CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204311Orig1s000

OTHER ACTION LETTERS

NDA 204311

COMPLETE RESPONSE

Mylan Pharmaceuticals Inc., a Viatris Company
U.S. Agent for Mylan Laboratories Limited, a Viatris Company, India
Attention: Beth Britton
Senior Director, Regulatory Affairs
3711 Collins Ferry Road
Morgantown, WV 26505

Dear Ms. Britton:

Please refer to your new drug application (NDA) dated and received December 23, 2013, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for the following drug product:

- Abacavir and Lamivudine Tablets for Oral Suspension, 60 mg/30 mg

We acknowledge receipt of your amendment dated February 6, 2019, which constituted a complete response to our October 23, 2014, tentative approval letter. We also acknowledge receipt of your amendment dated July 15, 2022, which constituted a complete response to our August 6, 2019, complete response letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

(1) Following surveillance inspection of Mylan Laboratories Limited Unit-8, a Viatris Company (FEI # 30002785310, Vizianagaram, Andhra Pradesh, India) manufacturing facility listed in this application, FDA conveyed deficiencies to the representatives of the facility. Satisfactory resolution of the observations is required before this NDA may be approved.

PRESCRIBING INFORMATION

(2) We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the

Prescription Drug Labeling Resources[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the Prescribing Information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at FDA.gov.[3]

CARTON AND CONTAINER LABELING

(3) We reserve comment on the proposed labeling until the application is otherwise adequate.

ADDITIONAL COMMENTS

We have the following comment and recommendation that are not approvability issues:

(4) Based on our regulatory and scientific review of your application, we have preliminarily determined that there is no need to rely for approval on FDA's finding of safety and/or effectiveness for (b) (4) (b) (4) because FDA's finding of safety and/or effectiveness for the other two relied-upon listed drugs, Ziagen (abacavir sulfate) oral solution, NDA 020978, and Epivir (lamivudine) oral solution, NDA 020596, appear adequate to support approval of your 505(b)(2) application. Therefore, in your future submissions to this application, including any resubmission, please update your Form FDA 356h (Field 20), cover letter, and annotated labeling to omit identification of (b) (4) as a basis for approval of your application.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

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[1] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources
[2] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule
[3] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The drug product is not eligible for procurement under the President's Emergency Plan for AIDS Relief (PEPFAR) program unless and until you have been notified in writing that, based on your resubmission, the application is tentatively approved.
If you have any questions, call Monica Zeballos, Sr. Program Consultant, at (301) 796-0840.

Sincerely yours,

{See appended electronic signature page}

Sarita Boyd, Pharm.D.
Associate Director for PEPFAR
Division of Antivirals
Office of Infectious Diseases
Office of New Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SARITA D BOYD
01/13/2023 03:17:43 PM

NDA 204311

COMPLETE RESPONSE

Mylan Pharmaceuticals Inc.
U.S. Agent for Mylan Laboratories Limited, India
Attention: Shane Shupe, Director, Regulatory Affairs
781 Chestnut Ridge Road, P.O. Box 4310
Morgantown, WV 26504-4310

Dear Mr. Shupe:

Please refer to your new drug application (NDA) dated and received December 23, 2013, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for the following drug product:

- Abacavir and Lamivudine Tablets for Oral Suspension, 60 mg/30 mg

We acknowledge receipt of your amendment dated February 6, 2019, which constituted a complete response to our October 23, 2014, tentative approval letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

(1) During a recent inspection of the Mylan Laboratories Limited, Unit 8 (FEI # 3002785310) manufacturing facility for this NDA, our field investigator observed objectionable conditions at the facility and conveyed that information to the representative of the facility at the close of the inspection. Satisfactory resolution of the observations is required before this NDA may be approved.

PRESCRIBING INFORMATION

(2) Your proposed Prescribing Information (PI) must conform to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57. As you develop your proposed PI, we encourage you to review the labeling review

resources on the PLR Requirements for Prescribing Information[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information in the PI on pregnancy, lactation, and females and males of reproductive potential
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

Submit draft labeling based on our proposed revisions sent to you separately via email correspondence on August 6, 2019.

Prior to resubmitting the labeling, use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at FDA.gov.[3]

To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should include annotations that support any proposed changes.

CARTON AND CONTAINER LABELING

(3) Submit draft carton and container labeling based on our proposed revisions sent to you separately via email on August 6, 2019.

[1] http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm
[2] http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm
[3] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

MEDICATION GUIDE

(4) Submit draft labeling based on our proposed revisions sent to you separately via email on August 6, 2019.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, please call Monica Zeballos, Pharm.D., Program Coordinator, at (301) 796-0840.

