the Ophthalmologist

Cataract Surgery Outcomes Optimization With Innovative Drugs and Technologies

September 15, 2014

NEVANAC® 0.1% (nepafenac 1 mg/mL) is indicated for the prevention and treatment, in adult patients, of postoperative pain and inflammation associated with cataract surgery and the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients.[1]

This document has been developed for promotional purposes as a summary of an Alcon-sponsored symposium, titled "Cataract Surgery Outcomes Optimization With Innovative Drugs and Technologies," on September 15, 2014, at the time of the ESCRS 2014 Congress, London, UK.

Alcon
a Novartis company

Nevanac
(nepafenac ophthalmic suspension) 0.1%

Introduction of Physicians

EDWARD J. HOLLAND, MD

Dr. Holland is the director of cornea services at Cincinnati Eye Institute and professor of ophthalmology at the University of Cincinnati. He has a reputation for his knowledge and expertise in the field of cornea and external disease. He is frequently invited to attend lectures both nationally and internationally. Dr. Holland is the author of over 200 articles in peer-reviewed journals and has edited *Cornea*, the most widely read textbook on corneal disease and surgery.

NICHOLAS LEE, BSc, MBBS, FRCS, FRCOphth

Dr. Lee is a retina specialist. He has been a National Health Service (NHS) consultant at The Hillingdon Hospital in Middlesex and the Western Eye Hospital in London since 1997, in the United Kingdom. He leads the diabetic eye services at The Hillingdon Hospital and the Western Eye Hospital and is actively involved in the diabetic screening programs of both Primary Care Trusts. He has been lead clinician at The Hillingdon Hospital for 15 years.

Introduction

Cataract surgery is one of the most prevalent and important surgical procedures in the European Union (EU) (Figure 1). Cataract is defined by the World Health Organization as clouding of the lens of the eye, which prevents clear vision.[1] Cataract surgery is the most common surgical procedure performed in the developed world, affecting approximately 20 million people globally, and is the leading cause of blindness (responsible for 51% of blindness) in the world.[2-4] Fortunately, blindness from cataract is generally treatable through cataract surgery, which removes the clouded crystalline lens and replaces it with an artificial lens, thereby restoring vision.[2] Because of the importance and prevalence of cataract surgery, improvements in cataract surgery and patient management are continually implemented. These improvements in cataract surgery techniques and pharmaceutical management have enhanced surgical outcomes and decreased patient burden by limiting patient pain. One of the important additions to cataract surgery is the routine use of nonsteroidal anti-inflammatory drugs (NSAIDs) for cataract patient management pre- and postoperatively. NSAIDs are potent anti-inflammatory agents that are used preoperatively and postoperatively to prevent pain and inflammation associated with cataract surgery.[4] Recent evidence suggests that NSAIDs may be useful agents to prevent postoperative complications in diabetic patients.[3]

NEVANAC® 0.1% (nepafenac 1 mg/mL) is indicated for the prevention and treatment, in adult patients, of postoperative pain and inflammation associated with cataract surgery and the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients.[1]

