EXECUTIVE SUMMARY

Application Type	NDA 19-845 NDA 20-963
Submission Numbers	S-020; S-010
Submission Code	SE5
Letter Date	12/15/06
Stamp Date	12/16/06
PDUFA Goal Date	6/18/07
Reviewer Name	Sonal D. Wadhwa, MD
Review Completion Date	5/4/07
Established Names	betaxolol hydrochloride ophthalmic suspension; timolol maleate ophthalmic gel forming solution
Trade Names	Betoptic S 0.25%; Timolol GFS 0.25% and 0.5%
Therapeutic Classes	beta-blockers
Applicant	Alcon Research, Ltd.
Priority Designation	P
Formulations	Ophthalmic suspension/solution
Dosing Regimen	Betoptic S one drop twice a day Timolol GFS one drop once a day

Indication	Treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma
Intended Population	Pediatric patients less than 6 y.o.

1 EXECUTIVE SUMMARY

1.1 Recommendation on Regulatory Action

NDA 19-845 S-020 and NDA 20-963 S-010 are recommended for approval. The clinical study contained in these supplements supports the use of betaxolol hydrochloride ophthalmic suspension 0.25% and timolol maleate ophthalmic gel forming solution 0.25% and 0.5% in the pediatric population. The benefits of using these drug products outweigh the risks in the treatment of elevated intraocular pressure in pediatric patients.

1.2 Recommendation on Post-marketing Actions

Not applicable-There are no recommendations for post-marketing actions.

1.2.1 Risk Management Activity

Not applicable-There are no recommendations for risk management activity.

1.2.2 Required Phase 4 Commitments

Not applicable-There are no recommendations for Phase 4 commitments.

1.2.3 Other Phase 4 Requests

Not applicable-There are no other recommendations for Phase 4 commitments.

1.3 Summary of Clinical Findings

1.3.1 Brief Overview of Clinical Program

Clinical study C-01-01 was conducted to obtain needed pediatric information on Betoptic S (betaxolol hydrochloride ophthalmic suspension 0.25%) and Timolol GFS (timolol maleate ophthalmic gel forming solution 0.25% and 0.5%) for the treatment of elevated intraocular pressure in children less than 6 years of age. This study was conducted in response to the Agency's Written Request of October 15, 1999 (original) and amendments on May 4, 2001, July 2, 2002, March 5, 2004, and May 7, 2004 for Betoptic S and issued October 15, 1999 (original) and amendments on May 14, 2001, July 3, 2002, March 12, 2004, and May 7, 2004 for Timolol GFS.

Study C-01-01 was designed to describe the safety and clinical response of Betoptic S 0.25% and Timolol GFS 0.25% and 0.5% in patients 0-6 years of age with a clinical diagnosis of glaucoma or ocular hypertension. The clinical safety and efficacy of Betoptic S and Timolol has been

established in adult and elderly patients with glaucoma or ocular hypertension in NDA 19-845 [Betoptic S (betaxolol hydrochloride ophthalmic suspension 0.25%)] and NDA 20-963 [Timolol GFS (timolol maleate ophthalmic gel forming solution 0.25% and 0.5%)]. The submission is based on data from a total of 107 patients: 35 exposed to Betoptic S 0.25%, 36 exposed to Timolol GFS 0.25%, and 36 exposed to Timolol GFS 0.5%.

1.3.2 Efficacy

The purpose of the trial contained in this pediatric supplement was to demonstrate the safety of Betoptic S and Timolol GFS when used in pediatric patients under 6 years old. The support for efficacy for both of these products was extrapolated from the adult trials. The limited clinical response data contained in the supplement showed the mean IOP reductions (in the ITT analysis) in patients treated with Betoptic S ranged from 1.7 - 2.3 mmHg, patients treated with Timolol GFS 0.25% ranged from 0.9 - 2.9 mmHg, and among patients treated with Timolol GFS 0.5% ranged from 2.4 - 3.7 mmHg.

1.3.3 Safety

- The study in these NDA supplements is adequate to establish the safety of the use of betaxolol hydrochloride ophthalmic suspension 0.25% and timolol maleate ophthalmic gel forming solution 0.25% and 0.5% in the pediatric population.

- The type of adverse events seen in pediatric patients treated with betaxolol and timolol are consistent with those seen in the adult population.

- There were no clinically relevant differences in the adverse event profile between the age group strata studied.

1.3.4 Dosing Regimen and Administration

The dosage and administration in the pediatric population is identical to that which has been established in the adult population. The applicant has not submitted data to support any change in the already established dose and frequency for either of these two products.

1.3.5 Drug-Drug Interactions

Drug/drug interaction analyses were not conducted for this trial.

1.3.6 Special Populations

There are no important considerations required for administering this product in special populations. The pediatric subpopulations analyzed were 1 week to <1 year, 1 year to <2 years, 2 years to <4 years, and 4 years to < 6 years of age. Adverse events and the safety profile for Betoptic S and Timolol GFS were consistent between these age groups.

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/s/

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