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## CME Activity

# Managing Ocular Pain and Inflammation After Cataract Surgery: Differentiating Among the Nonsteroidal Antiinflammatory Drugs Part 2

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## CONTENT SOURCE

This continuing medical education (CME) activity captures content from an event held in February of 2017 at the ACES/SEE meeting.

## TARGET AUDIENCE

This certified CME activity is designed for ophthalmologists involved in the comanagement of postoperative cataract patient management.

## LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- Describe the pharmacokinetic properties of the bromfenac molecule
- Assess the ability of topical ophthalmic NSAIDs to treat postoperative inflammation and pain in a cataract patient
- Analyze the safety profile of the bromfenac molecule
- Discuss the obstacles patients face in compliance and adherence
- Develop a plan to communicate compliance obstacles with patients

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# Managing Ocular Pain and Inflammation After Cataract Surgery: Differentiating Among the Nonsteroidal Antiinflammatory Drugs, Part 2

*Phacoemulsification with intraocular lens implantation has become the gold standard surgical procedure for cataract removal. Although there is potential for postoperative pain and inflammation, the benefits patients receive from the cataract surgery far outweigh these potential complications.[1] Risk factors for inflammatory complications may include those patients with anterior segment pathology, uveitis-related damage to the blood-aqueous barrier, diabetes, glaucoma, or those eyes previously exposed to surgery.[2]*

*Nonsteroidal antiinflammatory drugs (NSAIDs) can reduce postoperative pain and can reduce the risk of postoperative inflammation, thereby improving patient comfort.[3-7] The incidence of postoperative pain is estimated at about one-third during the early postoperative period, but almost 80% of those patients continue to experience pain even after they have left the surgical facility.[8] Postoperative inflammation—typically assessed as anterior chamber cell counts and flare—is also fairly common during the early-to-intermediate postoperative period. This, too, has been regarded as an acceptable risk profile given the benefits derived from cataract surgery.[1]*

*Bromfenac 0.075% (BromSite) is the latest entry in the NSAID market. Evolve gathered some leading cataract surgeons to discuss how this new NSAID differs from others, and its advantages.*

**—Eric Donnenfeld, MD, moderator**

**Eric Donnenfeld, MD:** Most of us use nonsteroidal antiinflammatory drugs (NSAIDs) in our practices. How important are they, and what role do—or should—NSAIDs play in cataract surgery?

**Sheri Rowen, MD:** I have used NSAIDs since I began cataract practice. In an early retrospective study I performed,[9] I found the rates of cystoid macular edema (CME) were much lower with NSAID use than after corticosteroid use alone, even with the earlier generation NSAIDs. I have been using NSAIDs ever since. When we consider pain control, pupil management, inflammation, and CME (even though that has not been studied as extensively), we know NSAIDs provide a great benefit.[10-15] For my patients who do develop CME, I have found NSAIDs can quickly resolve it. For all those reasons, I believe the use of NSAIDs is critical in my cataract practice.

**Cynthia Matossian, MD:** Studies have shown that starting NSAIDS prior to surgery, even by a day, will make a difference in maintaining mydriasis at the time of cataract surgery.[10,11,16-21] I tell my patients to start the NSAIDs 3 days before surgery, but I suspect many do not begin really using them until the day before surgery.

**Dr. Donnenfeld:** Dr. Singh, you see a lot of high-risk patients in your practice. How long do you continue your NSAIDS following cataract surgery? Should certain patients be prescribed NSAIDs for a longer course?

**Inder Paul Singh, MD:** That is an interesting debate. We evaluated our patients internally and looked at the optical coherence tomography images. We never published our data, but we compared outcomes after keeping patients on NSAIDs for 1 month postoperatively or 3 months postoperatively. We found a difference in the overall macular thickness—it was slightly thinner in the group on postoperative NSAIDs for 3 months. Based on our internal results, when patients have any kind of diabetic disease (controlled or not), any kind of epiretinal membrane or other macular pathology, or if I think patients are prone to fibrosis (especially for those who have opted for premium lenses), I now keep them on NSAIDs for 6 to 8 weeks, if not longer. But on average, after uncomplicated cases, I like keeping patients on postopeartive NSAIDs for 6 weeks.

**Dr. Donnenfeld:** We published a paper on the pharmacokinetic dose response to NSAIDs,[6] and found that initiating NSAIDs 1 to 3 days before surgery results in significantly more pupil dilation, less inflammation, more rapid healing, and less risk of macular thickening on OCT compared to starting at 1 hour or not using an NSAID. Based on that, I think 2 days preoperatively is the optimal time to start NSAIDs.

Numerous studies on the use of NSAIDs show they improve pupillary dilation, improve pain control, and improve short-term inflammation and short-term visual acuity (VA).[14,15,22-35] There has been some controversy on the longer-term effects on VA, however.[13,29,36] Others have questioned whether the body of evidence in the literature is convincing enough to warrant routine NSAID use.[36]

**Dr. Singh:** We have been involved with steroid trials for use after cataract surgery. When you are involved in these studies, you are not allowed to use NSAIDs as part of the postoperative care. We have found an amazing difference in the two sets of eyes—when you do not use an NSAID during either the preoperative or postoperative periods, the eyes are not as "happy," not as quiet. They are more likely to have hyperemia, the conjunctiva is often more edematous, and patients are more likely to complain about their postoperative course.

I was involved in the Dextenza study—this is a dexamethasone steroid implant that fits into the inferior punctum. When we placed it right after surgery, we found it helped reduce the need for steroid drops.[37]

When I first came out of fellowship, steroids were the standard of care. But then the data started being published on the outcomes after using NSAIDs, and I thought, 'How can I not use an NSAIDs in my postoperative cataract patients?' The results were just too positive. It definitely helped me grow my practice.