Sincerely yours,

{See appended electronic signature page}

Jeffrey Murray, M.D., M.P.H.
Deputy Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JEFFREY S MURRAY
08/06/2019 03:12:06 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204311 **TENTATIVE APPROVAL**

Mylan Pharmaceuticals Inc.
Attention: Shane Shupe, Senior Manager, Regulatory Affairs
U.S. Agent for Mylan Laboratories Limited in India
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

Dear Mr. Shupe:

Please refer to your New Drug Application (NDA) dated and received December 23, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for the following drug product:

- Abacavir and Lamivudine Tablets for Oral Suspension, 60 mg/30 mg

We also acknowledge receipt of your submissions dated:

May 15, 2014	August 1, 2014	September 12, 2014
June 26, 2014	August 22, 2014	October 1, 2014

This NDA provides for the use of Abacavir and Lamivudine Tablets for Oral Suspension, 60 mg/30 mg in combination with other antiretrovirals for the treatment of HIV-1 infection.

This NDA was reviewed under the President's Emergency Plan for AIDS Relief (PEPFAR).

We completed our review of this application. It is **tentatively approved** under 21 CFR 314.105 for use as recommended in the agreed-upon labeling (refer to the enclosed text for the package insert, medication guide, and immediate container and carton labels (b) (4) Also refer to the agreed-upon labeling submitted on October 21, 2014, for the package insert and medication guide and your September 12, 2014, submission for the revised immediate container and carton (b) (4). Based on the data provided, the expiration dating period is 24 months for Abacavir and Lamivudine Tablets for Oral Suspension, 60 mg/30 mg in the following packaging configuration when stored below 30ºC (86ºF): 1) HDPE bottle packs of 60 tablets with cotton, screw caps, induction seals, and desiccant (silica gel), 2) HDPE bottle packs of 60 tablets with cotton, screw caps, and induction seals for commercial packaging, and (b) (4) (b) (4)

This determination is based upon information available to the Agency at this time [i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in manufacturing and testing of the drug product]. This determination is subject to change on the basis of any new information that may come to our attention.

The listed reference drug products [Epivir (lamivudine), Ziagen (abacavir sulfate), (b) (4) (b) (4) upon which you base your application are subject to a period of patent and exclusivity protection and therefore, final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be made effective until the period has expired. If you have questions as to when this date will be, please contact the Agency at the information provided below.

Two or six months prior to the expiration of the patent and exclusivity protection, as appropriate, submit an amendment to this application identifying changes, if any, in the conditions under which your product was tentatively approved. Any changes to the conditions outlined in this NDA require our review before final approval and the goal date for our review will be set accordingly. Your amendment should include updated labeling, chemistry, manufacturing and controls data, and a safety update. This amendment should include draft final printed labels and labeling which comply with all U.S. regulations (uniqueness of drug product appearance per 21 CFR 206; child-resistant packaging per 16 CFR 1700, etc.). This amendment should be designated clearly in your cover letter as a "**FINAL APPROVAL REQUESTED**."

We remind you that you are expected to comply with the reporting requirements provided in 21 CFR 314.80 and 314.81. If the product is to be mass distributed in developing countries, a system of collecting and reporting adverse drug reactions by the distributor would be desirable (e.g., through governmental or nongovernmental agencies distributing the products).

We also remind you that, should you intend to market this product in the United States after the period of patent and exclusivity protection, you are required to comply with all applicable U.S. legislation, including the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), which requires that all NDAs, Biological License Applications (BLAs), or supplemental applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration contain a pediatric assessment unless this requirement is waived, deferred, or inapplicable. A pediatric assessment contains data gathered from pediatric studies using appropriate formulations for each age group for which the assessment is required, and other data that are adequate to: 1) assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and 2) support dosing and administration for each pediatric subpopulation for which the product has been assessed to be safe and effective. You must also join the antiretroviral pregnancy registry at that time and make the appropriate labeling change that references the existence of the pregnancy registry. In addition, an updated package insert (PI) must be submitted under the Structured Product Labeling requirements (http://www.fda.gov/oc/datacouncil/spl.html) as defined by the Physician's Labeling Rule [21 CFR 201.56, 201.57].

Until we issue a final approval letter, this NDA is not deemed approved. If you believe that there are grounds for issuing the final approval letter before the period of patents' protection has expired, you should amend your application accordingly.

Please note that this drug product may not be marketed in the United States without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d).

If you have any questions, please contact Monica Zeballos, Pharm.D., Senior Program Consultant, at (301) 796-0840 or email at monica.zeballos@fda.hhs.gov.

Sincerely yours,

{See appended electronic signature page}

Jeffrey Murray, M.D., M.P.H.
Deputy Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Draft PI, medication guide, and immediate container and carton labels (b) (4) (b) (4)

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

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JEFFREY S MURRAY
10/23/2014