CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22548Orig1s000

SUMMARY REVIEW

Division Director Review of NDA 22-548

Date	May 17, 2010
From	Wiley A. Chambers, M.D.
NDA#	22-548
Applicant	Allergan, Inc.
Date of Submission	July 30, 2009
PDUFA Goal Date	May 30, 2010
Proprietary Name / Established (USAN) names	Zymaxid (gatifloxacin ophthalmic solution) 0.5%
Dosage forms / Strength	ophthalmic solution
Proposed Indication(s)	Treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms: *Haemophilus influenzae, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mitis* group*, *Streptococcus oralis, Streptococcus pneumoniae* *Efficacy for this organism was studied in fewer than 10 infections.
Action:	Approval

1. Introduction

Gatifloxacin is an 8-methoxy fluoroquinolone that inhibits DNA gyrase and topoisomerase IV. Allergan's NDA 21-493 for Zymar (gatifloxacin ophthalmic solution) 0.3% was approved in March 2003 for the indication of bacterial conjunctivitis in adults and pediatric patients above the age of 1 year. In this NDA, a higher concentration (0.5%) of gatifloxacin ophthalmic solution has been formulated. The excipients are the same in both formulations. Differences between the formulations are an increased drug substance concentration, a small reduction in pH to insure adequate solubility of the drug substance and a slightly lower sodium chloride concentration for tonicity.

2. Background

Ophthalmic products currently approved for the treatment of bacterial conjunctivitis include azithromycin ophthalmic solution, ciprofloxacin ophthalmic solution and ointment, erythromycin ophthalmic ointment, gatifloxacin ophthalmic solution, gentamicin ophthalmic solution and ointment, levofloxacin ophthalmic solution, moxifloxacin ophthalmic solution, norfloxacin ophthalmic solution, ofloxacin ophthalmic solution, and tobramycin ophthalmic solution and ointment. Zymaxid (gatifloxacin ophthalmic solution) 0.5% is not marketed in any other country.

3. CMC

The drug substance, gatifloxacin (also referred to as AGN-198782), is a white to pale yellow (b) (4) Gatifloxacin has two pKa values of (b) (4) The chemical name is (±)-1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid sesquihydrate. The molecular weight of gatifloxacin sesquihydrate is 402.4 g/mol. Gatifloxacin is the same drug substance as is currently used in Zymar (gatifloxacin ophthalmic solution) 0.3% in NDA 21-493. The drug substance is manufactured at Kyorin Pharmaceutical Co. Ltd., Noshiro Plant, Akita, Japan.

The drug product, gatifloxacin ophthalmic solution 0.5% is a clear, pale yellow, sterile, preserved aqueous solution containing gatifloxacin (0.5% w/v (b) (4) The inactive ingredients include sodium chloride, edetate disodium, benzalkonium chloride and purified water. The pH of the bulk solution is adjusted using either (b) (4) sodium hydroxide or (b) (4) hydrochloric acid resulting in a final product release pH of 5.2 to 5.6. The osmolality of the drug product is at 265 - 315 mOsm/kg at release. All excipients are tested to USP/NF. Except for sodium hydroxide and hydrochloric acid, all excipients are tested for endotoxin.

Gatifloxacin ophthalmic solution 0.5% will be filled in a 5-mL multiple-dose bottle with a tip manufactured of low density polyethylene (LDPE, (b) (4) and a cap manufactured of high impact polystyrene (HIPS, (b) (4) The finished product is labeled with a pressure- sensitive label. The tamper evident security feature for the primary packaging container is a (b) (4) shrink seal surrounding the cap. The planned market configurations include a 1 mL fill in a 5-mL bottle (physician sample), and a 2.5 mL fill in a 5-mL bottle. The secondary packaging consists of a unit cardboard carton and an insert.

Stability data supports 24 months stability for a 2.5 mL (b) (4) and 12 months for a 1 mL fill. All sites were found "Acceptable".

