CLINICAL PHARMACOLOGY REVIEW

NDA: 21-493	Submission Date(s): 3/30/2009
Drug	Gatifloxacin ophthalmic solution 0.3%
Trade Name	ZYMAR
OCP Reviewers	Ryan P. Owen, Ph.D.
OCP Team Leader	Charles Bonapace, Pharm.D.
OCP Division	DCP4
OND division	DAIOP (520)
Sponsor	Allergan
Relevant IND(s)	59,408
Submission Type; Code	(b) (4) -009)
Formulation; Strength(s)	3 mg/mL Gatifloxacin (0.3%)
Indication	Bacterial Conjunctivitis
Dosage and Administration	(b) (4) : Days 1 through 6: 1 drop three times daily in the affected eye

Background

ZYMAR (Gatifloxacin ophthalmic solution, 0.3%) was originally approved on 3/28/03. The labeled dosing regimen of 0.3% gatifloxacin ophthalmic solution for patients greater than 1 year of age is as follows:

Days 1 and 2: Instill one drop every two hours in the affected eye(s) while awake, up to 8 times daily.
Days 3 through 7: Instill one drop up to four times daily in the affected eye(s) while awake.

In a Phase 1 pharmacokinetic study in six healthy adult volunteers, gatifloxacin ophthalmic solution at 0.3% or 0.5% was administered in an escalating dosing regimen starting with a single 2 drop dose, then 2 drops 4 times daily for 7 days, and finally 2 drops 8 times daily for 3 days. The serum gatifloxacin concentrations were below the lower limit of quantification (5 ng/mL) in all subjects at all time points.

(b) (4)

In order to comply with Section 505A of the Federal Food, Drug, and Cosmetic Act (and later the Best Pharmaceuticals for Children Act), the Agency asked that the Sponsor conduct a study with gatifloxacin in pediatric subjects aged 0 to 1 month. The current submission includes one Phase 4 study (Study 198782-003) that is intended to satisfy the Agency's request. Study 198782-003 was a 7-day, Phase 4, randomized, double-masked, parallel-group, multicenter study conducted to evaluate the safety and efficacy of topical gatifloxacin ophthalmic solution 0.3% compared

with topical moxifloxacin ophthalmic solution 0.5% for the treatment of presumed bacterial conjunctivitis in subjects from birth to 31 days of age.

On 10/30/06, a Pre-pediatric exclusivity supplement meeting was conducted between the Sponsor and the Agency. At that meeting, it was agreed that the dosing regimen of 0.3% gatifloxacin ophthalmic solution used in the trial for neonates would be one drop in the affected eye(s) three times a day for seven days.

If we assume a drop size to be 50 µL, then one drop of 0.5% gatifloxacin ophthalmic solution would be equivalent to 0.25 mg gatifloxacin, and one drop of 0.3% gatifloxacin ophthalmic solution would be equivalent to 0.15 mg gatifloxacin. Therefore, a regimen of 2 drops of 0.5% gatifloxacin given 8 times a day (the adult Phase 1 dosing regimen) would yield a net dose of 4 mg of gatifloxacin per day whereas a regimen of 1 drop of 0.3% of gatifloxacin given 3 times a day (the neonatal dosing regimen used in Study 198782-003) would yield a net dose of 0.45 mg gatifloxacin. The dosing regimen used in adults, which produced gatifloxacin concentrations below the limit of quantification, would be more than 8 times the neonatal dose. Thus, no pharmacokinetic blood samples were taken from neonates in Study 198782-003. (b) (4)

Labeling Recommendations

(b) (4)

Recommendation

(b) (4)

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Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 21493	SUPPL 9	ALLERGAN INC	ZYMAR (GATIFLOXACIN) OPHTHALMIC SOLUTION

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/s/

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07/29/2009

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07/29/2009