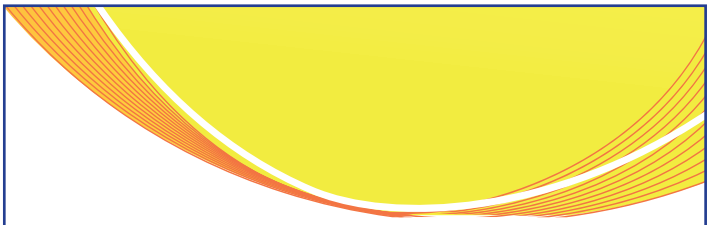
## POSTOPERATIVE PAIN

**Dr. Donnenfeld:** Let us discuss pain for a moment—for some patients, postoperative pain after cataract surgery may not be debilitating, but, for others with lower pain thresholds, it may be excruciating. It is probably safe to say that the less postoperative pain a patient endures, the more favorable the overall experience is likely to be. Do you think we talk about postoperative pain enough?

**Dr. Matossian:** There are two things by which patients judge their surgeon after undergoing cataract surgery. In the immediate postoperative period, it is how well they see compared to their preoperative vision. Later, it is whether or not they experienced pain or discomfort during the procedure or during the immediate postoperative period. If we are able to provide our patients with better visual outcomes and reduce the amount of postoperative inflammation, reduce their light sensitivity in the immediate postoperative period, and reduce the amount of pain and discomfort they are likely to experience, they are going to be more positive about their experience, and they are going to view their surgery as more successful.

**Dr. Rowen:** When we create a wound (whether it is for cataract surgery or a refractive procedure), in my experience, patients respond better when they have NSAIDs for pain control. Our incisions might be smaller than other types of surgeries, but we are still disrupting the epithelium. We are still creating a release of prostaglandins. Discomfort is a reality—patients do not tend to discuss this much. They expect pain, but the difference in what we see without postoperative NSAID use and with it is definitely noticeable. I think Dr. Matossian is correct when she notes that patients who have seamless surgery and do not really feel the postoperative effects as much are much happier. That is what we should address.

**Dr. Singh:** I always ask colleagues, what is your goal of cataract surgery? Is the goal spectacle independence after surgery? Or is it to have a happy patient? They do not have to be mutually exclusive, either. Everyone here has mimicked what we see in our practice as well. It is the overall experience—from preoperative, to intraoperative, to postoperative—that patients remember. We asked patients in our practice when they start discussing their surgery—how long before they start talking to their friends about their outcomes? In our patient population, it was within that first week. At postoperative day 1, they realize there is a difference, but they do not start talking to people about their experience for another few days. And their friends want to know—friends will ask about eye irritation or light sensitivity, and they want to know about the pain.



In cataract surgery, our threshold for comfort has gone down so much; patients expect to have a beautiful, easy course.
—Inder Paul Singh, MD

Everyone has some level of postoperative inflammation in the immediate postoperative period, but pain can be as simple as a patient noting their eye is a little sore when they wake up. It does not have to be patients complaining about throbbing or how opening their eyelids hurt. The definition of pain is going to vary. In cataract surgery, our threshold for comfort has gone down so much; patients expect to have a beautiful, easy course. We have found that to be particularly true with our premium IOL patients.

**Dr. Rowen:** Bromfenac 0.075% (BromSite) is approved as a twice-daily medication.[38] When we start to think about pain control, I use bromfenac 0.075% (BromSite) twice daily for the first week, and then taper to once daily after that. In our experience, it is that first week where the patient is most likely to feel pain. By dosing twice daily, you are giving the patient just a little bit longer control of pain/discomfort/irritation.

**Dr. Donnenfeld:** That is exactly what patients are looking for—they want quality vision and a quality experience, and they are both equally important. During their postoperative day 1 visit, they are already telling their friends about their experience. If the experience was not what they expected it to be, no matter how good the visual outcomes are from your perspective as a surgeon, the patient does not care. They care about their perception of how the operation went.

I discuss pain and that it is the enemy of surgery with my patients during our consult. When patients are uncomfortable, they tend to flinch or move their eyes or turn their heads, and it makes surgery much more dangerous. When we are in the operating room and patients are obviously in discomfort or they complain, we have increased the anesthesia. Sometimes that works, but sometimes it confuses the patients and may create some untoward movement as well. In my mind, controlling pain is not just a cosmetic discussion. It is a therapeutic discussion to have with the patient, because it will inevitably enable you to perform a safer surgery. It is another reason I believe in using NSAIDs and consider them invaluable in improving outcomes.

## DIFFERENTIATING NSAIDS

**Dr. Donnenfeld:** In your opinions, how should surgeons differentiate the available NSAIDS for use in cataract surgery? For me, there are three parameters that I consider when I am evaluating an NSAID. First, I evaluate the molecule. Then, I evaluate the concentration of that molecule. Lastly, I consider the vehicle in which the molecule is delivered. All three components are equally important to me. What are your priorities? How do you decide which NSAID to use?

**Dr. Matossian:** The bromfenac molecule has been available for a long, long time, both here in the United States and in other nations.[39-44] We know its safety profile. We know its efficacy. It is delivered in the DuraSite vehicle, which is an extended-release type of artificial tear that has various ingredients in it that make the eye feel comfortable and has been shown in studies to be safe and nontoxic.[45]

With the newest version of bromfenac (0.075%, BromSite) in DuraSite, I have been asked whether the twice-daily dosing will increase the amount of active ingredient on the surface of the eye. And will that, in turn, lead to negative problems?

