CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215596Orig1s000

OTHER REVIEW(S)

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

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

Memorandum

Date: 11/8/21

To: Alicia Moruf
Regulatory Project Manager
Division of Antivirals (DAV)

From: Nima Ossareh, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Sam Skariah, Team Leader, OPDP

Subject: OPDP Labeling Comments for:
LIVTENCITY (maribavir) tablets, for oral use

NDA: 215596

In response to DAVP consult request dated March 24, 2021, OPDP has reviewed the proposed product labeling (PI) for LIVTENCITY (maribavir) tablets, for oral use.

PI: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from Division of Antiviral Products (DAVP) on October 25, 2021 and are provided below.

Thank you for your consult. If you have any questions, please contact Nima Ossareh at (240) 402-2769 or nima.ossareh@fda.hhs.gov.

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NIMA OSSAREH
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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:	November 3, 2021
To:	Alicia Moruf, PharmD, MPH, RAC-US Senior Regulatory Project Manager **Division of Antivirals (DAV)**
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:	Jessica Chung, PharmD, MS Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Nima Ossareh, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	LIVTENCITY (maribavir)
Dosage Form and Route:	tablets, for oral use
Application Type/Number:	NDA 215596
Applicant:	Takeda Pharmaceuticals USA, Inc.

1 INTRODUCTION

On March 23, 2021, Takeda Pharmaceutical USA, Inc. submitted for the Agency's review an original New Drug Application (NDA) 215596 for LIVTENCITY (maribavir) tablets. The proposed indication for LIVTENCITY (maribavir) tablets is for the treatment of adults with post-transplant cytomegalovirus (CMV) infection and/or disease, including infections resistant and/or refractory to ganciclovir, valganciclovir, cidofovir or foscarnet.

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 Antivirals (DAV) on March 24, 2021, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for LIVTENCITY (maribavir) tablets.

2 MATERIAL REVIEWED

- Draft LIVTENCITY (maribavir) tablets PPI received on March 23, 2021, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 25, 2021.
- Draft LIVTENCITY (maribavir) tablets Prescribing Information (PI) received on March 23, 2021, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 25, 2021.

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. We reformatted the PPI document using the Arial font.

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)

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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BARBARA A FULLER
11/03/2021 10:14:18 AM

LASHAWN M GRIFFITHS
11/03/2021 10:22:53 AM

Clinical Inspection Summary

Date	10/20/2021
From	Jenn Sellers, M.D., Ph.D., Medical Officer Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations (OSI)
To	Christine Kim, Pharm.D., Regulatory Project Manager Andreas Pikis, M.D., Clinical Reviewer Mary Singer, M.D., Clinical Team Leader Division of Antiviral Products (DAV)
NDA #	215596
Applicant	Takeda Pharmaceuticals U.S.A, Inc.
Drug	Maribavir (TAK-620)
NME	Yes
Therapeutic Classification	Benzimidazole Riboside
Proposed Indication	Treatment of adults with post-transplant cytomegalovirus (CMV) infection and/or disease, including infections resistant and/or refractory to ganciclovir, valganciclovir, cidofovir or foscarnet
Consultation Request Dates	May 18, 2021
Summary Goal Date	October 22, 2021
Action Goal Date	November 23, 2021
PDUFA Date	November 23, 2021

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical investigators (CIs) Drs. Blumberg, Florescu, Silveira, Poiré and the sponsor, Takeda Pharmaceuticals U.S.A, Inc., were inspected in support of this application. At the site of Dr. Poiré, it was observed that few non-serious adverse events were not reported. We recommend that the review division take into account these adverse events in their safety evaluation of maribavir. At the site of Dr. Silveira, there were two observations related to treatment documentation and drug accountability. These violations are unlikely to affect the efficacy or safety results of the study (Protocol SHP-620-303). Overall, based on the results of these inspections, the studies (Protocols SHP-620-303 and 1263-203) appear to have been conducted adequately, and the clinical data generated from the CI sites and submitted by the sponsor appear to be reliable in support of this new drug application.

