

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022018Orig1s000

SUMMARY REVIEW

DATE: March 15, 2017

FROM: Jeffrey S. Murray M.D., M.P.H.
Division of Antiviral Products

SUBJECT: Deputy Director Memorandum for NDA 22018
Lamivudine and Zidovudine Tablets, 150 mg/300 mg
Applicant: Pharmicare Limited (Pharmacare)

TO: Division files

I. Background and Clinical Findings

(b) (4)

Subsequently Pharmicare submitted NDA 22018 for lamivudine and zidovudine tablets, (b) (4) FDA administratively chose to review NDA 22018 as a 505(b)(2), even though a reference listed drug (Combivir®) for these tablets existed, because the tablets had already been reviewed as a 505(b)(2) application (b) (4) NDA 22018 for lamivudine and zidovudine tablets was granted a tentative approval (TA) in August 2006. On Sept 17, 2016, Pharmicare made a class 2 resubmission to the previously granted TA to gain final approval and marketing in the United States after all the listed patents for Combivir® expired on 18 Nov 2016.

As stated in the labeling memorandum prepared by Monica Zeballos, on March 17, 2015, Pharmicare submitted a labeling amendment for the PLR (Physician's Labeling Rule) conversion of the package insert (PI). This approval will address the resubmission and the labeling amendment.

II. Summary of Findings

In this NDA (b) (4), Pharmicare's version of lamivudine and zidovudine tablets are bioequivalent (BE) to the reference product (Combivir®, GlaxoSmithKline), as concluded in the Clinical Pharmacology Review (b) (4). The BE study was conducted in the fasted condition only so the labeling will recommend use of lamivudine and zidovudine tablets without food. It should be noted that the Combivir® label has

no food recommendations. Had this product been reviewed as an ANDA, a fed BE study would have been required.

NDA 22018 (for tentative approval) contained some refinement of the manufacturing process for lamivudine and zidovudine tablets (b) (4) as mentioned in the Chemistry, Manufacturing and Controls (CMC) Review, prepared by Rao Kamhampati, Ph.D. With respect to the resubmission for final approval, refer to the Product Quality review prepared by Xinghua Wu, Ph.D., which summarizes updates in manufacturing processes and controls since the TA. (b) (4)

Monica Zeballos, and I reviewed the package insert labeling; the labeling should allow for safe and effective use of lamivudine and zidovudine tablets in combination with other antiretroviral drugs. The label is similar to that of the innovator product Combivir® and includes labeling compliant with the Pregnancy and Lactation Labeling Rule (PLLR). One difference in labeling for this product is the need to take drug on an empty stomach.

For final approval Pharmicare has agreed to join the Antiretroviral Pregnancy Registry.

III. Recommendations

In conclusion NDA 22018, providing for the use of lamivudine and zidovudine tablets in combination with other antiretroviral agents for the treatment of HIV-1 is recommended for Approval (final). Because the labeling has food restrictions that Combivir® and other generics do not have, it is expected that this product may receive a B rating in the Orange Book.

Jeffrey S. Murray M.D., M.P.H.

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/s/

JEFFREY S MURRAY
03/17/2017

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

DATE: August 23, 2006

FROM: Jeffrey S. Murray M.D., M.P.H.
Division of Antiviral Products

SUBJECT: Deputy Director memorandum for NDA 22-018
Lamivudine 150 mg/Zidovudine 300 mg Tablets (Pharmacare Limited)

TO: Division files

I. Background and Clinical Findings

The availability of a wide range of safe and effective antiretroviral drug products is hoped to facilitate a wider distribution of anti-HIV drugs to better meet the demands of the global HIV/AIDS pandemic. In May 2004 FDA published a draft guidance entitled "Fixed Dose Combinations (FDC) and Co-Packaged Drug Products for the Treatment of HIV." The guidance encourages sponsors to develop various drug product versions of previously approved antiretroviral drugs and encourages sponsors to submit drug applications for these products to FDA for review. Although many antiretroviral drug product versions of previously approved antiretrovirals cannot be currently marketed in the US because of patent and exclusivity restrictions, FDA is able to review these products for quality, safety and efficacy and potentially grant a tentative approval. The President's Emergency Plan for AIDS Relief will consider procurement of products reviewed by FDA that have been granted approval or tentative approval. Such products may be distributed outside the US, depending on legal requirements in other countries.

Pharmacare Limited (also known as Aspen Pharmacare) submitted this 505 (b)2 NDA for a fixed dose combination tablet, lamivudine/zidovudine tablets. (b) (4)

(b) (4) The lamivudine/zidovudine tablets (b) (4) with some recent refinement of manufacturing for NDA 22-018.

II. Recommendations

In this NDA (b) (4) Pharmacare's version of lamivudine/zidovudine tablets are bioequivalent to the reference product (Combivir, GlaxoSmithKline),

as concluded in the Clinical Pharmacology Review prepared by Arya Vikram Ph.D. NDA 22-018 contains some refinement of the manufacturing process for lamivudine/zidovudine tablets, (b) (4) as mentioned in the Chemistry, Manufacturing and Controls Review, prepared by Rao Kamhampati, Ph.D. Both Clinical Pharmacology and Chemistry Reviewers recommend tentative approval.

Vasavi Reddy, project management, and I reviewed the package insert labeling; the labeling should allow for safe and effective use of lamivudine/zidovudine tablets in combination with other antiretroviral drugs.

In conclusion NDA 22-018, providing for the use of lamivudine/zidovudine tablets in combination with other antiretroviral agents for the treatment of HIV, is recommended for Tentative Approval.

Jeffrey S. Murray M.D., M.P.H.

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/s/

JEFFREY S MURRAY
03/16/2017