CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-228

OTHER REVIEW(S)

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

Memorandum

*****Pre-Decisional Agency Information *****

Date: August 14, 2009

To: Raphael Rodriguez
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products

From: Beth Carr, Pharm.D., Regulatory Review Officer
Lynn Panholzer, Pharm.D., Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications (DDMAC)

Subject: Bepreve ™ (bepotastine besilate ophthalmic solution) 1.5%
NDA: 22-288

DDMAC has reviewed the proposed product labeling for Bepreve ™ (bepotastine besilate ophthalmic solution) 1.5% (Bepreve) submitted by Wiley Chambers via email on August 14, 2009 (attached); and we offer the following comments. Please feel free to contact me at (301) 796-3674 with any questions or clarifications.

Package Insert

HIGHLIGHTS OF PRESCRIBING INFORMATION

WARNINGS AND PRECAUTIONS

- *"Remove contact lenses prior to instillation of Bepreve."*

For clarification purposes, we recommend adding the sentence, "Lenses may be reinserted after 10 minutes following administration of Bepreve," to the above Warning and Precaution.

FULL PRESCRIBING INFORMATION

6 ADVERSE REACTIONS

In accordance with the January 2006 Guidance for Industry: Adverse Reactions Section of the Label for Human Prescription Drugs and Biologics – Content and Format, please include the following:

- Please include an adequate description of the data sources for the adverse event data, as outlined in the guidance. For example, please include information on whether the trials were double blinded, randomized, and placebo controlled trials, if available. Also, please include the dosage, frequency, and duration of therapy that patients received.

- Identify adverse reactions, if any, that resulted in a significant rate of discontinuation or other clinical intervention (e.g., dosage adjustment, need for other therapy to treat an adverse reaction) in clinical trials.

14 CLINICAL STUDIES

The description of the clinical studies is vague and may be used by the sponsor to promote in a misleading manner. We suggest rewriting this section with the following information: number of patients studied in each arm of the trial, age ranges of the patients, major study endpoints, descriptions of the measurement tools used to evaluate the outcomes (the measurable signs of ocular itching), actual results (tabular format), and any appropriate accompanying statistics.

We recommend that specific efficacy data be included to qualify the superiority claims made in the label. Broad claims about the superiority of the drug versus vehicle without the context of the actual data may be used to misleadingly overstate the efficacy of the drug in promotional materials.

- *"Bepreve (bepotastine besilate ophthalmic solution) 1.5% was more effective than its vehicle for relieving ocular itching induced by an ocular allergen challenge, both at CAC 15 minutes post-dosing and a CAC 8 hours post dosing of Bepreve."*

This claim is very vague and may be used promotionally to overstate the efficacy of Bepreve. Specifically, it does not identify the specific endpoint(s) that were measured. We recommend that the claim be revised to specify the measure of relief from ocular itching to which the claim refers.

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

/s/

BETH M CARR
08/27/2009

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 28, 2009
To:	Wiley Chambers, M.D., Acting Director Division of Anti-Infective & Ophthalmology Products
Through:	Laura Pincock, Pharm.D., Acting Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Raichell S. Brown, Pharm.D., J.D., Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Label and Labeling Review
Drug Name(s):	Bepreve (Bepotastine Besilate Ophthalmic Solution) 1.5%
Application Type/Number:	NDA # 22-288
Applicant/sponsor:	ISTA Pharmaceuticals
OSE RCM #:	2008-1998

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