II. BACKGROUND

Maribavir (TAK-620) is a selective orally bioavailable benzimidazole riboside antiviral drug. It directly inhibits UL97 kinase by binding to it at the adenosine triphosphate (ATP) binding site, eliminating phosphotransferase needed in processes such as DNA replication, encapsulation, and nuclear egress. Its anti-cytomegalovirus (CMV) activity has been demonstrated in vitro.

The sponsor, Shire, acquired by Takeda Pharmaceutical Company Limited in January 2019, developed maribavir for the treatment in transplant recipients with CMV infections that were refractory or resistant to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir. FDA

granted maribavir Orphan Drug Designation in June 2011 and Breakthrough Therapy Designation in December 2017.

The sponsor conducted a Phase 3 randomized, open-label, active-controlled study (Protocol SHP-620-303) and a Phase 2 randomized, dose-ranging study (Protocol 1263-203) in transplant recipients with CMV infections and submitted the study data to support the indication. Four CIs and the sponsor were inspected for these studies. The following is a brief description of these two studies.

Protocol SHP-620-303

Title: "A Phase 3, Multicenter, Randomized, Open-label, Active-controlled Study to Assess the Efficacy and Safety of Maribavir Treatment Compared to Investigator-assigned Treatment in Transplant Recipients with Cytomegalovirus (CMV) Infections that are Refractory or Resistant to Treatment with Ganciclovir, Valganciclovir, Foscarnet, or Cidofovir"

Subjects: 352 subjects were randomized

Study Sites: 94 sites in North America, Europe, and Asia Pacific.

Study Initiation and Completion Dates: 22 Dec 2016 and 17 Aug 2020

The primary study objective was to compare the efficacy of maribavir to investigator assigned anti-CMV treatment (IAT, which included ganciclovir, valganciclovir, foscarnet, or cidofovir) on CMV viremia clearance at the end of Study Week 8 in transplant recipients who were refractory or resistant to prior anti-CMV treatment.

The key secondary objective of the study was to compare the efficacy of the 2 treatment arms on CMV viremia clearance and symptomatic CMV infection (tissue-invasive disease and CMV syndrome) improvement or resolution at the end of Study Week 8 and maintenance of this treatment effect through Study Week 16.

This was a Phase 3, multicenter, randomized, open-label, active-controlled study to assess the efficacy and safety of maribavir compared to investigator assigned anti-CMV treatment in hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) recipients with CMV infections that were refractory to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir, including CMV infections with confirmed resistance to 1 or more anti-CMV agents.

The study had the following 3 phases: a screening phase of up to 2 weeks, an 8-week study treatment phase, and a 12-week follow-up phase. All subjects were required to visit the site up to 19 times for up to a 22-week period.

After screening, eligible subjects were stratified by transplant type (HSCT and SOT) and by the most recent screening CMV DNA viral load (qPCR result). Eligible subjects were then randomized in a 2:1 ration to open label maribavir 400 mg twice daily (BID) or the active control group, an investigator assigned anti-CMV treatment. Subjects in the investigator assigned anti-CMV treatment group could stop treatment at the discretion of the investigator for lack of confirmed viremia clearance and/or intolerance to the assigned treatment. Only subjects with clear evidence of virologic failure with or without clinical failure (i.e., not merely intolerance) after a minimum of 3 weeks of treatment could be evaluated by the medical monitor for entry into the rescue arm, starting at Visit 5/Week 3. Rescue treatment was with maribavir 400 mg BID for 8 weeks.

The ***primary efficacy endpoint*** was a confirmed CMV viremia clearance at the end of Study Week 8, defined as plasma CMV DNA concentration < lower limit of quantification, LLOQ (i.e., <137 IU/mL) per central laboratory result in 2 consecutive postbaseline samples, separated by at least 5 days.

- This endpoint was assessed regardless of whether subjects completed the stipulated 8 weeks of study-assigned treatment.

- Subjects who initiated alternative (non-study) anti-CMV therapy or rescue treatment before Week 8 were counted as non-responders.

The ***key secondary endpoint*** was the achievement of CMV viremia clearance and symptom control at the end of Study Week 8, followed by maintenance of this treatment effect for another 8 weeks of treatment (i.e., Follow-up Week 16).

