OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA:	203-510
Submission Date(s):	September 21, 2012
PUDFA:	March 21, 2013
Drug	Phenylephrine hydrochloride
Product/Formulation; Strength(s)	Phenylephrine hydrochloride ophthalmic solution 2.5% and 10%
Primary Reviewer	Yongheng Zhang, Ph.D.
Team Leader	Philip Colangelo, Pharm D, Ph D
OCP Division	DCP4
OND Division	DTOP/OAP
Applicant	Paragon Bioteck Inc.
Proposed indication	To dilate the pupil (b) (4)
Dose and Administration	One drop should be instilled at 3-5 minute intervals up to a maximum of 3 drops per eye; If necessary, this dose may be repeated (b) (4)
Submission Type	505(b)(2) ; Priority

BACKGROUND

Phenylephrine is an alpha-adrenergic receptor sympathetic agonist that has been used for more than 70 years to dilate the pupil in ocular diagnostic, therapeutic and surgical procedures. Phenylephrine hydrochloride ophthalmic solutions, 2.5% and 10%, are currently being marketed and supplied in the US for use as a mydriatic. However, these products are outside of the approved OTC monograph (i.e., between 0.08% and 0.2%) and have never been cleared by a FDA approval process. To address this unapproved drug product issue, the sponsor submitted this NDA as a 505(b)(2) application on 10/19/2011. The Refusal to File (RTF) letter was issued on 12/16/2011, citing CMC deficiencies. The sponsor resubmitted the NDA on 12/21/2012 and the application is now under the priority review.

Due to the wealth of scientific literature and extensive clinical use the sponsor considers that the safety and efficacy of phenylephrine hydrochloride ophthalmic solution, 2.5% and 10%, have been well established. Therefore, the sponsor believes it is unnecessary to conduct any additional clinical studies to support this literature-based NDA.

The sponsor did not conduct any clinical pharmacology related studies and did not request the waiver of evidence of in vivo bioavailability or bioequivalence. In accordance with the 21 CFR §320.22(e) – "*FDA, for good cause, may waive a requirement for the submission of evidence of in vivo bioavailability or bioequivalence if waiver is compatible with the protection of the public health*", the Clinical Pharmacology review team will grant the waiver of evidence of in vivo bioavailability or bioequivalence to this NDA, considering the extensive clinical experience of the product.

RECOMMENDATIONS

The office of Clinical Pharmacology, Division of Clinical Pharmacology IV has reviewed the submission, and it is acceptable from a clinical pharmacology perspective. Product labeling should be revised as indicated in **Appendix 1**.

Appendix 1. Proposed Labeling with Revisions

Sponsor's draft label version date: 11/2011

The following proposed labeling has been marked with revisions made by the Clinical Pharmacology Reviewer.

(underline =Clin Pharm reviewer's addition; ~~strikethrough~~ = Clin Pharm reviewer's deletion)

5 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

YONGHENG ZHANG
12/12/2012

PHILIP M COLANGELO
12/12/2012