DRUG PRODUCT COMPOSITION

Ingredient	Grade	Function	Concentration
Gatifloxacin Sesquihydrate (% w/v)	N/A	Active Ingredient	0.5
Benzalkonium Chloride (% w/v)	NF/Ph Eur	(b) (4)	
Edetate Disodium (% w/v)	USP/Ph Eur		
Sodium Chloride (% w/v)	USP/Ph Eur		
Hydrochloric Acid (b) (4) or Sodium Hydroxide (b) (4)	NF/Ph Eur		
Purified Water	USP/Ph Eur	(b) (4)	(b) (4)

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4. Nonclinical Pharmacology/Toxicology

The applicant, Allergan, Inc. (Irvine, CA), has requested that the Division cross-reference the nonclinical data from approved NDA 21-493 for Zymar (gatifloxacin ophthalmic solution) 0.3% to the current NDA. The Zymar NDA contains data from nonclinical studies that support the higher concentration of gatifloxacin to be used in the new product. One month repeat dose ocular toxicity studies in the rabbit used gatifloxacin concentrations up to 1% and ocular toxicity studies up to 3 months duration in the dog used concentrations up to 0.5%. There were no adverse findings in the rabbits and the only finding in the dogs was mild, reversible conjunctival hyperemia that was not considered toxicologically significant by the reviewer, Dr. Zhou Chen. The only nonclinical study that the sponsor has submitted to the current NDA is a study conducted in-house entitled "Comparison of Ocular Pharmacokinetics of Gatifloxacin in Dutch-Belted Rabbits Following 0.3% QID and 0.5% BID Dosing," Study No. PK-08-P029.

5. Clinical Pharmacology/Biopharmaceutics

This NDA does not contain any new clinical pharmacology studies. Reference is made to the clinical pharmacology program conducted under NDA 21-493. In support of the increased formulation strength of gatifloxacin, the applicant has submitted two identical Phase 3 studies which examined the safety and efficacy of the new formulation. Under the previous clinical pharmacology program, systemic concentrations were undetectable (< 5 ng/mL) following a total topical daily dose of 2.56 mg/day for three days.

A waiver of the requirement for submission of evidence of in vivo bioavailability for the drug product gatifloxacin ophthalmic solution 0.5% is granted under CFR 320.22 (e). Pharmacokinetic information from NDA 21-493 and from the previously marketed oral tablet of gatifloxacin supports this recommendation.

6. Sterility Assurance

The drug product is an aqueous formulation containing benzalkonium chloride (b) (4) (b) (4). The drug product is formulated, (b) (4) Component plastic 5ml bottles and dropper tips are sterilized (b) (4) Caps (b) (4) (b) (4) The drug product (b) (4) (b) (4) to fill volumes of either 1 mL, 2.5 mL or (b) (4).

Endotoxin Test Method Validation Results

Linear Regression	Acceptance Criteria	Result
Correlation Coefficient (r)	(b) (4)	(b) (4)
Slope		
Intercept		
Control Standard Endotoxin (CSE) Standard		

[1] (b) (4) The 2.5 mL in 5 mL bottle commercial configuration contains adequate drug product for a course of therapy.

Curve		
% PPC Recovery	**Acceptance Criteria**	**Result**
Lot 56874	(b) (4)	(b) (4)
Lot 56875		
Lot 56876		
Endotoxin Test Results	**Acceptance Criteria**	
Bulk Lot 56874		
Bulk Lot 56875	(b) (4)	
Bulk Lot 56876		(4)

Although the bacterial endotoxin acceptance criterion of (b) (4) is greater than the Division's currently recommended level of (b) (4) the applicant has demonstrated sufficient control of the drug product manufacturing process to minimize endotoxin contamination. The raw materials and the container closure are controlled for endotoxins by application of individual internal limits. Except for the sodium hydroxide and hydrochloric acid used for pH adjustments during compounding, all formulation excipients are tested for bacterial endotoxins. The USP purified water used in formulation is also tested, and meets, the acceptance criterion for bacterial endotoxins in water for injection. The worst case maximum weighted contribution for endotoxin based on raw material and component internal limits is (b) (4). The applicant stated that, as more history and manufacturing experience with the drug product and raw materials are gained they intend to further evaluate the endotoxin levels in the raw materials and their contribution to the drug product.

7. Clinical/Statistical - Efficacy

The Phase 3 clinical development program included two identically designed studies (198782-004 and 198782-005). The two studies only differ in their definition of the window around the day 6 efficacy endpoint.

The primary statistical objective of the studies was to demonstrate that gatifloxacin ophthalmic solution 0.5% is more effective than vehicle in the treatment of bacterial conjunctivitis.
The primary efficacy variable was clinical success, defined as achievement of a score of zero for both conjunctival hyperemia and conjunctival discharge in the study eye.