- Symptom control was defined as resolution or improvement of tissue-invasive CMV disease or CMV syndrome for subjects symptomatic at baseline or no new symptoms of tissue-invasive CMV disease or CMV syndrome for subjects asymptomatic at baseline.

- This endpoint was assessed regardless of whether subjects completed the required 8 weeks of study-assigned treatment.

- Subjects who initiated alternative (non-study) anti-CMV therapy before Week 16 were counted as non-responders.

Protocol 1263-203

Title: "A Phase 2, Randomized, Dose-ranging Study to Assess the Safety and Anti-cytomegalovirus (CMV) Activity of Maribavir Versus Valganciclovir for Treatment of CMV Infections in Transplant Recipients Who Do Not Have CMV Organ Disease."

Subjects: 119 subjects were randomized

Study Sites: 38 total centers in Austria, Belgium, Germany, France, Spain, and the UK.

Study Initiation and Completion Dates: 14 May 2012 and 25 Jul 2014

The primary study objective was to evaluate the safety and tolerability of different doses of maribavir versus valganciclovir, administered orally for up to 12 weeks, for treatment of CMV infections in recipients of stem cell or solid organ transplants who did not have CMV organ disease.

This was a Phase 2, multicenter, randomized, dose-ranging, parallel-group study of maribavir versus valganciclovir for the treatment of CMV infections in stem cell transplant or solid organ transplant recipients. Eligible subjects were stratified by transplant type (SCT or SOT) and randomized in a 1:1:1:1 allocation ratio to receive oral maribavir at 1 of 3 dose strengths (400 mg twice a day (BID), 800 mg BID, or 1200 mg BID) or valganciclovir (Weeks 1-3: 900 mg BID, after Week 3: 900 mg once daily; with dose adjustment for renal function) for up to 12 weeks. For those subjects assigned to receive maribavir, only dose strength was blinded; valganciclovir administration was open label.

The primary efficacy endpoints:

- Confirmed undetectable plasma CMV DNA (central laboratory) within 3 weeks
- Confirmed undetectable plasma CMV DNA (central laboratory) within 6 weeks

III. RESULTS

1. Emily Blumberg, M.D.
Site #008
3400 Spruce Street
Philadelphia, PA 19104
Inspection dates: June 07-10, 2021

At this site for Protocol SHP-620-303, a total of 11 subjects were screened and enrolled, and 4 subjects completed the study. Six subjects discontinued the study, and one subject was transferred to a different study site. The subjects and the reasons for discontinuations were verifiable, i.e., there were no discrepancies between the source records and the line listings submitted by the sponsor for discontinuations.

The inspection reviewed the source records for all enrolled subjects for the following: informed consent, study eligibility, efficacy endpoint data, adverse events, and investigational product received. The other records reviewed included, but were not limited to, electronic case report forms (eCRFs), protocol deviations, concomitant medications, randomization, drug accountability records, site correspondence with the sponsor/monitor/Institutional Review Board (IRB), FDA 1572, and financial disclosure records.

The primary and the key secondary efficacy endpoint data were verifiable. There was no evidence of underreporting of adverse events.

2. Diana Florescu, M.D.
Site #006
985400 Nebraska Medical Center
Omaha, NE 68198-5400
Inspection dates: May 16-20, 2021

At this site for Protocol SHP-620-303, 19 subjects were screened, 17 were enrolled, and 16 subjects completed the study. One subject discontinued the study due to a schedule conflict.

The inspection reviewed all 17 enrolled subject records. Source records reviewed included, but were not limited to, the informed consent forms, study inclusion/exclusion, study efficacy endpoint data, adverse events, eCRFs, protocol deviations, concomitant medications, progress notes, study drug accountability, and randomization procedures.

The primary and the key secondary efficacy endpoint data were verifiable. There was no evidence of underreporting of adverse events.

