CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-278

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA	22-278
Submission Date	October 1, 2007
Brand Name	MembraneBlue
Generic Name	Trypan blue
Primary Reviewer	Sarah Robertson, Pharm.D.
Team Leader	Charles R. Bonapace, Pharm.D.
OCP Division	DCP4
OND Division	DAIOP
Applicant	Dutch Ophthalmic Research Center (DORC) International b.v.
Submission Type; Code	Original NDA
Formulation; Strength	0.15% ophthalmic solution
Indication(s)	Selective staining of epiretinal membranes during ophthalmic surgical vitrectomy procedures.

EXECUTIVE SUMMARY

Trypan blue is an acid di-azo group dye used to selectively stain dead tissues or cells. NDA 21-670 for VisionBlue® (0.06% trypan blue ophthalmic solution) was submitted by Dutch Ophthalmic Research Center (DORC) and approved in December 2004 for staining the anterior capsule of the lens as an aid in ophthalmic surgery. The Sponsor submitted the current NDA for MembraneBlue (0.15% trypan blue ophthalmic solution) for staining the epiretinal membranes during ophthalmic surgical vitrectomy procedures, to facilitate removal of the tissue [redacted] b(4)
[redacted] MembraneBlue solution is comprised of trypan blue in [redacted] the same as VisionBlue®.

MembraneBlue is packaged in a volume of 0.5 mL in a 2.25 mL single-use syringe for application to the retinal membrane by blunt cannula. The actual dosage of MembraneBlue is determined by the ophthalmic surgeon, but is in the range of 0.3 to 0.5 mL. Trypan blue is not absorbed by viable cells, but traverses the membrane of dead cells. Excess dye is washed out of the eye by irrigation, while the stained membranes are removed from the eye, leaving only a minimal amount of trypan blue in the eye following surgery.

No clinical PK studies evaluating the systemic absorption of trypan blue following administration of MembraneBlue have been conducted. A waiver of the in vivo bioavailability requirement is granted, based on the expected negligible systemic exposure of trypan blue following use of MembraneBlue (0.15% trypan blue ophthalmic solution) during ophthalmic surgical vitrectomy procedures.

RECOMMENDATION

The Clinical Pharmacology and Biopharmaceutics information provided by the Applicant is acceptable. A waiver of the in vivo bioavailability requirement is granted, based on the expected negligible exposure of trypan blue following the use of MembraneBlue (0.15% trypan blue ophthalmic solution) during ophthalmic surgical vitrectomy procedures.
Recommended changes to the proposed label should be forwarded to the Sponsor.

PHASE IV COMMITMENTS

No Phase IV commitments are recommended

SPONSOR'S PROPOSED LABEL (v. 1/17/08) WITH ANNOTATED CHANGES

5 Page(s) Withheld

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

√ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Sarah M. Robertson
3/12/2008 01:05:09 PM
BIOPHARMACEUTICS

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3/12/2008 01:58:56 PM
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