

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

211284Orig1s000

OTHER REVIEW(S)

**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: October 11, 2018

To: Debra Birnkrant, MD
Director
Division of Antiviral Products (DAVP)

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: Ruth Lidoshore, PharmD
Patient Labeling Reviewer
Division of Medical Policy Programs (DMPP)

Wendy Lubarsky, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: Review of Patient Labeling: Patient Package Insert (PPI)

Drug Name (established name): TEMIXYS (lamivudine and tenofovir disoproxil fumarate)

Dosage Form and Route: tablets, for oral use

Application Type/Number: NDA 211284

Applicant: Celltrion, Inc. C/O ELC Group s.r.o

1 INTRODUCTION

On January 16, 2018, Celltrion, Inc. C/O ELC Group s.r.o., submitted for the Agency's review a 505(b)(2) New Drug Application (NDA) 211284 for TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets. The Reference Listed Drugs (RLDs) are EPIVIR (lamivudine) tablets NDA 020564 and VIREAD (tenofovir disoproxil fumarate) tablets NDA 021356. The proposed indication for TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets is for use in combination with other antiretrovirals for the treatment of HIV-1 infection in adults and pediatric patients (b) (4) weighing at least 35 kg.

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 Antiviral Products (DAVP) on April 5, 2018, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets.

2 MATERIAL REVIEWED

- Draft TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets PPI received on January 16, 2018, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 3, 2018.
- Draft TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets Prescribing Information (PI) received on January 16, 2018, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 3, 2018.
- Approved CIMDUO (lamivudine and tenofovir disoproxil fumarate) tablets comparator labeling dated February 28, 2018.

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 APFont to make medical information more accessible for patients with vision loss. We reformatted the PPI document using the Arial font, size 10.

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 comparator 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.

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

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/s/

RUTH I LIDOSHORE
10/11/2018

WENDY R LUBARSKY
10/11/2018

BARBARA A FULLER
10/12/2018

LASHAWN M GRIFFITHS
10/12/2018

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

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

Memorandum

Date: October 11, 2018

To: Kyong Hyon, Regulatory Project Manager
Division of Antiviral Products (DAVP)

From: Wendy Lubarsky, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Sam Skariah, Team Leader, OPDP

Subject: OPDP Labeling Comments for TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets, for oral use

NDA: 211284

In response to DAVP consult request dated April 5, 2018, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), and carton and container labeling for the original NDA submission for TEMIXYS (lamivudine and tenofovir disoproxil fumarate) tablets, for oral use (Temixys).

PI and PPI: OPDP's comments on the proposed labeling are based on the draft PI and PPI received by link (in OPDP consult request form) from DAVP (Kyong Hyon) on October 3, 2018 (PI was downloaded from link on October 9, 2018), and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed PPI will be sent under separate cover.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling received by link (in OPDP consult request form) from DAVP (Kyong Hyon) on October 3, 2018, and we agree with attached comments and do not have any additional comments.

Thank you for your consult. If you have any questions, please contact Wendy Lubarsky at (240) 402-7721 or wendy.lubarsky@fda.hhs.gov.

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/s/

WENDY R LUBARSKY
10/11/2018

MEMORANDUM

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

DATE: 2/26/2018

TO: Division of Antiviral Products
Office of Antimicrobial 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 211284

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 site listed below. The inspectional outcome from the inspections was classified as No Action Indicated (NAI).

Inspection Site

Facility Type	Facility Name	Facility Address
Clinical	PAREXEL International	Early Phase Clinical Unit, Campus Avenue South, University of the Free State, Bloemfontein, 9301, South Africa
Analytical	(b) (4)	

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/s/

SHILA S NKAH
02/26/2018