3. Fernanda Silveira, M.D.
Site number # 003
200 Lothrop Street
Pittsburgh, PA 15213
Inspection dates: June 22-25, 28-29, and July 1, 2021

At this site for Protocol SHP-620-303, 15 subjects were screened and enrolled, and 11 subjects completed the study. Four subjects discontinued the study for the following reasons: Subject # (b) (6) (IAT group) discontinued due to the adverse event of neutropenic fever. Three subjects discontinued due to lack of efficacy: # (b) (6) in IAT group, # (b) (6) in maribavir 400mg BID group, and # (b) (6) in maribavir 400mg BID group. All these discontinuations were verifiable against the data line listings.

The inspection reviewed study records for all 15 screened subjects. Records reviewed included, but were not limited to, informed consent forms, subject eligibility, home health care reports, electronic medical records, efficacy data, adverse events, pharmacy log, concomitant medications, eCRFs, investigational product accountability, randomization, site correspondence, FDA form 1572, financial disclosure, study monitoring report and staff training records.

The primary and the key secondary efficacy endpoint data were verifiable. There was no evidence of underreporting of adverse events.

However, there were two observations for the inspection:

1. The site did not maintain adequate records for three of the four subjects randomized to investigator assigned treatment (ganciclovir, valganciclovir, foscarnet or cidofovir) to show that they received the prescribed doses.

2. The site did not maintain adequate records related to subject compliance with maribavir dosing and drug accountability at the individual count level. The records include the number of tablets returned by subjects, but the site did not reconcile the number of tablets returned by subjects with the dosing recorded in the electronic diary (eDiary) to identify discrepancies. There was a note to file in some subject records indicating that they did not complete all the required dosing information in the eDiary.

Reviewer's comment: These findings regarding treatment documentation and drug accountability are unlikely to have an effect on the efficacy or safety results of the study.

4. Xavier Poiré, M.D.
Site # M20315
Avenue Hippocrate 10
Hématologie Bruxelles, 1200
Belgium
Inspection dates: June 6-11, 2021

At this site for Protocol 1263-203, 10 subjects were screened and enrolled, and 8 subjects completed the study. Two subjects discontinued the study due to adverse events: Subject # (b) (6) in the valganciclovir group discontinued due to septic shock, and Subject # (b) (6) in maribavir 800mg BID group discontinued due to liver toxicity. These discontinuations and the adverse events were verifiable against the data line listings.

The inspection reviewed subject study records for all 10 screened subjects. Records reviewed included, but were not limited to, Independent Ethics Committee (IEC) oversight, informed consent, eligibility, protocol adherence, concomitant medications, test article accountability, adverse events and the efficacy endpoint data.

The primary efficacy endpoint data were verifiable. All serious adverse events were reported. However, a few adverse events in 6 subjects (all in maribavir group) were not reported to the sponsor and FDA. Please see Table 1 below.

Table 1. Adverse Events Not Reported to the Sponsor and FDA

Subject #	Maribavir Dose	Adverse Events
(b) (6)	800 mg BID	Significant loss of appetite Nausea Headache within 15 minutes of taking the pill
	800 mg BID	Dyspnea
	800 mg BID	Decreased appetite
	1200 mg BID	Decreased appetite
	1200 mg BID	Increased fatigue Thrush Headache Loss of appetite
	1200 mg BID	Worsening anorexia Diarrhea

Reviewer's comment: We recommend that the review division consider adding these adverse events to their assessment of the overall safety of maribavir.

5. Sponsor

Takeda Pharmaceutical Company Limited
55 Hayden Avenue
Lexington, MA 02421
Inspection dates: July 19-28, 2021

The sponsor Takeda was inspected in accordance with Compliance Program 7348.810 Bioresearch Monitoring (BIMO) for Sponsor, CRO, and Monitors. Activities and records reviewed included, but were not limited to, organizational charts, standard operating procedures, investigator selection, monitoring plans, monitoring reports, transfer of responsibilities, correspondence, training records, FDA 1572s, financial disclosure forms, electronic case report forms (eCRFs), protocol adherence, subject protection and ethical oversight, safety plans, adverse events, data management, primary efficacy endpoint, and investigational product accountability records. No issues of concern were found.

