CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-278

OTHER REVIEW(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Internal Consult

Pre-decisional Agency Information

To: Mike Puglisi
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Division of Anti-Infective and Ophthalmology Products (DAIOP)

From: Lynn Panholzer, PharmD
Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications (DDMAC)

Date: March 31, 2008

Re: NDA 22-278, MembraneBlue™ (0.15% trypan blue ophthalmic solution)
Labeling Review

Thank you for forwarding this consult request, dated November 8, 2007, to DDMAC. We have reviewed the draft package insert, box and peel pouch label, syringe label, and patient record label dated January 30, 2008 (obtained from the Electronic Document Room) and have the following comments.

Package Insert

- The close proximity of the "DORC" logo to the trade and established names at the beginning of each page of the package insert confuses the communication of these names. We recommend that the logo be moved, such as to the end of the package insert.

- **Indications and Usage**
  "MembraneBlue is indicated for use as an aid in ophthalmic surgery by staining the epiretinal membranes during ophthalmic surgical vitrectomy procedures, **facilitating removal of the tissue** ——————————." (emphasis added; Full Prescribing Information, and similar presentation in Highlights) b(4)

  The bolded phrase above would allow the drug to be promoted as facilitating removal of tissue and as —————————— Has the drug been shown by substantial evidence to facilitate removal of tissue? To —————————— We recommend that any statements not supported by substantial evidence be deleted from the indication. b(4)

- **Warnings and Precautions**

  We note that the Highlights section of the draft label says to remove excess MembraneBlue from the vitreous cavity, whereas the Full Prescribing Information says to remove it from the posterior chamber of the eye. Are "vitreous cavity" and "_____" synonymous? We recommend that the sections be revised to be consistent with each other. b(4)

- **Description**
  "MembraneBlue selectively stains epiretinal membranes during ophthalmic surgical vitrectomy procedures."

  This statement suggests that the staining effects of MembraneBlue are very specific to epiretinal membranes, and would allow the drug to be promoted as being selective for these membranes. This implication is echoed in the indicated use of the product. However, the Clinical Pharmacology section of the draft label is inconsistent with this description, stating that "MembraneBlue selectively stains membranes in the human eye during posterior surgery, such as epiretinal membranes (ERM) and Internal Limiting Membranes (ILM)." This seems to indicate that the staining is not just specific to epiretinal membranes and that the drug stains other membranes in the human eye. How selective is the drug for epiretinal membranes and what are the implications of selectivity (or lack thereof) for the safety and efficacy of the drug? We recommend that the statements in these sections of the label be revised if needed for accuracy and consistency.

  Also, the Description and Clinical Pharmacology sections state that the drug is used during ophthalmic surgical vitrectomy procedures or during posterior surgery, respectively. Is it appropriate to describe the drug's use in surgical procedures in these sections of the label?

- **Clinical Pharmacology**
  _____

  This statement is potentially problematic in the Clinical Pharmacology section of the label, which generally addresses issues such as the absorption, distribution, metabolism, and excretion of a drug. It claims that _____ but is not clear as to how this happens, and may suggest that the body does this naturally. However, the Precautions, General and Dosage and Administration sections of the draft label suggest that this is done by the person administering the drug. Furthermore, this statement in the Clinical Pharmacology section of the label may imply that no dye is absorbed from the eye into the body. This is important given the carcinogenicity and teratogenicity seen in animals. Claiming or implying in promotional materials that no drug is absorbed could be used to minimize the risks of the drug. Is there adequate evidence to support that no dye is absorbed into the body? If not, we recommend that this claim be removed from the clinical pharmacology section. b(4)

Box and Peel Pouch Label, Syringe Label, and Patient Record Label

- The trade name and established name for the product are indistinguishable from each other on the labels because they are run together and lack any distinguishing characteristics, like brackets around the established name. Additionally, the logo for the manufacturer (DORC) is placed above and in very close proximity to the trade name, making it look as though it is part of the trade name. We recommend that the manufacturer's logo be moved and that the identities of the trade name and established names be made clear.

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/s/

Lynn Panholzer
3/31/2008 04:18:10 PM
DDMAC REVIEWER