The primary analysis for efficacy was the day 6 visit analysis for Study 198782-004, which included all data collected for the day 6 visit. This analysis method defined a visit window in the statistical analysis plan. An "Up-to-Day 6" analyses, including all data collected up to and including day 6 but excluding data collected after day 6 was conducted as sensitivity analyses.

Prior to unblinding the data for Study 198782-005, the Applicant revised the primary efficacy analysis for Study 005 to correspond with the more successful Up-to-Day 6 visit analysis in Study 004.The Up-to-Day 6 analysis was the primary efficacy analysis for Study 198782-005.[2]

[2] On January 14, 2009, Allergan notified the FDA of significant cGCP violations at a study site in India in Study 198782-005. The investigator at this site was Shanta Motwane, MD. At Site 13020 was found to have significant data integrity issues. This site enrolled 72 patients, of whom 31 were included in the mITT population. At Site 13020, the clinical success rates in both groups at the day 6 time point in the mITT population using the up to day

This analysis included all data collected up to and including day 6, but excluded any day-6 visit data that was collected after the day 6 time point. The day 6 visit analysis includes all day 6 visit data in the pre-defined window. The day 6 visit analysis is considered a secondary.

As planned in the protocols, there were 4 analysis populations. The intent to treat (ITT) population included all randomized patients. The primary population for efficacy analysis was the modified intent to treat (mITT) population, which consisted of randomized patients who had a positive bacterial culture from the conjunctiva at baseline. The per protocol (PP) population included all mITT patients without major protocol violations who had at least 1 follow-up visit. The ITT and PP populations were secondary populations for efficacy analysis.

Clinical Cure by Organisms – Studies 04 and 05 Combined

Organism	Gatifloxacin		Vehicle	
	Clinical Success n/N (%)	Microbiological Cure n/N (%)	Clinical Success n/N (%)	Microbiological Cure n/N (%)
Haemophilus influenzae	38/43 (88%)	42/43 (98%)	19/45 (43%)	26/45 (58%)
(b) (4)				
Pseudomonas aeruginosa	2/7 (29%)	6/7 (86%)	4/10 (40%)	9/10 (90%)
Staphylococcus aureus	26/52 (50%)	45/52 (87%)	13/37 (35%)	22/37 (60%)
Staphylococcus epidermidis	21/35 (60%)	31/35 (89%)	14/27 (52%)	22/27 (82%)
(b) (4)				
Staphylococcus hominis	3/7 (43%)	7/7 (100%)	7/15 (47%)	15/15 (100%)
Staphylococcus warneri	5/11 (46%)	10/11 (91%)	1/2 (50%)	2/2 (100%)
(b) (4)				
Streptococcus pneumoniae	21/34 (62%)	30/34 (88%)	22/38 (58%)	24/38 (63%)
Streptococcus mitis group	8/9 (89%)	9/9 (100%)	3/4 (75%)	3/4 (75%)
Streptococcus oralis	7/12 (59%)	10/12 (83%)	1/6 (17%)	5/6 (83%)

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6 analysis method (84.6% [11/13] in the gatifloxacin group and 83.3% [15/18] in the vehicle group) were somewhat higher than at most other sites with comparable enrollment.

During monitoring of the site, significant cGCP violations were observed. These violations involved source documentation anomalies which in the sponsor's judgment did not adequately support the data in the Case Report Forms. In contrast to other study sites, this site reported no adverse events, concomitant medications, and/or medical/ophthalmic history for any randomized patients. As such Allergan was concerned the site was not sufficiently diligent in querying the patients for safety and history information and was concerned about the data quality at the site.

All efficacy analyses are presented with data from Site 13020 excluded.