Simply put, no. Bromfenac 0.075% (BromSite) is suspended within the DuraSite vehicle. With sheer blinking the active ingredient is released, and it penetrates immediately into the cornea and into the anterior chamber. The active ingredient is not just 'spending time' on the surface of the eye.

**Dr. Rowen:** Bromfenac has one of the most potent penetration profiles of any molecule on the market. The cLogP of this molecule shows it can penetrate the cornea almost instantaneously. As Dr. Matossian said, it is released with a blink, it penetrates the cornea, and because it is an extremely potent COX-1 and COX-2 blocker, there is an almost immediate response.

**Dr. Singh:** It is a well-known point that less than 5% of a drug is actually absorbed in the eye when you instill a drop.[46,47] There are multiple factors that account for that—blink reflex, nasal lacrimal evacuation, tear turnover, etc. So when we evaluate how a drug can be delivered more effectively or absorbed more effectively, the options are to change how long it can be absorbed or change the vehicle. Due to its lipophilic properties, bromfenac 0.075% (BromSite) does not need to be hydrolyzed by corneal esterases; therefore, it can be absorbed fairly rapidly. Also, with the DuraSite vehicle increasing residence time, the bromfenac molecule has more potential opportunities for absorption. It is important to note that DuraSite does not increase corneal toxicity due to the ability of the vehicle to sequester the nonabsorbed molecule within its matrix and prevent it from residing directly on the epithelium.[45] When comparing absorption data, bromfenac 0.075% (BromSite) with DuraSite demonstrated higher concentrations in the aqueous compared to a bromfenac 0.09% (Bromday) without DuraSite, suggesting the vehicle allows for greater absorption at a lower concentration.

**Dr. Donnenfeld:** There are several NSAIDs approved for use in ophthalmic surgery: bromfenac, diclofenac, ketorolac, nepafenac, and suprofen.[39,40] We tend to use ketorolac, nepafenac, and bromfenac after cataract surgery. All three are potent NSAIDs, but as Dr. Singh pointed out, bromfenac is the most potent so its concentration is lower than the others.

There are several NSAIDs approved for use in ophthalmic surgery: bromfenac, diclofenac, ketorolac, nepafenac, and suprofen.
—Eric Donnenfeld, MD

Ketorolac was really the first NSAID we used routinely, but it is not as potent, and it is much more toxic to the cornea.[6,48,49]

As currently available, ketorolac 0.5% is very toxic molecule—during the registration trials, up to 40% of subjects had significant burning and stinging associated with ketorolac.[50] That is about what you are going to see if you use a generic NSAID. Ketorolac was also highly associated with epitheliopathy, corneal melts, and decreased visual acuity.[6] I strongly counsel against using this molecule, especially in people with ocular surface disease.

**Dr. Singh:** In our patient population after an internal review of our diagnosis codes looking for patients with a diagnosis of dry eye-related diseases, we found almost 80% of our patients may have some type of ocular surface disease. As glaucoma specialists, we tend to see a higher population of patients with surface issues due to glaucoma medications and systemic comorbidities.

**Dr. Rowen:** There is nothing worse than doing a perfect surgery and 3 weeks later the patient comes in with his or her corneal epithelium completely disrupted from the ketorolac.

**Dr. Donnenfeld:** We heard from this panel and know from the literature that bromfenac is safe and exceptionally well tolerated. The DuraSite vehicle is a mucoadhesive molecule that adheres to the surface and is an extraordinarily potent ocular surface protectant.

**Dr. Singh:** Other NSAIDs use vehicles that make the residence time on the cornea longer,[5] but may also cause more tolerability issues. When I have used eye drops with some of these polymers, like guar gum or hyaluronic acid, I hear more complaints from patients than when I have used other NSAIDs.

**Dr. Matossian:** Plus, as Dr. Rowen noted, some patients note a little bit of a foreign body sensation during the immediate postoperative period, especially at the site of the incision. In my expereince, adding the mucoadhesive vehicle that is used in DuraSite really soothes the eye with each blink.

**Dr. Donnenfeld:** And the mucoadhesive stays on the ocular surface a longer period of time. We know that the turnover time with the tear film is just minutes.[51-54] There is evidence that DuraSite helps lengthen the time a solution stays on the surface.[55,56] Other medications use DuraSite as well, including azithromycin and besifloxacin.[57,58] Tear film studies have shown that antibiotics can remain for 3 to 5 days.[59,60] Those levels cannot be achieved without the use of a vehicle. Let me ask, in your opinion, what is the effect of having DuraSite vehicle on the penetration rates of the active ingredient (drug) into the eye?

**Dr. Singh:** As Dr. Matossian pointed out earlier, that vehicle helps keep the drug on the surface longer, but it also keeps it in a "protective pocket" of sorts in the DuraSite vehicle itself. With any vehicle, our concerns should be that something that is kept on the surface for any length of time can cause epitheliopathy over the long term. But that is not the case here—the active ingredient is protected within a small pocket of the DuraSite molecule. When the DuraSite reacts with the tear film, an ionization occurs to release the drug. Bromfenac is highly lipophilic, so it will absorb quickly. It does not have a lot of time to contact the epithelium. Every blink replenishes the surface and releases the drug, it goes back into the conjunctival cul-de-sac, the patient blinks again, and the whole process is repeated resulting in a chronic, slow release throughout the day. For me, that is an important point. We are not getting this big bolus of medicine in the morning and then nothing throughout the day. This particular vehicle ensures there is a slow release throughout the waking hours. I think that is a main reason this drug helps control pain and discomfort a little bit more continuously than having a bolus in the morning.

