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APPLICATION NUMBER:

203168Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	See electronic stamp date
From	Renata Albrecht, MD Division of Transplant and Ophthalmology Products
Subject	Division Director Summary Review
BLA Number	NDA 203168
Related IND	IND 60295
Related NDA	NDA 21664, NDA 20535
Review type	Standard
Applicant Name	Bausch & Lomb, previously ISTA
Date of Submission **Date of Receipt**	June 5, 2012 June 7, 2012
PDUFA Goal Date	April 7, 2013
Proprietary Name / **Established (USAN) Name**	Prolensa bromfenac
Formulation **Concentration** **Dosing Regimen**	Topical ophthalmic solution 0.07% One drop in the affected eye one time daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the post-operative period.
Therapeutic Class **Proposed Indication**	Nonsteroidal anti-inflammatory agent For the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery
Action for NME	*Approval*

NDA 203168 Prolensa (bromfenac ophthalmic solution) 0.07%
Indication: For the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
Medical Officer Review	Bill Boyd 3/20/2013
CDTL Review	Bill Boyd 4/5/2013
Deputy Director Review	Wiley Chambers 4/5/2013
Statistical Review Team Leader Review	Abel Eshete, Yan Wang 3/4/2013 Yan Wang, Daphne Lin 4/4/2013
Pharmacology/Toxicology Review	Robeena Aziz, Lori Kotch 3/4/2013
Clinical Pharmacology Review	Yoriko Hayigaya, Philip Colangelo 2/19/2013
ONDQA CMC Review	Rao Kambhampati, Rapti Madurawe 2/26/2013, 4/4/2013 Rapti Madurawe 4/5/2013
Quality Microbiology Review	Stephen Langille, Bryan Riley 1/22/2013
OSI/DGCPC	Kassa Ayalew, Susan Leibenhaut, Susan Thompson 2/4/2013, 2/20/2013
OSE/DMEPA Proprietary Name Letter Final Review	Jung Lee, Zachary Oleszczuk, Carol Holquist 11/7/2012 Carol Holquist 11/9/2012 Jung Lee, Jamie Wilkins Parker 3/4/2013
OSE/DMEPA Label, Labeling and Packaging Review	Jung Lee, Jamie Wilkins Parker, Carol Holquist 2/8/2013
OPDP/DPDP Review	Christine Corser 3/20/2013
Pediatric Review Committee	This application did not trigger PREA

OND=Office of New Drugs
CDTL=Cross-Discipline Team Leader
ONDQA=Office of New Drug Quality Assessment
OSI/DGCPC=Office of Scientific Investigations/Division of Good Clinical Practice Compliance (formerly Division of Scientific Investigation (DSI)
OSE=Office of Surveillance and Epidemiology
OMEPARM=Office of Medication Error Prevention and Risk Management
DMEPA=Division of Medication Error Prevention and Analysis
OPDP/DPDP=Office of Prescription Drug Promotion/Division of Professional Drug Promotion; formerly, DDMAC=Division of Drug Marketing, Advertising and Communication

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1. Summary and Recommendations

Bromfenac ophthalmic solution, 0.07% has been shown to be effective and safe for the treatment of pain and inflammation associated with cataract surgery based on two Phase 3 trials showing superiority of the product to vehicle. The treatment regimen evaluated in these trials and recommended for approval is one drop in the affected eye one time daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the post-operative period.

Key Efficacy Results of Phase 3 Studies in Prolensa NDA (ITT Population)
Proportion of Subjects with Cleared Ocular Inflammation (0 cell and no flare)

Study	Visit	Bromfenac 0.07%	Vehicle	Difference (%) (Asymptotic 95% CI)
Study 1	Day 8	27/112 (24.1%)	7/108 (6.5%)	17.6 (8.4, 26.8)
	Day 15	51/112 (45.5%)	14/108 (13.0%)	32.5 (21.4, 43.8)
Study 2	Day 8	33/110 (30.0%)	14/110 (12.7%)	17.3 (6.7, 27.9)
	Day 15	50/ 110 (45.4%)	30/ 110 (27.3%)	18.2 (5.7, 30.7)
		Proportion of Subjects Who Were Pain Free		
Study 1	Day 1	91/112 (81.3%)	47/108 (43.5%)	37.7 (25.9, 49.6)
Study 2	Day 1	84/110 (76.4%)	61/110 (55.5%)	20.9 (8.7, 33.1)

The safety of the 0.07% bromfenac formulation was evaluated in 222 patients treated with this product and compared to 218 patients who received vehicle. This represents a new concentration of bromfenac. The safety of bromfenac 0.09% given twice daily (Xibrom) and once daily (Bromday) was evaluated in NDA 21-664 for the same indication(s).

The labeling will include information on adverse reactions in these trials, and other safety information. The Warnings and Precautions includes information that the product contains sodium sulfite and may cause allergic reactions in susceptible people, NSAIDs may slow or delay healing, there is a potential cross-sensitivity with aspirin, increase bleeding time, and potential for keratitis and corneal erosion, ulceration and perforation. Common adverse reactions after cataract surgery associated with Prolensa use included anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and blurred vision. These adverse reactions were reported in 3 to 8% of patients.

All reviewers recommend approval. OSI recommends that clinical site data are considered reliable. As summarized in the CMC review, OC recommends that manufacturing facilities are

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