Clinical Success in the Study Eye by Population and Analysis Method 198782-004 [3]

	Day 6 Visit Analysis (Primary Analysis Method)			Up to Day 6 Analysis		
Population (Analysis) Time point	Gatifloxacin	Vehicle	P Value [a]	Gatifloxacin	Vehicle	P Value [a]
mITT (LOCF)						
Day 4 n/N (%)	56/167 (33.5)	33/158 (20.9)	0.011	56/167 (33.5)	33/158 (20.9%)	0.011
Day 6 n/N (%)	**125/167 (74.9)**	**103/158 (65.2)**	**0.057**	107/167 (64.1)	79/158 (50.0)	0.010
PP						
Day 4 n/N (%)	48/137 (35.0)	32/135 (23.7)	0.040	48/137 (35.0)	32/135 (23.7)	0.040
Day 6 n/N (%)	107/138 (77.5)	89/132 (67.4)	0.063	80/102 (78.4)	67/94 (71.3)	0.248
ITT (LOCF)						
Day 4 n/N (%)	105/287 (36.6)	88/291 (30.2)	0.106	105/287 (36.6)	88/291 (30.2)	0.106
Day 6 n/N (%)	220/287 (76.7)	199/291 (68.4)	0.026	190/287 (66.2)	160/291 (55.0)	0.006
mITT (As treated LOCF)						
Day 4 n/N (%)	55/168 (32.7)	34/157 (21.7)	0.025	55/168 (32.7)	34/157 (21.7)	0.025
Day 6 n/N (%)	126/168 (75.0)	102/157 (65.0)	0.048	106/168 (63.1)	80/157 (51.0)	0.027
ITT (As treated LOCF)						
Day 4 n/N (%)	104/288 (36.1)	89/289 (30.8)	0.176	104/288 (36.1)	89/289 (30.8)	0.176
Day 6 n/N (%)	221/288 (76.7)	198/289 (68.5)	0.027	189/288 (65.6)	161/289 (55.7)	0.015

ITT = intent to treat; LOCF = last observation carried forward; mITT = modified intent to treat; PP = per protocol
Bolding shows primary comparison.
a: P value is from Pearson's chi-square test, unless ≥ 25% of the cells had expected counts < 5, then Fisher's exact test was used.
Source: Table 14.2-1.1, 14.2-1.2, 14.2-1.3, 14.5-10.1, 14.5-10.2, 14.5-10.3, 14.5-17.1, 14.5-17.2, 14.5-20.1, 14.5-20.2

[3] Section 11.1.1.1, CSR 198782-004

Clinical Success in the Study Eye by Population and Analysis Method 198782-005 [4]

	Day 6 Visit Analysis			Up to Day 6 Analysis (Primary Analysis Method)		
Population (Analysis) Time point	Gatifloxacin	Vehicle	P Value [a]	Gatifloxacin	Vehicle	P Value [a]
mITT (LOCF)						
Day 4 n/N (%)	23/166 (13.9%)	17/167 (10.2%)	0.302	23/166 (13.9%)	17/167 (10.2%)	0.302
Day 6 n/N (%)	99/166 (59.6%)	78/167 (46.7%)	0.018	**86/166 (51.8%)**	**69/167 (41.3%)**	**0.055**
PP						
Day 4 n/N (%)	23/155 (14.8%)	16/148 (10.8%)	0.295	23/155 (14.8%)	16/148 (10.8%)	0.295
Day 6 n/N (%)	93/156 (59.6%)	72/146 (49.3%)	0.072	76/138 (55.1%)	61/134 (45.5%)	0.115
ITT (LOCF)						
Day 4 n/N (%)	65/394 (16.5%)	58/393 (14.8%)	0.502	65/394 (16.5%)	58/393 (14.8%)	0.502
Day 6 n/N (%)	226/394 (57.4%)	199/393 (50.6%)	0.058	200/394 (50.8%)	184/393 (46.8%)	0.269
mITT (As treated LOCF)						
Day 4 n/N (%)	23/166 (13.9%)	17/167 (10.2%)	0.302	23/166 (13.9%)	17/167 (10.2%)	0.302
Day 6 n/N (%)	96/166 (59.6%)	78/167 (46.7%)	0.018	86/166 (51.8%)	69/167 (41.3%)	0.055
ITT (As treated LOCF)						
Day 4 n/N (%)	65/393 (16.5%)	58/392 (14.8%)	0.502	65/393 (16.5%)	58/392 (14.8%)	0.502
Day 6 n/N (%)	226/393 (57.5%)	199/392 (50.8%)	0.058	200/393 (50.9%)	184/392 (46.9%)	0.268

ITT = intent-to-treat; LOCF = last observation carried forward; mITT = modified intent-to-treat; PP = per protocol

Note: Bolding shows primary comparison.

a: P value is from Pearson's chi-square test, unless ≥25% of the cells had expected counts <5, then Fisher's exact test was used.