**Dr. Rowen:** In addition, it was shown that aqueous humor concentrations of bromfenac did increase over a generic formulation using the Durasite vehicle on the ocular surface. It goes to the point that one drop continues to enter through the cornea to the anterior chamber, and you get that aqueous concentration exactly where you need it. You have the DuraSite residence time coating the cornea, you have the bromfenac going into the eye to the target tissue where the COX-1 and COX-2 enzymes reside and are released. Having twice as much active ingredient could be a bonus in controlling inflammation.

**Dr. Donnenfeld:** Getting twice as much nonsteroidal to the eye is obviously an advantage, but what is the effect of having both DuraSite and bromfenac on the ocular surface? What does that do for ocular surface pain after surgery? Does it have a significant effect on controlling pain because you have increased contact time?

**Dr. Matossian:** Yes—having the DuraSite on the surface definitely decreases the pain, and that is our goal for our patients—to minimize pain and discomfort.

**Dr. Rowen:** The interesting part of what of you raised is: would the DuraSite be comparable to the bromfenac 0.075% (BromSite) in terms of the foreign body irritation on the surface? We do not think we actually know that directly. That would be something worthy of future investigation.

**Dr. Donnenfeld:** How important do you think preventing pain is as an indication?

**Dr. Singh:** To me, that is an extremely important issue for a number of reasons. We try to educate our patients about the medications we prescribe, about the brand-name medications. They want to know how long they have to take the medication and why. Up until this indication on this NSAID, though, I could not tell them anything I prescribed would prevent pain. Now I have a way to put a better value on their purchase, so to speak: "Is this prevention of pain worth it to me?" Giving our patients enough value for that purchase is important.

Patients are most fearful of losing vision or going blind after cataract surgery, but their second biggest fear is always pain. Even though most of our patients do not have high pain levels postoperatively, I think it is a big benefit for patients to know that they can take something to alleviate and prevent the pain. It is also why I tell my patients I am prescribing a name brand and not a generic alternative, even though generics are available.

**Dr. Matossian:** I think that is really key. Patients are worried about going blind and the pain of surgery. If we can get them engaged in the process, in the decision-making process of purchasing a branded product whose indication is prevention of inflammation and prevention of pain—that is great.

The bottle size is also very important. That is another key feature.

**Dr. Singh:** Why do you consider bottle size a key feature?

**Dr. Matossian:** Because one of the things that our patients complain about most is how little medicine they get and that it does not last long enough. This is especially true for our cataract-age, elderly patients. They have a harder time getting the drops into their eye, and they tell us they often miss, so they end up using more drops than they anticipated. Or their hands shake. They are frustrated that, yet again, they have to go to the pharmacy, and purchase another bottle, and then we get the call backs.

So, my technicians are tied up trying to get another bottle certified or preapproved for that patient, because they have gone through it too quickly. And then the patient gets upset at us. That negativity and anger is directed at the practice and at the surgeon when we have nothing to do with it. I would rather not have that

dialogue at all, and instead find an alternative. A bigger 5-ml bottle is welcomed. Hopefully, it is a big enough bottle. It has about 100 drops in it to get the patient through both eyes and the second sequential cataract surgery.

## ON- AND OFF-LABEL USES

**Dr. Donnenfeld:** What are the FDA indications? How do you actually prescribe it clinically yourselves?

**Dr. Rowen:** Well, the FDA indication is at twice a day for 14 days.[38] I think most of us prescribe NSAIDs for a longer period postoperatively, especially if there are complications or if the patient is at a higher risk.[61]

We want to control the blood-aqueous barrier after cataract surgery. I have been telling patients to use this for 2 days prior to surgery, and once or twice daily for the first week, followed by once daily for the next 4 to 5 weeks.

**Dr. Donnenfeld:** Does anyone have any different uses of the medication?

**Dr. Matossian:** I prescribe it once a day because I know how potent bromfenac is, and we have used that molecule in the past. But I do tell patients to use it for 8 weeks to ensure we are past the 6-week point where we might see some CME.

**Dr. Singh:** I am kind of a hybrid. I prescribe it twice a day, but after the first week, I drop it to once daily. But I also recommend patients dose twice a day for 3 days before surgery.

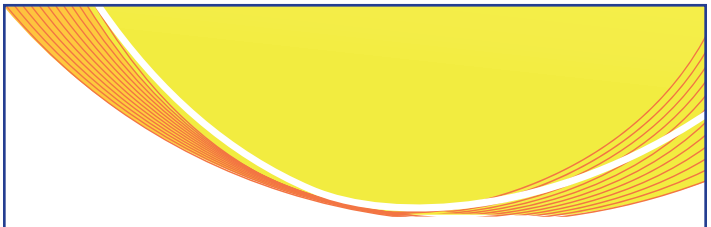
**Dr. Matossian:** That is what I prefer, too.

**Dr. Rowen:** I recommend predosing for 2 days before surgery.

**Dr. Matossian:** I do 3 days before, twice a day. Then once a day thereafter.

**Dr. Singh:** There are a lot of us who have incorporated using a femtosecond laser in our cataract surgeries to make the arcuate incisions. There are studies that now show an increased risk of prostaglandin release after the femtosecond portion when compared to standard cases.[21,62,63] Clinically, I have found NSAIDs do help prevent miosis from occurring. But for pain, in general whenever we are doing any kind of surface or conjunctival work, or when we need to use a peripheral iridotomy, recommending patients predose is a good idea. I am especially cognizant of that with my femtosecond laser cataract patients. It is really important to have that twice-a-day dosing beforehand.

