CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-154

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	April 27, 2009
To:	Debra Birnkrant, MD Director, Division of Anti-Viral Products
Through:	Todd Bridges, RPh, Team Leader Denise P. Toyer, PharmD, Deputy Director Carol A. Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Denise V. Baugh, PharmD, BCPS, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Tyzeka (Telbivudine) Oral Solution 20 mg/mL
Application Type/Number:	NDA# 22-154
Applicant:	Novartis Pharmaceuticals
OSE RCM #:	2009-737

CONTENTS

1 INTRODUCTION

This review is in response to the Applicant's proposal to provide [redacted] with each 300 mL bottle of Tyzeka Oral Solution. One device is a measuring cup that contains increments of 5 mL and can measure the doses of 10 mL, 20 mL, and 30 mL. [redacted] b(4)

2 REGULATORY HISTORY

The Division of Medication Error Prevention and Analysis (DMEPA) reviewed the container label, carton and insert labeling, and the measuring device (30 mL clear plastic cup) for Tyzeka Oral Solution and provided recommendations for improvement in OSE# 2008-1074 dated October 17, 2008.

The Agency issued the Applicant a Complete Response letter dated October 21, 2008, which indicated that [redacted] b(4)

On March 2, 2009, the Applicant submitted a proposal that included a dosing cup calibrated in 5 mL increments (i.e., capable of measuring doses of 5 mL to 30 mL) [redacted] b(4) They proposed to provide [redacted]

Upon analysis of the Applicant's proposal DMEPA found the provision of [redacted] b(4) Specifically, the applicant proposal [redacted] b(4)

2.1 PRODUCT INFORMATION

Tyzeka (telbivudine) is indicated for the treatment of chronic hepatitis B in adult patients with evidence of viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. The recommended dose is 600 mg orally once daily, with or without food. This regimen is adjusted for renally compromised patients as follows:

Creatinine Clearance	Oral Solution (20 mg/mL)
> 50	30 mL daily
30 - 49	20 mL daily
< 30	10 mL daily
End stage renal disease (ESRD)	[redacted] b(4)

It will be supplied as a 20 mg/mL oral solution in a 300 mL bottle.

3 DISCUSSION

DMEPA discussed their safety concerns pertaining to the [redacted] with the Division of Anti-Viral Products (DAVP). DAVP agreed that the applicant's proposal [redacted] was unacceptable. The Division indicated that prescribers can dose patients with end stage renal disease (ESRD) using the currently approved 'tablet' dosage form. Additionally, DMEPA stated that the current device could be improved upon as well (e.g., increased visibility of numbers and the deletion of extraneous markings). Subsequent to that decision, DAVP and DMEPA discussed the safety concerns concerning the [redacted] with the Applicant in an April 17, 2009 teleconference. At that time, the Applicant agreed [redacted] b(4)

Thus, upon approval Tyzeka Oral Solution will only include the dosing cup for doses of 10 mL, 20 mL, and 30 mL. To address DMEPA's concerns with the legibility of the increments on the dosing cup and the extraneous measurements, the Applicant agreed to develop a dosing device that addressed these concerns and that would measure all of the prescribed doses [redacted] b(4) , 10 mL, 20 mL, and 30 mL]. DAVP and the Applicant are currently finalizing the dates associated with a post-marketing commitment (PMC) that reads:

> Develop a dosing cup for distribution with Tyzeka oral solution that has clearly marked units of measure and contains only those units that correspond to dosing recommendations. If this dosing cup does not conform to these specifications, then conduct a failure mode and effects analysis (FMEA) of the proposed dosing cup to evaluate the potential for medication errors.

4 CONCLUSIONS

The [redacted] in addition to the PMC to develop a dosing device that does not contain extraneous measurements and provides clearly marked measurements for the approved doses addresses DMEPA's safety concerns. b(4)

If you have questions or need clarifications, please contact Marlene Hammer, OSE project manager, at 301-796-0757.

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/s/

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