Sources: Tables 14.2-1.1, 14.2-1.2, 14.2-1.3, 14.5-1.2, 14.5-3.1, 14.5-3.2, 14.5-4.1, 14.5-4.2, 14.5-4.3, 14.5-5.1, 14.5-5.2

Analysis of Secondary Endpoints(s)

Microbiological Cure in the Study Eye mITT Population 198782-004

	Day 6 Visit Analysis (Primary Analysis Method)		
Visit / Time point	**Gatifloxacin**	**Vehicle**	**p value [a]**
Day 4 n/N (%)	145/167 (86.8)	81/158 (51.3)	< 0.001
Day 6 n/N (%)	149/167 (89.2)	97/158 (61.4)	< 0.001

198782-005

	Up to Day 6 Visit Analysis (Primary Analysis Method)		
Visit / Time point	**Gatifloxacin**	**Vehicle**	**p value [a]**
Day 4 n/N (%)	144/166 (88.0%)	123/167 (73.3%)	< 0.001
Day 6 n/N (%)	153/166 (92.2%)	134/167 (80.2%)	0.002

A patient was considered to have microbiological cure if all bacterial species present at Day 1 (baseline) were eradicated.

198782-004 and 198782-004 Efficacy Conclusions

The two clinical trials 198782-004 and 198782-005 show borderline statistical significance in their specified primary efficacy endpoints; the sensitivity analyses for each trial are unquestionably statistically significant. Zymaxid (gatifloxacin ophthalmic solution) 0.5% when dosed twice daily on days 2 to 5 in clinical trials appears less effective than Zymar (gatifloxacin ophthalmic solution) 0.3% dosed four times daily on days 2 to 5 in clinical trials. Although this reformulation of Zymar has a higher concentration of gatifloxacin at 0.5%, Allergan dosed the Zymaxid drug product less frequently after Day 1 (BID versus QID). There is adequate pharmacologic and pharmacokinetic information in the original Zymar NDA 21-493 to support the dosing of the Zymaxid product one drop two to four times daily in the affected eye(s) while awake on Days 2 through 7. The recommended dosing of Zymaxid (gatifloxacin ophthalmic solution) 0.5% will be: Patients 1 year of age or older: Instill one drop every two hours in the affected eye(s) while awake, up to 8 times on Day 1. Instill one drop two to four times daily in the affected eye(s) while awake on Days 2 through 7.

8. Safety

The safety database includes all randomized and treated patients, 717 patients treated with gatifloxacin 0.5% and 716 patients treated with vehicle. Gatifloxacin ophthalmic solution 0.5% is not marketed in any country. Zymar (gatifloxacin ophthalmic solution, 0.3% was approved in the U.S. in 2003. A review of the postmarketing reports does not raise concern that there is a new unknown safety risk associated with gatifloxacin since the spontaneous postmarketing reports for gatifloxacin were consistent with its known safety profile.

Adverse Events Occurring in ≥ 1% of Patients (Pooled Safety Population)[5]

Preferred Term [a]	Primary SOC of PT [a]	Gatifloxacin (N= 717)	Vehicle (N= 716)
Overall	---	83 (11.6%)	95 (13.3%)
Conjunctivitis bacterial	Infections and Infestations	19 (2.6%)	32 (4.5%)
Eye irritation	Eye disorders	15 (2.1%)	8 (1.1%)
Dysgeusia	Nervous system disorders	8 (1.1%)	1 (0.1%)*
Eye pain	Eye disorders	7 (1.0%)	9 (1.3%)
Conjunctivitis	Eye disorders	2 (0.3%)	9 (1.3%)**

a: MedDRA 10.0
* $p < 0.05$, Fisher's exact test
** $p < 0.05$, Pearson's chi-square test
Source: Module 2.7.4 Table 2.7.4.2-2

9. Advisory Committee Meeting

No Advisory Committee Meeting was necessary for Zymaxid (gatifloxacin ophthalmic solution) 0.5%.

10. Pediatrics

Zymaxid has been demonstrated in clinical trials to be safe and effective for the treatment of bacterial conjunctivitis in pediatric patients one year or older. The Agency considers patients below one month of age with bacterial conjunctivitis to be a different diagnostic condition (ophthalmia neonatorum).