Postoperatively, I tend to recommend only once a day because the data show we are getting twice as much of the bromfenac molecule in the anterior chamber. The bromfenac 0.09% (Bromday) studies compared once daily in each arm, with predosing.[43,55,64,65] So I am comfortable with dosing before twice daily, but then only once a day after surgery.



> Our higher risk patients need more predosing and postoperative dosing. I also increase the pre- and postdosing for any patient who has a history of macular or inflammatory issues.
>
> —Cynthia Matossian, MD

**Dr. Rowen:** My treatment recommendations do not change if my patients have chosen the femtosecond laser option. I have prescribed once daily but tell patients if they are feeling any discomfort to increase the dosing to twice daily. If there are confounding issues—epiretinal membrane or diabetic macular edema—then I keep patients on the NSAID for much, much longer.[61] I also have them start much earlier, up to a week before surgery.

**Dr. Donnenfeld:** I start my patients on NSAIDs 2 to 3 days before surgery and I continue it postoperatively. When I use bromfenac 0.075% (BromSite), I use it once a day. I feel that the molecule is so potent, that even if it is approved twice a day, I think I am getting very good drug delivery. I have patients generally use it for 4 weeks if it is an uncomplicated case, and for 3 months in patients with diabetic macular edema. I also follow what Dr. Rowen does: prescribe NSAIDs for up to a week preoperatively in these more difficult cases.

**Dr. Matossian:** I agree—our higher risk patients need more predosing and postoperative dosing. I also extend the pre- and postdosing for any patient who has a history of macular or inflammatory issues.

**Dr. Singh:** That is also where having a bigger bottle helps.

## WHY CHANGE?

**Dr. Singh:** A lot of our colleagues say the data are great, but if their surgery is successful, then patients do not complain about pain, the eyes look quiet postoperatively, and everyone's at 20/20 at 1 week after surgery. Do we really need to consider a different medication?

One reason for the pushback is that all the commercially available NSAIDs marketed in the United States work well. We are kind of splitting hairs, it seems.

> Any time we are manipulating the ocular surface, I think there is great potential to use an NSAID.
>
> —Inder Paul Singh, MD

I will say, anecdotally, however, that I notice a difference, particularly with my femtosecond laser-assisted patients. When we see them on postoperative day 1, the conjunctiva can sometimes look a little boggy from the suction clip. But after using bromfenac 0.075% (BromSite), it was nice to see the conjunctiva—more than the anterior chamber—looked rather quiet. It was not that the anterior chamber was much quieter or that the complaints of pain were much less, but it really struck me how quiet the conjunctiva looked, how relaxed it seemed. With all the options we have, it is not that one is good and another is not, but there are some nuanced differences among our choices that may lead us to choose one NSAID over another.

**Dr. Donnenfeld:** Any other case examples?

**Dr. Matossian:** This is not a specific patient, but, overall, my patients comment on how good their eye feels after surgery, where I have not had that comment from a previous branded NSAID. They definitely talk about the gel, the mucoadhesive characteristics of the drop. They specifically say the drug feels good, which I have never heard about any other medication.

**Dr. Rowen:** Soothing is the word my patients use most often.

**Dr. Matossian:** I have also found it useful (off-label) for my dry eye patients. I use it mostly after intense pulsed laser, where these patients already have a pre-existing ocular surface disease and a fairly compromised corneal surface. They are already uncomfortable. After an intense pulsed laser, I am manually expressing their meibomian glands, and I am causing some kind of mechanical pressure on those glands. That can lead to increased irritation for patients, and I have found bromfenac 0.075% (BromSite) really eases that discomfort. I recommend it twice daily for 7 days after the intense pulsed laser procedure.

**Dr. Singh:** Any time we are manipulating the ocular surface, I think there is great potential to use an NSAID. Off-label uses outside of cataract surgery make sense to me—I also use it when there are sutures on the conjunctiva.

**Dr. Donnenfeld:** In closing, I think we can all agree that NSAIDs play an extraordinarily significant role in the management of inflammation and the prevention of pain following cataract surgery. Bromfenac 0.075% (BromSite) is a very welcome addition to the NSAID market. And we find that, because the DuraSite vehicle increases contact time on the ocular surface, there are higher aqueous humor concentrations. And we look forward to more clinical evidence about the efficacy of this medication and (perhaps) its efficacy in areas other than postoperative cataract surgery. ■


