



NDA 22-541

TENTATIVE APPROVAL

Macleods Pharmaceuticals Limited
Attention: Pooja Kulkarni, Regulatory Affairs
304, Atlanta Arcade, Marol Church Road
Andheri East, Mumbai - 400059
India

Dear Ms. Kulkarni:

Please refer to your new drug application (NDA) 22-541 dated May 21, 2010, received on May 26, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Lamivudine and Stavudine Tablets, 150 mg/30 mg.

We acknowledge receipt of your submissions dated:

June 10, 2009
July 6, 2009
October 23, 2009

March 22, 2010
April 14, 2010
May 12, 2010

June 19, 2010
July 12, 2010

This NDA provides for the use of Lamivudine and Stavudine Tablets, 150 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, as amended. 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, patient package insert, and immediate carton and container labels). Also, refer to your original submission for the immediate carton and container labels and the agreed-upon labeling emailed on July 31, 2010, for the package insert and patient package insert. Based on the data provided, the expiration dating period is 24 months for Lamivudine and Stavudine Tablets, 150 mg/30 mg in a HDPE container of 60 tablets and for the bulk package triple laminate pouch containing 2000 tablets (for repacking within 6 months) when stored at 20°-25°C (68° to 77°F).

The tentative approval is contingent upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices of the facilities used in manufacturing and testing of the drug product) and is, therefore, subject to change on the basis of any new information that may come to our attention.

We have the following recommendation regarding carton labels:

1. It is our understanding that a few PEPFAR recipient nations have expressed a preference for antiretroviral drugs to be supplied in an individual carton containing a bottle and the package insert. If you wish, you may submit color images of carton label(s) as a labeling amendment for review. If they are found to be acceptable, you would have an option to provide bottles alone and bottles within cartons. No additional stability data would be required because the addition of a cardboard carton is not expected to have a measurable effect on the protection provided by the bottle.

One of the listed reference drug products [Epivir[®] (lamivudine)] upon which you base your application is subject to a period of patent 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's 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 United States 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.**"

Failure to submit this amendment will prompt a review of this application that may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

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 remind you that, should you intend to market this product in the United States after the period of patents protection, you are required to 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].

Before 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 expiration of the patents protection, you should amend your application accordingly.

This product may be considered misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed in the United States before final approval.

If you have any questions, please contact David Araujo, Pharm.D., Senior Program Consultant, at (301) 796-0669 or by email at david.araojo@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: PI, PPI, and immediate container label

Email CC: Andrej Gasperlin, AB Pharmaceuticals
U.S. Agent for Macleods Pharmaceuticals Limited

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22541	ORIG-1	MACLEODS PHARMACEUTICA LS LTD	Lamivudine/Stavudine FDC Tabs (150mg/30mg)

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
08/05/2010