{See appended electronic signature page}

Jenn W. Sellers, M.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Phillip Kronstein, M.D.
Team Leader
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Kassa Ayalew, M.D., M.P.H
Branch Chief and Division Director (acting)
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

cc:
DARRTS: NDA 215596
DAV/Project Manager/Christine Kim
DAV/Medical Officer/Andreas Pikis
DAV/Clinical Team Leader/Mary Singer
OSI/Office Director/David Burrow
OSI/Deputy Office Director/Laurie Muldowney
OSI/DCCE/Division Director (acting)/Kassa Ayalew
OSI/DCCE/Branch Chief/Kassa Ayalew
OSI/DCCE/Team Leader/Phillip Kronstein
OSI/DCCE/GCP Reviewer/Jenn Sellers
OSI/GCP Program Analyst/Yolanda Patague

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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:	July 6, 2021
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215596
Product Name and Strength:	Livtencity (maribavir) tablet, 200 mg
Applicant/Sponsor Name:	Takeda Pharmaceuticals USA, Inc.
OSE RCM #:	2021-595-1
DMEPA Safety Evaluator:	Melina Fanari, RPh
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on June 22, 2021 for Livtencity. The Division of Antivirals (DAV) requested that we review the revised container labels and carton labeling for Livtencity (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

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] Fanari, M. Label and Labeling Review for Livtencity (NDA 215596). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 Jun 8. RCM No.: 2021-595.