1. Monnet D, Tepenier L, Brezin AP. Objective assessment of inflammation after cataract surgery: comparison of 3 similar intraocular lens models. *J Cataract Refract Surg.* 2009;35(4):677-681.
2. Schalnus R. Topical nonsteroidal anti-inflammatory therapy in ophthalmology. *Ophthalmologica.* 2003;217(2):89-98.
3. Prolensa [package insert]. Tampa, FL: Bausch & Lomb Incorporated, 2013.
4. European Medicines Agency. Nevanac (nepafenac). 2012.
5. Ilevro [package insert]. Fort Worth, Texas: Alcon Laboratories, Inc., 2013.
6. Donnenfeld ED, Perry HD, Wittpenn JR, et al. Preoperative ketorolac tromethamine 0.4% in phacoemulsification outcomes: pharmacokinetic-response curve. *J Cataract Refract Surg.* 2006;32(9):1474-1482.
7. American Academy of Ophthalmology Cataract and Anterior Segment Panel. Preferred Practice Patterns: Cataract in the Adult Eye. San Francisco, CA: American Academy of Ophthalmology, 2011.
8. Porela-Tiihonen S, Kaarniranta K, Kokki M, et al. A prospective study on postoperative pain after cataract surgery. *Clin Ophthalmol.* 2013;7:1429-1435.
9. Rowen S. Preoperative and postoperative medications used for cataract surgery. *Curr Opin Ophthalmol.* 1999;10(1):29-35.
10. Duan P, Liu Y, Li J. The comparative efficacy and safety of topical non-steroidal anti-inflammatory drugs for the treatment of anterior chamber inflammation after cataract surgery: a systematic review and network meta-analysis. *Graefes Arch Clin Exp Ophthalmol.* 2017;255(4):639-649.
11. Hoffman RS, Braga-Mele R, Donaldson K, et al. Cataract surgery and nonsteroidal antiinflammatory drugs. *J Cataract Refract Surg.* 2016;42(9):1368-1379.
12. Kessel L, Tendal B, Jorgensen KJ, et al. Post-cataract prevention of inflammation and macular edema by steroid and nonsteroidal anti-inflammatory eye drops: a systematic review. *Ophthalmology.* 2014; 121(10):1915-1924.
13. Kim SJ, Schoenberger SD, Thorne JE, et al. Topical nonsteroidal anti-inflammatory drugs and cataract surgery: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2015;122(11):2159-2168.
14. Quintana NE, Allocco AR, Ponce JA, Magurno MG. Non steroidal anti-inflammatory drugs in the prevention of cystoid macular edema after uneventful cataract surgery. *Clin Ophthalmol.* 2014;8:1209-1212.
15. Sheppard JD. Topical bromfenac for prevention and treatment of cystoid macular edema following cataract surgery: a review. *Clin Ophthalmol.* 2016;10:2099-2111.
16. Carreno E, Portero A, Galarreta DJ, Herreras JM. Update on twice-daily bromfenac sodium sesquihydrate to treat postoperative ocular inflammation following cataract extraction. *Clin Ophthalmol.* 2012;6:637-644.
17. Dick HB, Schultz T. [New Developments in Cataract Surgery] [published online ahead of print January 13, 2017]. *Klin Monbl Augenheilkd.* doi: 10.1055/s-0042-121423.
18. Gonzalez-Salinas R, Guarnieri A, Guirao Navarro MC, Saenz-de-Viteri M. Patient considerations in cataract surgery - the role of combined therapy using phenylephrine and ketorolac. *Patient Prefer Adherence.* 2016;10:1795-1801.
19. Jung JW, Chung BH, Kim EK, et al. The effects of two non-Steroidal anti-Inflammatory drugs, bromfenac 0.1% and ketorolac 0.45%, on cataract surgery. *Yonsei Med J.* 2015;56(6):1671-1677.
20. Liu C, Liu Y, Ye S, et al. Effect of topical nonsteroidal anti-inflammatory drugs and nuclear hardness on maintenance of mydriasis during phacoemulsification surgery. *J Ocul Pharmacol Ther.* 2014;30(10):831-836.
21. Schultz T, Joachim SC, Szuler M, et al. NSAID Pretreatment inhibits prostaglandin release in femtosecond laser-assisted cataract surgery. *J Refract Surg.* 2015;31(12):791-794.
22. Lane SS, Holland EJ. Loteprednol etabonate 0.5% versus prednisolone acetate 1.0% for the treatment of inflammation after cataract surgery. *J Cataract Refract Surg.* 2013;39(2):168-173.
23. Lee TH, Choi W, Ji YS, Yoon KC. Comparison of ketorolac 0.45% versus diclofenac 0.1% for macular thickness and volume after uncomplicated cataract surgery. *Acta Ophthalmol.* 2016;94(3):e177-182.
24. Lim BX, Lim CH, Lim DK, et al. Prophylactic non-steroidal anti-inflammatory drugs for the prevention of macular oedema after cataract surgery. *Cochrane Database Syst Rev.* 2016;11:CD006683.
25. McCafferty S, Harris A, Kew C, et al. Pseudophakic cystoid macular edema prevention and risk factors; prospective study with adjunctive once daily topical nepafenac 0.3% versus placebo. *BMC Ophthalmol.* 2017;17(1):16.
26. Moschos MM, Chatziralli IP, Pantazis P, et al. Is topical diclofenac essential before and after uneventful phacoemulsification cataract surgery? *J Ocul Pharmacol Ther.* 2012;28(4):335-339.
27. Ramakrishnan S, Baskaran P, Talwar B, Venkatesh R. Prospective, randomized study comparing the effect of 0.1% nepafenac and 0.4% ketorolac tromethamine on macular thickness in cataract surgery patients with low risk for cystoid macular edema. *Asia Pac J Ophthalmol (Phila).* 2015;4(4):216-220.
28. Sahu S, Ram J, Bansal R, et al. Effect of topical ketorolac 0.4%, nepafenac 0.1%, and bromfenac 0.09% on postoperative inflammation using laser flare photometry in patients having phacoemulsification. *J Cataract Refract Surg.* 2015;41(10):2043-2048.
29. Shorstein NH, Liu L, Waxman MD, Herrinton LJ. Comparative effectiveness of three prophylactic strategies to prevent clinical macular edema after phacoemulsification surgery. *Ophthalmology.* 2015;122(12):2450-2456.
30. Ticly FG, Lira RP, Zanetti FR, et al. Prophylactic use of ketorolac tromethamine in cataract surgery: a randomized trial. *J Ocul Pharmacol Ther.* 2014;30(6):495-501.
31. Turan-Vural E, Halili E, Serin D. Assessing the effects of ketorolac and acetazolamide on macular thickness by optical coherence tomography following cataract surgery. *Int Ophthalmol.* 2014;34(3):525-531.
32. Tzelikis PF, Vieira M, Hida WT, et al. Comparison of ketorolac 0.4% and nepafenac 0.1% for the prevention of cystoid macular oedema after phacoemulsification: prospective placebo-controlled randomised study. *Br J Ophthalmol.* 2015;99(5):654-658.
33. Wang QW, Yao K, Xu W, et al. Bromfenac sodium 0.1%, fluorometholone 0.1% and dexamethasone 0.1% for control of ocular