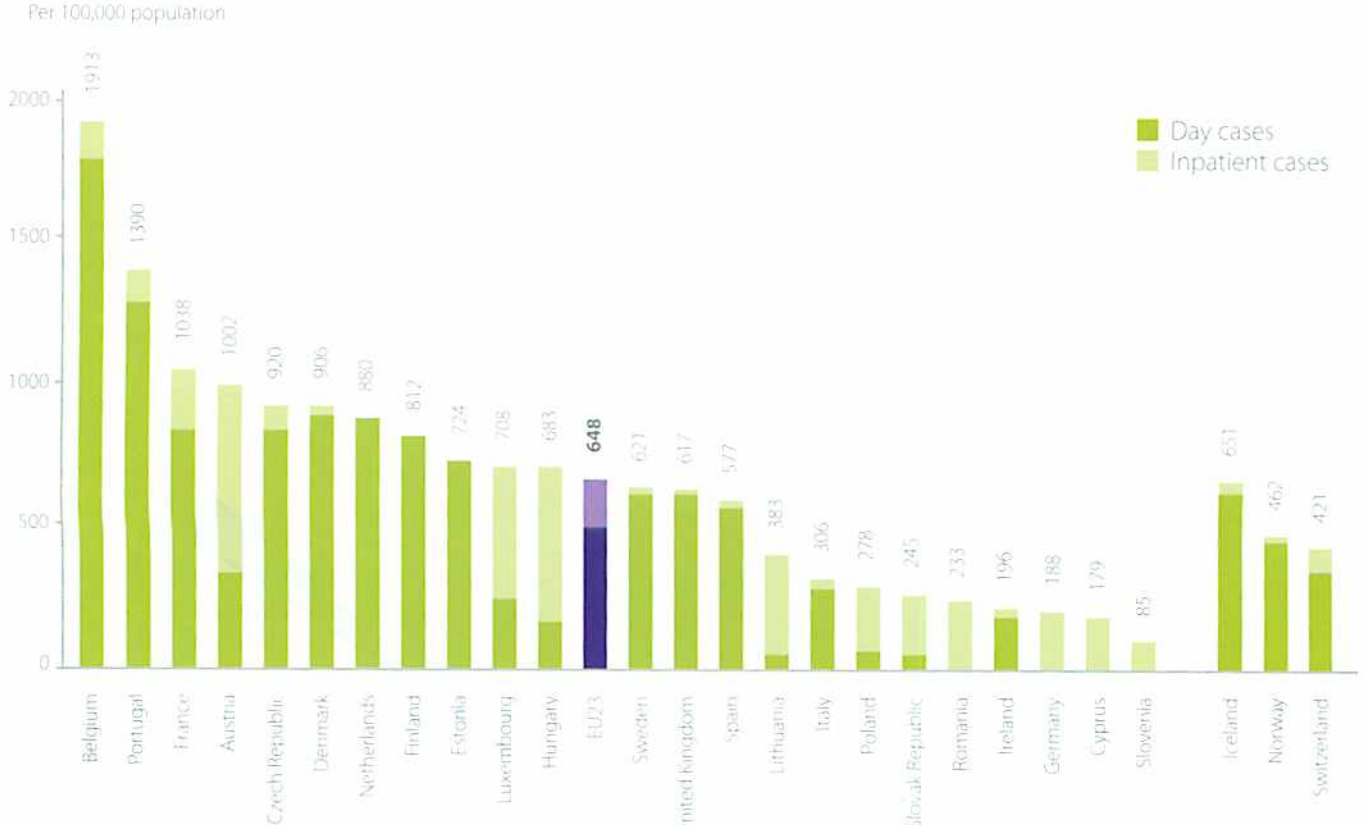
The recommended dosage in adults (including the elderly) for prevention and treatment of pain and inflammation is 1 drop of NEVANAC® 0.1 mg/mL in the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and up to 21 days of the postoperative period as directed by the clinician. An additional drop should be administered 30 to 120 minutes prior to surgery. For the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients, the dose is 1 drop of NEVANAC® 0.1 mg/mL in the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and up to 60 days of the postoperative period as directed by the clinician. An additional drop should be administered 30 to 120 minutes prior to surgery.

Due to population growth, longer life expectancy, sedentary lifestyles, and increasing prevalence of obesity, the diabetic patient population is quickly growing.[5] The number of people with diabetes mellitus is expected to increase to 366 million people in 2030.[6] This patient population is commonly plagued by visual impairment—most often cataracts.[7] In diabetic patients, cataracts occur at an earlier age and two to five times more frequently than in patients without diabetes mellitus.[5] Overall, approximately 20% of all patients undergoing cataract surgery also have diabetes mellitus, making this condition an important concern in cataract surgery.[8] Although advancements in cataract surgery have made it a very effective procedure with minimal adverse events, there are still some important complications associated with cataract surgery to consider (Figure 2).

Introduction *(continued)*

The diabetic patient population is at a greater risk for some of the complications that may arise after cataract surgery, including posterior synechiae, pupillary block, severe iritis, and macular oedema.[1] Many of the complications that may occur following cataract surgery are associated with inflammation, and for this reason, increased NSAID use may be one important consideration to improve patient outcomes.[1] Increased NSAID use may be especially important in diabetic patients because these patients are at greater risk of developing postoperative complications such as macular oedema.[1,3] Macular oedema is the leaking of fluid from the blood vessels in the eye, which can cause increased retinal thickness and decreased visual acuity.[3,4] Macular oedema is one of the most common reasons for decreased visual acuity following cataract surgery and can occur even in successful, uneventful cataract surgery.[5] Recently, two physicians—Edward Holland, MD, and Nicholas Lee, MD—participated as faculty at an Alcon-sponsored symposium during the 32nd annual meeting of the European Society of Cataract & Refractive Surgeons (ESCRS), to discuss the importance of managing inflammation in cataract surgery. In particular, the physicians stressed the importance of NSAID use in diabetic patients to reduce the risk of macular oedema, treating diabetic patients with NSAIDs up to 60 days following cataract surgery. This material is a summary of the discussion that occurred during this symposium.