Based on the review of the original NDA for Zymar (gatifloxacin ophthalmic solution, 0.3%), there is no evidence that the ophthalmic administration of gatifloxacin has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

11. Other Relevant Regulatory Issues

The Statistical Review and Evaluation raised no new issues for the studies.
Division of Scientific Investigations (DSI) audit was requested. The following sites were reviewed.

[5] NDA 22-548 Section 2.5.5.5.1 All Adverse Events

Name of CI, IRB, or Sponsor Location	Protocol #: and # of Subjects:	Inspection Date	Field Classification/Final Classification
Yasmin Rusi Bhagat, M.D. Head of Ophthalmology Department St. George's Hospital Fort, Mumbai , India	Protocol 198782-005 Site # 13008 84 Subjects	11/09/2009- 11/11/2009	NAI/VAI
Nita Shanbhag, M.D. Omkar Eye Care Center 302/303 Koteshwar Plaza Junc of Jawaharlal Nehru road and RHB road, Mulund (West) Mumbai – 400080, India	Protocol 198782-005 Site # 13014 90 Subjects	11/16/2009- 11/17/09	NAI/NAI
Daniel A. Long, MD Dr. Daniel A Long – A Professional Medical Corporation 120 Meadowcrest St. #330 Gretna, LA 70056	Protocol 198782-004 Site # 10008 50 Subjects	10/19/2009- 10/21/2009	OAI/OAI-Untitled

On January 14, 2009, Allergan notified the FDA of significant cGCP violations at a study site in India in Study 198782-005. The investigator at this site was Shanta Motwane, MD. At Site 13020 was found to have significant data integrity issues. This site enrolled 72 patients, of whom 31 were included in the mITT population. At Site 13020, the clinical success rates in both groups at the day 6 time point in the mITT population using the up to day 6 analysis method (84.6% [11/13] in the gatifloxacin group and 83.3% [15/18] in the vehicle group) were somewhat higher than at most other sites with comparable enrollment.

During monitoring of the site, significant cGCP violations were observed. These violations involved source documentation anomalies which in the sponsor's judgment did not adequately support the data in the Case Report Forms. In contrast to other study sites, this site reported no adverse events, concomitant medications, and/or medical/ophthalmic history for any randomized patients. As such Allergan was concerned the site was not sufficiently diligent in querying the patients for safety and history information and was concerned about the data quality at the site.

In general, the studies appear to have been conducted adequately and the data in support of the NDA appear reliable. The final classification of the inspection for Dr. Shanbhag is NAI. The final classification of the Clinical Investigator inspection of Dr. Bhagat is VAI. Although regulatory violations were noted at Dr Bhagat's site, it is unlikely that they significantly affect overall data reliability from the site. The data from Dr. Long's clinical site documented several regulatory violations due to the clinical investigator's failure to conduct the study according to the signed investigator statement and the investigational plan. However, the violations are unlikely to affect overall data reliability from the site. The classification of the Clinical

Investigator inspection of Dr. Long is OAI-Untitled. Review of the findings demonstrated that these findings did not result in adverse outcomes that would otherwise impact subject safety and/or efficacy. Dr. Long submitted a written response that provided adequate corrective actions for the violations noted during the inspection. The data in support of the application are considered reliable.

Allergan, Inc. has adequately disclosed financial arrangements with clinical investigators as recommended in the FDA guidance for industry on *Financial Disclosure by Clinical Investigators*. There is no evidence to suggest that the results of the study were impacted by any financial payments.

The results of the Proprietary Name Risk Assessment raised no issues related to the proposed name, Zymaxid.

12. Labeling

Labeling was submitted by Allergan, Inc. on 4/20/2010 and found to be acceptable. A copy of the labeling is included in the Cross-Discipline Team Leader Review.

13. Regulatory Action

NDA 22-548 is to be approved for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms: *Haemophilus influenzae, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mitis* group*, *Streptococcus oralis*, *Streptococcus pneumoniae.* *Efficacy for this organism was studied in fewer than 10 infections. There are no postmarketing agreements for this application.

Wiley A. Chambers, MD
Acting Director
Division of Anti-Infective and Ophthalmology Products

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22548	ORIG-1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%

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/s/

WILEY A CHAMBERS
05/17/2010