

Therapeutic Class Overview

Ophthalmic Nonsteroidal Anti-Inflammatory Drugs

Therapeutic Class

- Overview/Summary:** This review encompasses the ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) bromfenac sodium (Prolensa[®], generic), diclofenac sodium, flurbiprofen sodium (Ocufen[®]), ketorolac tromethamine (Acular[®], Acular LS[®], Acuvail[®]) and nepafenac (Ilevro[®], Nevanac[®]).¹⁻¹¹ These agents are indicated for use prevention of intraoperative miosis during cataract surgery, management of postoperative inflammation, and the reduction of pain and discomfort following cataract and refractive surgery. Although not Food and Drug Administration (FDA)-approved, ophthalmic NSAIDs are also used for the prevention and treatment of cystoid macular edema following cataract surgery.^{12,13} Ophthalmic NSAIDs exert their anti-inflammatory activity primarily by nonselective inhibition of cyclooxygenase-1 and cyclooxygenase-2 enzymes.¹⁻¹⁰ Topical administration of anti-inflammatory agents for ocular conditions is preferred over systemic administration due to higher ocular drug concentrations with minimal systemic adverse events.¹⁴⁻¹⁶

The American Academy of Ophthalmology and the American Optometric Association both recommend using ophthalmic NSAIDs for preventing and treating cystoid macular edema following cataract surgery. Neither organization recommends one ophthalmic NSAID over another.^{17,18} The American Academy of Ophthalmology also recommends the use of NSAIDs in before and after several refractive surgeries.¹⁹ Both organizations note that ophthalmic NSAIDs are effective in treating the signs and symptoms of allergic conjunctivitis.^{20,21} The most common adverse events associated with ophthalmic NSAIDs include conjunctival hyperemia, burning and stinging.¹⁵ Corneal ulceration and full-thickness corneal melts associated with the use of these agents is a serious complication. Ophthalmic NSAIDs were first reported to cause corneal melting in 1999. The majority of cases were related to the generic ophthalmic diclofenac sodium solution manufactured by Falcon Laboratories, and ultimately this product was removed from the market. There have been reports of corneal melts and keratitis associated with the use of other ophthalmic NSAIDs; however, available evidence does not alter the favorable benefit-risk ratio of the appropriate use of ophthalmic NSAIDs.¹⁵

Table 1. Current Medications Available in the Therapeutic Class¹⁻¹⁰

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Bromfenac sodium ophthalmic* (Prolensa [®])	Treatment of pain and inflammation associated with cataract surgery	Ophthalmic solution: 0.09% (1.7 mL, 2.5 mL, 5 mL) 0.07% (1.6 mL, 3 mL)	✓
Diclofenac sodium ophthalmic	Temporary relief of pain and photophobia in patients undergoing corneal refractive surgery; treatment of postoperative inflammation in patients undergone cataract extraction	Ophthalmic solution: 0.1% (2.5 mL, 5 mL)	✓
Flurbiprofen sodium ophthalmic (Ocufen [®] *)	Inhibition of intraoperative miosis	Ophthalmic solution: 0.03% (2.5 mL)	✓
Ketorolac tromethamine ophthalmic (Acular [®] *, Acular LS [®] *, Acuvail [®])	Reduction of ocular pain and burning/stinging following corneal refractive surgery (0.4%); temporary relief of ocular itching due to seasonal allergic conjunctivitis (0.5%); treatment of pain and inflammation associated with cataract surgery (0.45%); treatment of postoperative inflammation in patients who have undergone cataract extraction (0.5%)	Ophthalmic solution: 0.4% (5 mL) 0.45% (0.4 mL single-use vials in package of 30) 0.5% (3 mL, 5 mL, 10 mL)	✓

Nepafenac ophthalmic (Ilevro [®] , Nevanac [®])	Treatment of pain and inflammation associated with cataract surgery	Ophthalmic suspension: 0.1% (3 mL) 0.3% (1.7 mL, 3 mL)	-
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*Generic available in one dosage form or strength.

Evidence-based Medicine

- The ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to be safe and effective in inhibiting intraoperative miosis, reducing postoperative inflammation and pain associated with cataract surgery, relieving pain and photophobia following corneal refractive surgery and relieving seasonal allergic conjunctivitis symptoms in placebo-controlled trials.^{22-49,56-64} Although not Food and Drug Administration (FDA)-approved, there is evidence to support the use of ophthalmic NSAIDs for preventing or treating cystoid macular edema and for reducing pain associated with various other refractive surgeries.⁵¹⁻⁵⁴
- The results of head-to-head trials comparing ophthalmic NSAIDs have not consistently demonstrated any one agent to be more efficacious than another for a given indication.^{31,32,34,35,48,49,51,52,57,58,61}
- With regard to safety, not one agent was consistently reported to be better tolerated than another across trials, although there is some evidence that the preservative-free products may be associated with less ocular irritation.⁴⁵
- Corneal complications have been reported to occur with all of the agents in the class and the risk does not appear to be higher with one agent vs another.
- Consensus guidelines established by the American Academy of Ophthalmology and the American Optometric Association recommend the use of topical NSAIDs for preventing and treating cystoid macular edema due to cataract surgery. Available evidence suggests that ophthalmic NSAIDs either alone or in combination with ophthalmic corticosteroids are more effective than ophthalmic corticosteroids alone. The ophthalmic NSAIDs are not associated with an increase in intraocular pressure, which may occur with the use of corticosteroids.^{17,18}

Key Points within the Medication Class

- According to Current Clinical Guidelines:
 - The use of topical nonsteroidal anti-inflammatory drugs (NSAIDs) for preventing and treating cystoid macular edema due to cataract surgery is recommended.^{17,18}
 - For refractive surgery, specifically surface ablation techniques and laser in situ keratomileusis, the use of ophthalmic NSAIDs is recommended. Judicious NSAID application should be done after surface ablation to reduce pain and inflammation and to delay corneal epithelialization NSAID application should be done before laser in situ keratomileusis to ameliorate postop pain. No NSAID is recommended over another.¹⁹
 - Both organizations note that ophthalmic NSAIDs are effective in treating the signs and symptoms of allergic conjunctivitis.^{20,21}
- Other Key Facts:
 - Bromfenac 0.09%, diclofenac sodium, flurbiprofen sodium, and ketorolac tromethamine 0.5 and 0.4% are available generically.
 - Diclofenac sodium and ketorolac tromethamine 0.45% are the only ophthalmic NSAIDs that are formulated as preservative-free.^{4,6}
 - Nepafenac 0.3% and two formulations of bromfenac sodium (0.09% and Prolensa[®]) are approved for once daily dosing.^{1,2,10}
 - Ketorolac Tromethamine 0.4% is the only ophthalmic NSAID used as needed.⁸

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