inflammation and prevention of cystoid macular edema after phacoemulsification. *Ophthalmologica.* 2013;229(4):187-194.
34. Yasuda K, Miyazawa A, Shimura M. A comparison of preservative-free diclofenac and preserved diclofenac eye drops after cataract surgery in patients with diabetic retinopathy. *J Ocul Pharmacol Ther.* 2012;28(3):283-289.
35. Zaczek A, Artzen D, Laurell CG, et al. Nepafenac 0.1% plus dexamethasone 0.1% versus dexamethasone alone: effect on macular swelling after cataract surgery. *J Cataract Refract Surg.* 2014;40(9):1498-1505.
36. Kim SJ, Patel SN, Sternberg P, Jr. Routine use of nonsteroidal anti-inflammatory drugs with corticosteroids in cataract surgery: beneficial or redundant? *Ophthalmology.* 2016;123(3):444-446.
37. Gira JP, Sampson R, Silverstein SM, et al. Evaluating the patient experience after implantation of a 0.4 mg sustained release dexamethasone intracanalicular insert (Dextenza): results of a qualitative survey. *Patient Prefer Adherence.* 2017;11:487-494.
38. BromSite [prescribing information]. Alameda, CA: InSite Vision, 2016.
39. Waterbury LD, Silliman D, Jolas T. Comparison of cyclooxygenase inhibitory activity and ocular anti-inflammatory effects of ketorolac tromethamine and bromfenac sodium. *Curr Med Res Opin.* 2006;22(6):1133-1140.
40. Cho H, Wolf KJ, Wolf EJ. Management of ocular inflammation and pain following cataract surgery: focus on bromfenac ophthalmic solution. *Clin Ophthalmol.* 2009;3:199-210.
41. Bronuck [package insert]. Osaka, Japan: Senju Pharmaceutical Co., 2009.
42. Xibrom [package insert]. Irvine, CA: ISTA Pharmaceuticals, 2010.
43. Bromday [package insert]. Irvine, CA: ISTA Pharmaceuticals, 2011.
44. Committee for Medicinal Products for Human Use (CHMP). Yellox Assessment Report. Report No.: EMA/431843/2011. 2011 May 19.
45. Bowman LM, Si E, Pang J, et al. Development of a topical polymeric mucoadhesive ocular delivery system for azithromycin. *J Ocul Pharmacol Ther.* 2009;25(2):133-139.
46. Ghate D, Edelhauser HF. Ocular drug delivery. *Expert Opin Drug Deliv.* 2006;3(2):275-287.
47. Mishima S, Gasset A, Klyce SD, Jr., Baum JL. Determination of tear volume and tear flow. *Invest Ophthalmol.* 1966;5(3):264-276.
48. Donnenfeld E. Current use of non-steroidal anti-inflammatory drugs in the treatment of ocular inflammation related to cataract surgery. *European Ophthalmic Review.* 2012;6(3):173-177.
49. Donnenfeld ED, Nichamin LD, Hardten DR, et al. Twice-daily, preservative-free ketorolac 0.45% for treatment of inflammation and pain after cataract surgery. *Am J Ophthalmol.* 2011;151(3):420-426.
50. Solomon KD, Cheetham JK, DeGryse R, et al. Topical ketorolac tromethamine 0.5% ophthalmic solution in ocular inflammation after cataract surgery. *Ophthalmology.* 2001;108(2):331-337.
51. Khanal S, Tomlinson A, Diaper CJ. Tear physiology of aqueous deficiency and evaporative dry eye. *Optom Vis Sci.* 2009;86(11):1235-1240.
52. Occhipinti JR, Mosier MA, LaMotte J, Monji GT. Fluorophotometric measurement of human tear turnover rate. *Curr Eye Res.* 1988;7(10):995-1000.
53. Sack RA, Sathe S, Beaton A. Tear turnover and immune and inflammatory processes in the open-eye and closed-eye environments: relationship to extended wear contact lens use. *Eye Contact Lens.* 2003;29(1 Suppl):S80-82; discussion S3-4, S192-194.
54. Sorbara L, Simpson T, Vaccari S, et al. Tear turnover rate is reduced in patients with symptomatic dry eye. *Contact Lens and Anterior Eye.* 2003;27:15-20.
55. Hosseini K, Hutcheson J, Bowman LM. Aqueous humor concentration of Bromfenac 0.09% (Bromday) compared with Bromfenac in DuraSite 0.075% (Bromsite) in cataract patients undergoing phacoemulsification after 3 days dosing. Presented at: Association for Research in Vision and Ophthalmology; May 5-9, 2013; Seattle, Washington.
56. Krenzer KL, Zhang JZ, Coffey MJ, Richardson ME. Safety of repeated topical ocular administration of a polycarbophil-based formulation in several models of ocular surgery in rabbits. *J Cataract Refract Surg.* 2012;38(4):696-704.
57. Luchs J. Azithromycin in DuraSite for the treatment of blepharitis. *Clin Ophthalmol.* 2010;4:681-688.
58. Malhotra R, Gira J, Berdy GJ, Brusatti R. Safety of besifloxacin ophthalmic suspension 0.6% as a prophylactic antibiotic following routine cataract surgery: results of a prospective, parallel-group, investigator-masked study. *Clin Ophthalmol.* 2012;6:855-863.
59. Akpek EK, Vittitow J, Verhoeven RS, et al. Ocular surface distribution and pharmacokinetics of a novel ophthalmic 1% azithromycin formulation. *J Ocul Pharmacol Ther.* 2009;25(5):433-439.
60. Solomon R, Perry HD, Donnenfeld ED, Greenman HE. Slitlamp biomicroscopy of the tear film of patients using topical Restasis and Refresh Endura. *J Cataract Refract Surg.* 2005;31(4):661-663.
61. Singh RP, Narvekar A. Efficacy and safety of nepafenac 0.1% (Nevanac) for the reduction in risk of macular edema (ME) following cataract surgery in patients with diabetic retinopathy: results from 2 multicenter trials. Presented at: Euretina; September 11-14, 2014; London.
62. Schultz T, Joachim SC, Kuehn M, Dick HB. Changes in prostaglandin levels in patients undergoing femtosecond laser-assisted cataract surgery. *J Refract Surg.* 2013;29(11):742-747.
63. Schultz T, Joachim SC, Stellbogen M, Dick HB. Prostaglandin release during femtosecond laser-assisted cataract surgery: main inducer. *J Refract Surg.* 2015;31(2):78-81.
64. Henderson BA, Gayton JL, Chandler SP, et al. Safety and efficacy of bromfenac ophthalmic solution (Bromday) dosed once daily for postoperative ocular inflammation and pain. *Ophthalmology.* 2011;118(11):2120-2127.
65. Silverstein SM, Cable MG, Sadri E, et al. Once daily dosing of bromfenac ophthalmic solution 0.09% for postoperative ocular inflammation and pain. *Curr Med Res Opin.* 2011;27(9):1693-1703.

