

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
203168Orig1s000

MEDICAL REVIEW(S)

CLINICAL REVIEW

Application Type	NDA
Application Number(s)	203168
Priority or Standard	Standard
Submit Date(s)	June 6, 2012
Received Date(s)	June 7, 2012
PDUFA Goal Date	April 7, 2013
Division / Office	OAP/DTOP
Reviewer Name(s)	William M. Boyd, M.D.
Review Completion Date	March 20, 2013
Established Name	bromfenac ophthalmic solution 0.07%
(Proposed) Trade Name	Prolensa
Therapeutic Class	nonsteroidal anti-inflammatory
Applicant	Bausch & Lomb, Inc.
Formulation(s)	bromfenac ophthalmic solution 0.07%
Dosing Regimen	one drop into the affected eye once daily
Indication(s)	treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery
Intended Population(s)	patients who have undergone cataract surgery

Template Version: March 6, 2009

Table of Contents

1	RECOMMENDATIONS/RISK BENEFIT ASSESSMENT	5
1.1	Recommendation on Regulatory Action	5
1.2	Risk Benefit Assessment	5
1.3	Recommendations for Postmarket Risk Evaluation and Mitigation Strategies ...	5
1.4	Recommendations for Postmarket Requirements and Commitments	5
2	INTRODUCTION AND REGULATORY BACKGROUND	5
2.1	Product Information	6
2.2	Tables of Currently Available Treatments for Proposed Indications	6
2.3	Availability of Proposed Active Ingredient in the United States	6
2.4	Important Safety Issues With Consideration to Related Drugs	6
2.5	Summary of Presubmission Regulatory Activity Related to Submission	6
2.6	Other Relevant Background Information	7
3	ETHICS AND GOOD CLINICAL PRACTICES.....	7
3.1	Submission Quality and Integrity	7
3.2	Compliance with Good Clinical Practices	8
3.3	Financial Disclosures.....	8
4	SIGNIFICANT EFFICACY/SAFETY ISSUES RELATED TO OTHER REVIEW DISCIPLINES	8
4.1	Chemistry Manufacturing and Controls	9
4.2	Clinical Microbiology.....	10
4.3	Preclinical Pharmacology/Toxicology	10
4.4	Clinical Pharmacology	11
4.4.1	Mechanism of Action.....	11
4.4.2	Pharmacodynamics/Pharmacokinetics	11
5	SOURCES OF CLINICAL DATA.....	12
5.1	Tables of Studies/Clinical Trials	12
5.2	Review Strategy	14
5.3	Discussion of Individual Studies/Clinical Trials.....	14
6	REVIEW OF EFFICACY	24
6.1	Indication	24
6.1.1	Methods	24
6.1.2	Demographics.....	25
6.1.3	Subject Disposition.....	26
6.1.4	Analysis of Primary Endpoint(s)	28
6.1.5	Analysis of Secondary Endpoints(s)	30
6.1.6	Other Endpoints	32
6.1.7	Subpopulations	34

6.1.8	Analysis of Clinical Information Relevant to Dosing Recommendations	34
6.1.9	Discussion of Persistence of Efficacy and/or Tolerance Effects.....	34
6.1.10	Additional Efficacy Issues/Analyses	34
7	REVIEW OF SAFETY.....	35
7.1	Methods.....	35
7.1.1	Studies/Clinical Trials Used to Evaluate Safety	35
7.1.2	Categorization of Adverse Events.....	35
7.1.3	Pooling of Data Across Studies/Clinical Trials to Estimate and Compare Incidence.....	36
7.2	Adequacy of Safety Assessments	37
7.2.1	Overall Exposure at Appropriate Doses/Durations and Demographics of Target Populations	37
7.2.2	Explorations for Dose Response.....	38
7.2.3	Special Animal and/or In Vitro Testing	38
7.2.4	Routine Clinical Testing	38
7.2.5	Metabolic, Clearance, and Interaction Workup	38
7.2.6	Evaluation for Potential Adverse Events for Similar Drugs in Drug Class ..	38
7.3	Major Safety Results	39
7.3.1	Deaths.....	39
7.3.2	Nonfatal Serious Adverse Events	39
7.3.3	Dropouts and/or Discontinuations	40
7.3.4	Significant Adverse Events	46
7.3.5	Submission Specific Primary Safety Concerns	46
7.4	Supportive Safety Results	47
7.4.1	Common Adverse Events	47
7.4.2	Laboratory Findings	53
7.4.3	Vital Signs	53
7.4.4	Electrocardiograms (ECGs)	53
7.4.5	Special Safety Studies/Clinical Trials	53
7.4.6	Immunogenicity.....	53
7.5	Other Safety Explorations.....	53
7.5.1	Dose Dependency for Adverse Events	53
7.5.2	Time Dependency for Adverse Events.....	53
7.5.3	Drug-Demographic Interactions	54
7.5.4	Drug-Disease Interactions.....	54
7.5.5	Drug-Drug Interactions.....	54
7.6	Additional Safety Evaluations	54
7.6.1	Human Carcinogenicity.....	54
7.6.2	Human Reproduction and Pregnancy Data.....	54
7.6.3	Pediatrics and Assessment of Effects on Growth	54
7.6.4	Overdose, Drug Abuse Potential, Withdrawal and Rebound.....	55
7.7	Additional Submissions / Safety Issues.....	55
8	POSTMARKET EXPERIENCE.....	55

9	APPENDICES	56
9.1	Literature Review/References	56
9.2	Advisory Committee Meeting.....	56
9.3	Labeling Recommendations	56

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.