



Therapeutic Class ReviewSM

Ophthalmics - Nepafenac ophthalmic suspension 0.1% (NevanacTM) and Bromfenac ophthalmic solution 0.09% (XibromTM) April 2006

New Product for Review:

Nepafenac ophthalmic suspension 0.1%
(NevanacTM) [Alcon Laboratories]
Bromfenac ophthalmic solution 0.09%
(XibromTM) [ISTA Pharmaceuticals]

Dossier Provided by Manufacturer: Yes/Yes

Dossier Evaluation: (Dossier ranked 1 to 3) 1/1

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

Executive Summary

- Marketing
 - Bromfenac ophthalmic solution (Xibrom)
 - Marketing effort are likely to emphasize twice daily dosing and decreased ocular irritation/stinging.
 - Company representatives state that only ophthalmologists that perform cataract surgeries will be targeted by detailing.
 - Nepafenac ophthalmic suspension (Nevanac)
 - Marketing efforts are likely to emphasize thrice daily dosing and decreased ocular irritation/stinging. Alcon may also emphasize increased ocular penetration, which is based on rabbit data.
 - Alcon did not comment on the physician population it intends to target with marketing for this drug. It should be noted that Alcon has other ophthalmic products with indications that might be useful to physicians other than ophthalmologists.
- Both products are indicated only for ocular inflammation after cataract surgery. Nevertheless, ocular NSAIDs are used for a number of other indications, including inflammation after refractive surgery, seasonal allergic conjunctivitis, and numerous other ocular inflammatory conditions. Bromfenac ophthalmic solution (Xibrom) has been available in Japan since 2000 and is used for many conditions outside of cataract surgery. The potential for off-label use is high.

Evidence

- There is possibly useful evidence that bromfenac ophthalmic solution (Xibrom) is effective for the treatment of ocular inflammation due to cataract extraction and lens replacement.
- There is no useful evidence that either bromfenac ophthalmic solution (Xibrom) or nepafenac ophthalmic suspension (Nevanac) is more effective than existing formulary ophthalmic NSAID's.

- There is no useful evidence that either bromfenac ophthalmic solution (Xibrom) or nepafenac ophthalmic suspension (Nevanac) is safer than existing formulary ophthalmic NSAID's.
- Safety and efficacy of bromfenac ophthalmic solution (Xibrom) has not been established for patients less than 18 years of age.
- Safety and efficacy of nepafenac ophthalmic suspension (Nevanac) has not been established for patients less than 10 years of age.
- There was no evidence found that either bromfenac ophthalmic solution (Xibrom) or nepafenac ophthalmic suspension (Nevanac) significantly differs in safety or efficacy based on race, ethnicity, or gender.

Decision

- Recommend maintaining non-preferred/non-formulary status.

Products

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^b
diclofenac sodium ophthalmic solution 0.1% (Voltaren®)	03/91	Post-op inflammation following cataract extraction Post-op pain and photophobia following corneal refractive surgery	1 gtt QID beginning 1 day post-op x 14 days. 1-2 gtt 1hr pre-op, then QID x 3 days post-op	<ul style="list-style-type: none"> - Corneal abrasion - keratitis - laser photocoagulation - light intolerance - pain associated with foreign body - cystoid macular edema
flurbiprofen ophthalmic solution 0.03% (Ocufen®)	12/86	Inhibition of intraoperative miosis.	1 gtt q30min 2hrs prior to surgery x 4 gtt.	<ul style="list-style-type: none"> - cystoid macular edema - inflammation post cataract surgery - uveitis syndrome
ketorolac tromethamine ophthalmic solution - (Acular® ophthalmic solution 0.5%) - (Acular LS™ ophthalmic solution 0.4%) - (Acular® PF ophthalmic dropperette 0.5%)	11/92 05/03 11/97	<ul style="list-style-type: none"> - Seasonal allergic conjunctivitis - Post-op inflammation following cataract extraction - Post-op pain and stinging following corneal refractive surgery. - Post-op pain and photophobia following incisional refractive surgery 	<p>1 gtt QID</p> <p>1 gtt QID beginning 1 day post-op x 14 days.</p> <p>1 gtt QID PRN for up to 4 days post-op</p> <p>1 gtt QID PRN for up to 3 days post-op</p>	<ul style="list-style-type: none"> - cystoid macular edema - pain due to corneal abrasion
bromfenac ophthalmic solution 0.09% (Xibrom®)	03/05	Post-op pain and inflammation following cataract extraction	1 gtt BID beginning 1 day post-op x 14 days.	<ul style="list-style-type: none"> - conjunctivitis - blepharitis - episcleritis - scleritis
nepafenac ophthalmic suspension 0.1% (Nevanac®)	08/05	Post-op pain and inflammation following cataract extraction	1 gtt TID beginning 1 day PRE-op, continued on day of surgery then 14 days post-op.	

