CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-436

OTHER 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:	July 10, 2009
To:	Debra Birnkrant, M.D., Director **Division of Antiviral Drug Products**
Through:	Jodi Duckhorn, MA, Team Leader **Division of Risk Management**
From:	Jessica M. Diaz, BSN, RN Patient Product Information Reviewer **Division of Risk Management**
Subject:	DRISK Review of Patient Labeling (Patient Package Insert)
Drug Name(s):	TRADENAME (acyclovir/hydrocortisone)
Application Type/Number:	NDA 22-436
Applicant/sponsor:	Medivir AB
OSE RCM #:	2008-1864 (associated RCM 2008-1862)

1 INTRODUCTION

Medivir AB submitted a New Drug Application 505(b)(2), (NDA 22-436) for a cream September 30, 2008. TRADENAME (acyclovir, 5%/hydrocortisone, 1%) is used to treat the early signs and symptoms of recurrent herpes labialis (cold sores) in adults and adolescents (12 years of age and older).

The Division of Antiviral Drug Products (DAVP) requested the Division of Risk Management review the Patient Package Insert (PPI) for "TRADENAME". This review was written in response to that request from DAVP.

2 MATERIAL REVIEWED

- TRADENAME (acyclovir, 5%/hydrocortisone, 1%) Patient Package Insert (PPI) submitted September 30, 2008 and revised by the Review Division throughout the current review cycle.
- TRADENAME (acyclovir, 5%/hydrocortisone, 1%) Prescribing Information (PI) submitted September 30, 2008 and revised by the Review Division throughout the current review cycle.

3 DISCUSSION

The purpose of patient directed labeling is to facilitate and enhance appropriate use and provide important risk information about medications. Our recommended changes are consistent with current research to improve risk communication to a broad audience, including those with lower literacy.

The draft PPI submitted by the Applicant has a Flesch Kinkaid grade level of 7.4, and a Flesch Reading Ease score of 62.4%. To enhance patient comprehension, materials should be written at a 6^{th} to 8^{th} grade reading level, and have a reading ease score of at least 60% (60% corresponds to an 8^{th} grade reading level). The reading scores as submitted by the Applicant are acceptable.

In our review of the PPI, we have:

- reformatted the PPI to a three page document,
- simplified wording and clarified concepts where possible,
- ensured that the PPI is consistent with the PI,
- removed unnecessary or redundant information
- Although not required for Patient Information, we have put this PPI in the question-and-answer format specified in the

Medication Guide Regulations (21 CFR 208.20) that we recommend for all FDA approved patient labeling.

- ensured that the PPI meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

In 2008, The American Society of Consultant Pharmacists Foundation in collaboration with The American Foundation for the Blind published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. They recommend using fonts such as Arial, Verdana, or APHont to make medical information more accessible for patients with low vision. We have reformatted the PPI document using the font APHont, which was developed by the American Printing House for the Blind specifically for low vision readers.

See the attached document for our recommended revisions to the PPI. Comments to the review division are ***bolded, underlined and italicized***.

We are providing the review division a marked-up and clean copy of the revised PPI. We recommend using the clean copy as the working document.

All future relevant changes to the PI should also be reflected in the PPI.

4 CONCLUSIONS AND RECOMMENDATIONS

1. In the header, the Applicant should insert the phonetic spelling of TRADENAME and make established name lower case.
2. In the introductory paragraph, we deleted "[redacted] We instead inserted, "TRADENAME is for cold sores, on lips and around the mouth only. TRADENAME should not be used in eyes, mouth, nose or on genitals." to replace this statement. b(4)
3. In the section "What is TRADENAME?" we inserted a pediatric statement consistent with the PI.
4. The section "[redacted] is typically reserved for labeled contraindications. Therefore, we deleted the [redacted] as there are no contraindications listed in the PI. b(4)
5. In the section, "What should I tell my doctor before using TRADENAME?" we added the information about pregnancy, breast-feeding and immune compromised patients because it is included in the section of PI "Use in Specific Populations". In

addition, the pediatric information in this section was moved to "What is TRADENAME?" section (as noted above).

6. In the section, "How should I use TRADENAME?" we:
   - recommend inserting "thin" or "thick" to describe the word "layer" as appropriate
   - deleted the statement "[redacted]" We generally do not like to include specific dosing instructions because it may contradict with the Healthcare Provider's instructions. b(4)
7. The information in the section "[redacted] was deleted and moved to the section "How should I use TRADENAME?" b(4)
8. In the section, "What are the possible side effects of TRADENAME?" we:
   - added "pigmentation changes" because it is in PI and the PI/PPI should be consistent.
   - deleted the comment "[redacted]" from PPI because it is not patient friendly. b(4)
   - inserted and modified the statement "Tell your doctor..." with standard wording to be consistent with patient information.
   - inserted "Call your doctor for medical advice about side effects. You may reports side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch." Although this statement is not required for voluntary PPIs like TRADENAME, we recommend adding it to all patient labeling for consistency.
9. In the section, "How should I store TRADENAME?" we deleted [redacted] is more appropriate. b(4) This information must be added to the PI so that it can be added to the PPI. The PI/PPI must be consistent.
10. The last section of PPI should include the following information RX only, Issue Month Year and COMPANY Name and Address.

Please let us know if you have any questions.

7 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

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7/10/2009 01:53:35 PM
LABELING REVIEWER

Jodi Duckhorn
7/10/2009 02:34:18 PM
DRUG SAFETY OFFICE REVIEWER

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/s/

NICKEISHA S BURFORD
09/15/2009