Date of first opening" vs. (b) (4)

4 CONCLUSION

Our evaluation of the proposed dosing syringe did not identify any areas of vulnerability that would lead to medication errors. However, the labels and labeling identified areas of vulnerability that may lead to medication errors. Above, we have provided recommendations in Table 2 for DRTM and Table 3 for Therakind Limited (Therakind). We ask that the Division convey Table 3 in its entirety to Therakind Limited (Therakind) so that recommendations are implemented prior to approval of this NDA supplement.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Jylamvo received on March 1, 2021 from Therakind Limited (Therakind).

Table 2. Relevant Product Information for Jylamvo	
Initial Approval Date	N/A
Active Ingredient	methotrexate
Indication	JYLAMVO is a dihydrofolate reductase inhibitor indicated for the: • Treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen • Treatment of adults with mycosis fungoides • Treatment of adults with relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen • Treatment of adults with rheumatoid arthritis • Treatment of adults with severe psoriasis
Route of Administration	oral
Dosage Form	oral solution
Strength	2 mg/mL
Dose and Frequency	Instruct patients and caregivers to take the recommended dosage as directed, because medication errors have led to deaths. Verify pregnancy status in females of reproductive potential before starting JYLAMVO. ALL: The recommended dosage is 20 mg/m^2 orally once weekly as a part of a combination chemotherapy maintenance regimen. Mycosis fungoides: The recommended dosage is 25 to 75 mg orally once weekly as monotherapy; 10 mg/m2 orally twice weekly as part of combination chemotherapy. Relapsed or refractory non-Hodgkin lymphoma: The recommended dosage is 2.5 mg orally two to four times per week as part of metronomic combination chemotherapy.

	Rheumatoid Arthritis: The recommended starting dosage is 7.5 mg orally once weekly; adjust dose to achieve an optimal response. Psoriasis: The recommended dosage is 10 to 25 mg orally once weekly until adequate response is achieved.
How Supplied	Supplied as a clear yellow oral solution that contains 2 mg of methotrexate per milliliter. It is packaged in a 75 ml amber type III glass bottle with tamper evident child-resistant closure (polypropylene with expanded polyethylene liner) containing 60 mL of oral solution. Each pack contains one bottle, a low-density polyethylene (LDPE) bottle adaptor and a 10 mL white polypropylene dosing syringe (with major graduations at every 1 mL and minor graduations at every 0.25 mL) (NDC 55792-020-01).
Storage	Store JYLAMVO at 20°C to 25°C (68°F to 77°F). Keep the bottle tightly closed. Discard three months after first opening. JYLAMVO is a cytotoxic drug. Follow applicable special handling and disposal procedures.

APPENDIX B. PREVIOUS DMEPA REVIEWS-N/A
APPENDIX C. HUMAN FACTORS STUDY-N/A

APPENDIX D. ISMP NEWSLETTERS-N/A

APPENDIX E. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)-N/A

APPENDIX F. N/A

APPEARS THIS WAY IN ORIGINAL

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,[a] along with postmarket medication error data, we reviewed the following Jylamvo labels and labeling submitted by Therakind Limited (Therakind).

- Container label received on March 1, 2021
- Carton labeling received on March 1, 2021
- Prescribing Information (Image not shown) received on March 1, 2021 , available from \\CDSESUB1\evsprod\nda212479\0005\m1\us\114-lab\1141-dra-lab\11413-dra-lab-tex\draft-labeling-text-word.docx

G.2 Label and Labeling Images

\\CDSESUB1\evsprod\nda212479\0005\m1\us\114-lab\1141-dra-lab\11411-dra-car-and-con-lab\draft-carton-container-labels.pdf

Container label

(b) (4)

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

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

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/s/

TERESA S MCMILLAN
10/27/2021 12:32:56 PM

IDALIA E RYCHLIK
10/27/2021 01:53:09 PM

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: 8/2/2021

TO: Division of Rheumatology and Transplant Medicine (DRTM)
Office of Immunology and Inflammation (OII)

FROM: Division of New Drug Study Integrity (DNDSI)
Office of Study Integrity and Surveillance (OSIS)

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

RE: NDA 212479

The Division of New Drug Study Integrity (DNDSI) within the Office of Study Integrity and Surveillance (OSIS) determined that inspections are not warranted at this time for the site listed below. The rationale for this decision is noted below.

Rationale

OSIS conducted a Remote Record Review (RRR) for the site in (b) (4), which falls within the surveillance interval. The RRR was conducted under the following submissions: ANDAs (b) (4).

OSIS concluded that data from the reviewed studies were reliable.

Therefore, based on the rationale described above, inspections are not warranted at this time.

Site

Facility Type	Facility Name	Facility Address
Clinical	FARMOVS Pty., Ltd.	Clinical Research Organisation, Pharmacology Building, University of the Free State, Nelson Mandela Drive, Bloemfontein, Free State, 9301, South Africa
Analytical	(b) (4)	

Ting Wang -S

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Date: 2021.08.02 09:33:21 -04'00'

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/s/

TING WANG
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