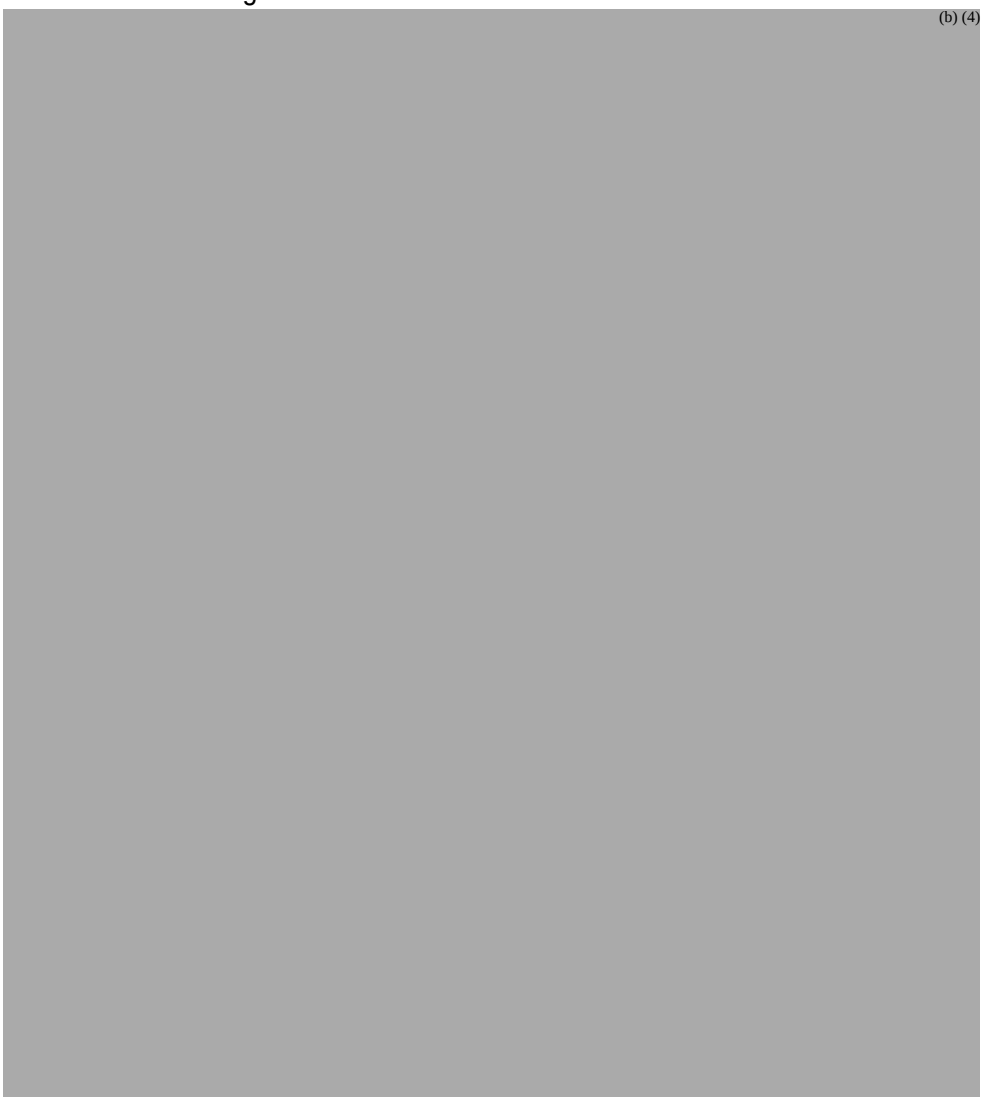
APPENDIX A. IMAGES OF LABELS AND LABELING RECEIVED ON JUNE 22, 2021

Container labels

(b) (4)

Carton labeling

(b) (4)



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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:	June 8, 2021
Requesting Office or Division:	Division of Antivirals (DAV)
Application Type and Number:	NDA 215596
Product Name and Strength:	Livtencity (maribavir) tablet, 200 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Takeda Pharmaceuticals USA, Inc.
FDA Received Date:	March 23, 2021
OSE RCM #:	2021-595
DMEPA Safety Evaluator:	Melina Fanari, RPh
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS

1 REASON FOR REVIEW

As part of the approval process for Livtencity (maribavir) tablet, the Division of Antivirals (DAV) requested that we review the proposed Livtencity prescribing information (PI),patient prescribing information (PPI), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS 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
ISMP Newsletters*	C-N/A
FDA Adverse Event Reporting System (FAERS)*	D-N/A
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

3 FINDINGS AND RECOMMENDATIONS

Our evaluation of the proposed Livtencity PI and PPI did not identify any medication error issues. Tables 3 below includes the identified medication error issues with the submitted container labels and carton labeling, our rationale for concern, and the proposed recommendation to minimize the risk for medication error.

Table 2. Identified Issues and Recommendations for Takeda Pharmaceuticals USA, Inc. (entire table to be conveyed to Applicant)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels and Carton Labeling			
1.	Net quantity and Rx only statements are located in close proximity to strength statement.	Prevent risk of numerical confusion between the strength and net quantity.	Decrease prominence (remove (b) (4)) of the net quantity and Rx only statements and relocate them away from the product strength statement.

Table 2. Identified Issues and Recommendations for Takeda Pharmaceuticals USA, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
2.	Container label barcode is in horizontal orientation.	Barcodes placed in a horizontal position may not scan due to vial curvature.	Consider reorienting the linear barcode (container labels only) to a vertical position to improve the scannability of the barcode.

4 CONCLUSION

Our evaluation of the proposed Livtencity PI and PPI did not identify any areas of vulnerability that may lead to medication errors. However, our review of the container labels and carton labeling identified areas of vulnerability that may lead to medication errors. Above, we have provided recommendations in Table 2 for the Applicant. We ask that the Division convey Table 2 in its entirety to Takeda Pharmaceuticals USA, Inc. so that recommendations are implemented prior to approval of this NDA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 3 presents relevant product information for Livtencity that Takeda Pharmaceuticals USA, Inc. submitted on March 23, 2021.

Table 3. Relevant Product Information for Livtencity	
Initial Approval Date	N/A
Active Ingredient	maribavir
Indication	The treatment of adults with post-transplant cytomegalovirus (CMV) infection and/or disease, including infections resistant and/or refractory to ganciclovir, valganciclovir, cidofovir or foscarnet. (b) (4)
Route of Administration	Oral
Dosage Form	Tablet
Strength	200 mg
Dose and Frequency	400 mg (two 200 mg tablets) orally twice daily
How Supplied	Bottle of 28 and 56 tablets
Storage	Store at 20 to 25°C (68 to 77°F), (b) (4) 15 to 30°C (59 to 86°F) *[see USP Controlled Room Temperature]*

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,[a] along with postmarket medication error data, we reviewed the following Livtencity labels and labeling submitted by Takeda Pharmaceuticals USA, Inc..