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# MANAGING OCULAR PAIN AND INFLAMMATION AFTER CATARACT SURGERY: DIFFERENTIATING AMONG THE NONSTEROIDAL ANTIINFLAMMATORY DRUGS PART 2

1 *AMA PRA Category 1 Credit*™ Expires May 2018

1. **Nonsteroidal antiinflammatory drugs (NSAIDs) have been used after cataract surgery for what purpose? (Choose all that apply)**
   a. Prevention of pain
   b. Prevention of cystoid macular edema
   c. Improve visual acuity
   d. IOP control
   e. Avoid corticosteroid use

2. **Initiating NSAID use ___ day(s) before surgery has been shown to result in a decreased risk of macular thickening on optical coherence tomography.**
   a. 0
   b. 0-2
   c. 1-3
   d. 3-5

3. **According to the panel, using only a steroid and not a concurrent NSAID(s) during the postoperative period can lead to _____**
   a. increased hyperemia
   b. reduced edema
   c. reduced amount of time for wound healing
   d. increased IOP spikes

4. **The panel recommends using which parameters to differentiate among the various NSAIDs? (Choose all that apply)**
   a. Molecule safety
   b. Molecule concentration
   c. Vehicle used to deliver molecule
   d. Time on market
   e. Molecule pharmacokinetic data

5. **In general, what percentage of a drug is absorbed in the eye after a topical drop is instilled?**
   a. 1%
   b. 3%
   c. 5%
   d. 7%

6. **Studies on NSAIDs have shown which is most toxic to the cornea?**
   a. Bromfenac
   b. Diclofenac
   c. Ketorolac
   d. Nepafenac

7. **The use of femtosecond lasers in cataract surgery has increased, and with it an increased risk of prostaglandin release after the femtosecond laser portion of the surgery. Incorporating the use of NSAIDs during the preoperative period _____**
   a. Is not necessary when using femtosecond lasers
   b. Should be done 3 to 4 days earlier than for patients undergoing standard phaco
   c. Should be limited to the "day of" surgery only
   d. Can help prevent miosis

8. **An 82-year-old patient with well-controlled diabetes presents for cataract surgery. An ocular examination does not find any evidence of diabetic macular edema or diabetic retinopathy. How long would the panelists recommend you keep this patient on NSAIDs after surgery?**
   a. No difference in postoperative course from nondiabetic patients
   b. 6 to 8 weeks after surgery, with a preplanned taper to coincide with corticosteroid use
   c. 4 weeks after surgery, with corticosteroid use planned for an additional month
   d. 3 months after surgery

## ACTIVITY EVALUATION

| **Did the program meet the following educational objectives?** | Agree | Neutral | Disagree |
|---|---|---|---|
| Describe the pharmacokinetic properties of the bromfenac molecule | _____ | _____ | _____ |
| Assess the ability of topical ophthalmic NSAIDs to treat postoperative inflammation and pain in a cataract patient | _____ | _____ | _____ |
| Analyze the safety profile of the bromfenac molecule | _____ | _____ | _____ |
| Discuss the obstacles patients face in compliance and adherence | _____ | _____ | _____ |
| Develop a plan to communicate compliance obstacles with patients | _____ | _____ | _____ |

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Do you feel the information presented will change your patient care? ❒ Yes ❒ No

Please identify how you will improve/change: _____

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_____

_____

Create/revise protocols, policies, and/or procedures. Please specify:

_____

_____

Please identify the barriers to change.

_____ Cost ___ Lack of consensus or professional guidelines _____ Lack of administrative support _____ Lack of experience

_____ Lack of time to assess/counsel patients _____ Lack of opportunity (patients) _____ Reimbursement/insurance issues

_____ Lack of resources (equipment) _____ Patient compliance issues _____ No barriers _____ Other

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