^a Date applies to approval date for the original brand name medication where there are now generics available. .

^b As listed in © 1974 - 2005 Thomson MICROMEDEX database or as referenced.

References

1. Nevanac™ [package insert]. Fort Worth, TX: Alcon Laboratories; August 2005
2. Xibrom™ [package insert]. Irvine, CA: ISTA Pharmaceuticals, Inc; July 2005
3. Klasco RK (Ed): DRUGDEX® System (electronic version). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at: <http://www.thomsonhc.com> (cited: 2/7/06).
4. ISTA-BR-CS001. Product Dossier: Xibrom™ (bromfenac ophthalmic solution 0.9%), ISTA Pharmaceuticals; Irvine CA. Data reviewed February 1, 2006.
5. Personal Communication. Clara K. Song, PharmD Medical Affairs Medical Communications Manager ISTA Pharmaceuticals, Inc. February 7, 2006.
6. Alcon Study # C-03-32. Product Dossier: Nevanac™ (nepafenac ophthalmic suspension 0.1%), Alcon Laboratories; Fort Worth, TX. Data reviewed February 1, 2006.
7. Alcon Study #C-02-53. Product Dossier: Nevanac™ (nepafenac ophthalmic suspension 0.1%), Alcon Laboratories; Fort Worth, TX. Data reviewed February 1, 2006.
8. Alcon Study # C-95-93. Product Dossier: Nevanac™ (nepafenac ophthalmic suspension 0.1%), Alcon Laboratories; Fort Worth, TX. Data reviewed February 1, 2006.
9. Alcon Study # C-97-30 Product Dossier: Nevanac™ (nepafenac ophthalmic suspension 0.1%), Alcon Laboratories; Fort Worth, TX. Data reviewed February 1, 2006.
10. Alcon Study # C-95-91 Product Dossier: Nevanac™ (nepafenac ophthalmic suspension 0.1%), Alcon Laboratories; Fort Worth, TX. Data reviewed February 1, 2006.
11. Kashiwagi T, Kida T, et al. Effect of bromfenac ophthalmic solution on ocular inflammation and corneal epithelial barrier function following cataract surgery. *Folia Ophthalmol Jpn* 54: 276-279, 2--3
12. Takamatsu F, Shiroyama N, et al. Efficacy and adverse effects of bromfenac ophthalmic solution following cataract surgery. *Rinsho Ganka Jpn J Clin Ophthalmol* (57)7: 1233-1237, 2003
13. Ohara K, Ohkubo A, et al. Prevention of miosis during caract surgery by topical bromfenac sodium. *Rinsho Ganka Jpn J Clin Ophthalmol* 58(7): 1325-1328, 2004
14. Ohara K, Ohkuba A, et al. Effect of Bromfenac Sodium on Postoperative Inflammation. Manuscript Pending. Product Dossier: Xibrom™ (bromfenac ophthalmic solution 0.9%), ISTA Pharmaceuticals; Irvine CA. Data reviewed February 1, 2006.
15. Kashiwagi K, Tsukahara S. Effect of non-steroidal anti-inflammatory ophthalmic solution on intraocular pressure reduction by latanoprost. *Br J Ophthalmol*. 2003 Mar;87(3):297-301.
16. Product Dossier: Xibrom™ (bromfenac ophthalmic solution 0.9%), ISTA Pharmaceuticals; Irvine CA. Data reviewed February 1, 2006.
17. Product Dossier: Nevanac™ (nepafenac ophthalmic suspension 0.1%), Alcon Laboratories; Fort Worth, TX. Data reviewed February 1, 2006.