- Container labels and Carton Labeling received on March 23, 2021
- Prescribing Information (Images not shown) received on March 23, 2021 located at \\CDSESUB1\evsprod\NDA215596\0001\m1\us

F.2 Label and Labeling Images

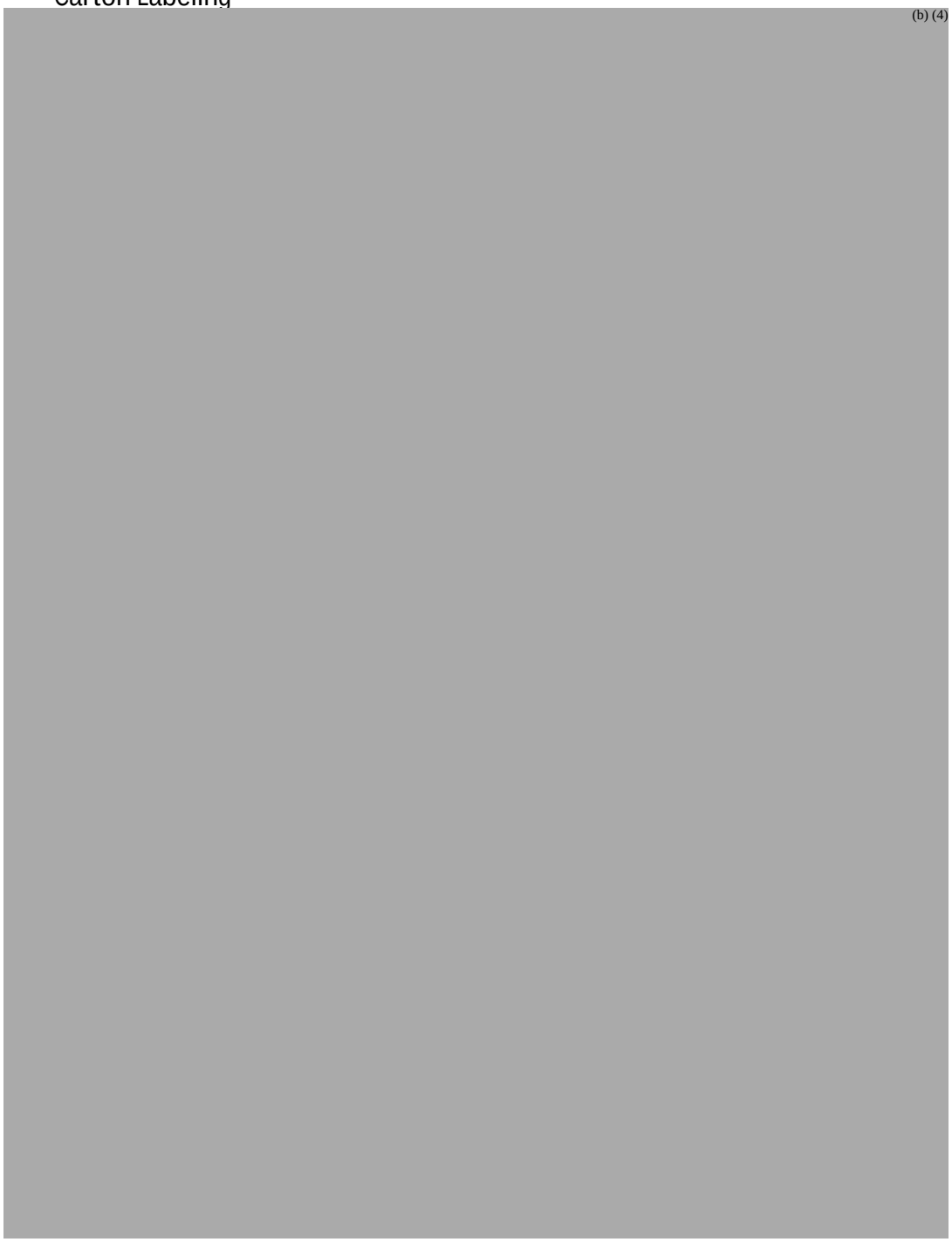
Container labels

(b) (4)

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

Carton Labeling

(b) (4)



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