FIGURE 1:
Cataract surgery rates for different European countries from the Organisation for European Co-operation and Development (OECD).[9]



Common Complications Post Cataract Surgery

Cystoid macular oedema, corneal oedema, endophthalmitis and persistent iritis are several complications that are related to inflammation.[10] NEVANAC® 0.1% (nepafenac 1 mg/mL) is indicated for the prevention and treatment, in adult patients, of postoperative pain and inflammation associated with cataract surgery and the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients.[1]

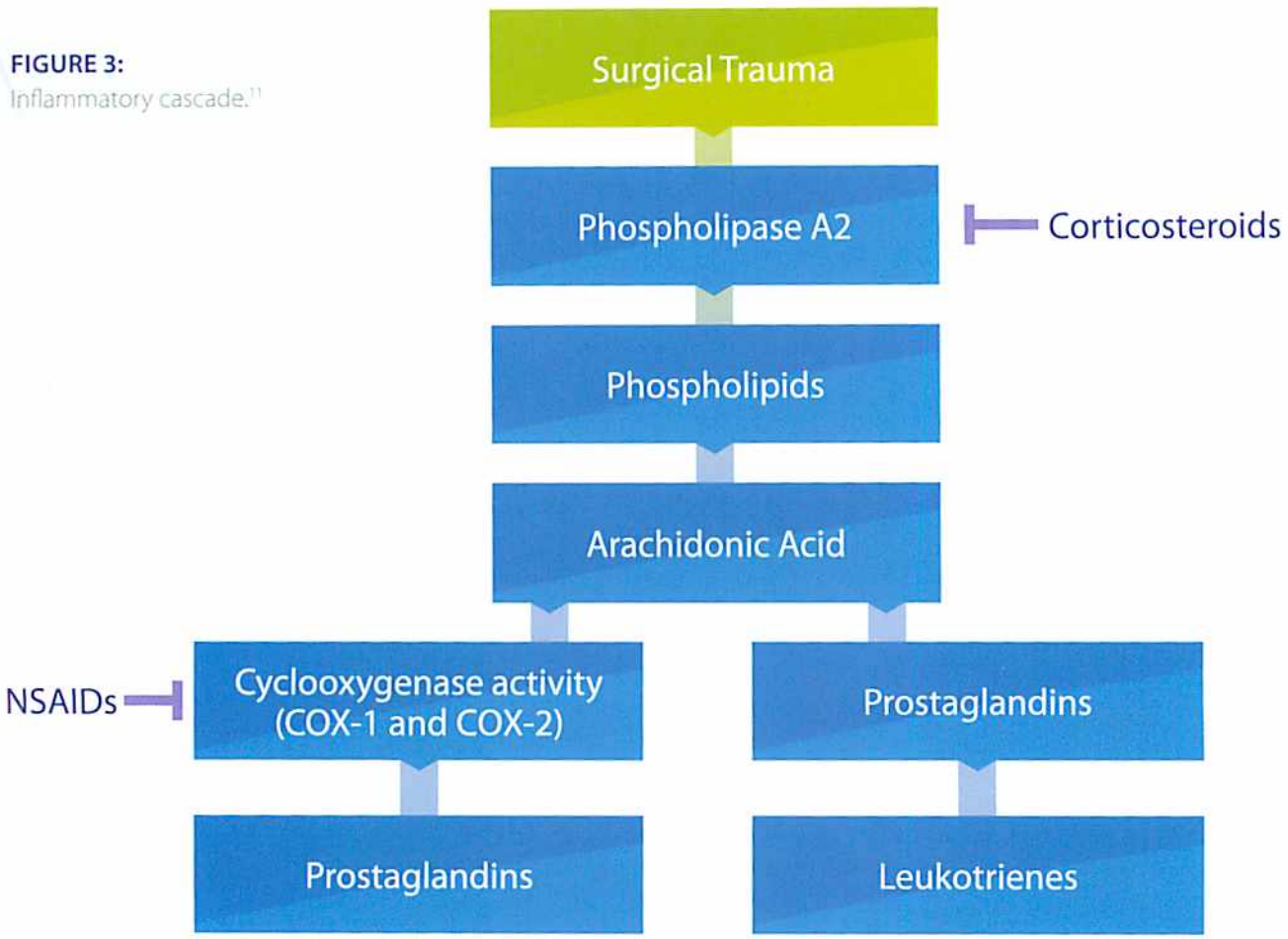
FIGURE 2:

Common postoperative cataract complications.[10]

Postoperative Complication	Range of Estimated Incidences (%)
Cystoid macular oedema	1.2 – 3.5
Corneal oedema	0.03 – 5.18
IOL dislocation, removal, or exchange	0.19 – 1.1
Endophthalmitis	0.03
Retinal tear, break, or detachment	0.14 – 0.9
Persistent iritis	1.1

Complications: The Role of Inflammation

FIGURE 3:
Inflammatory cascade.[11]



Like many other types of traumas or surgical procedures, cataract surgery causes an inflammatory response which, if left untreated, may contribute to serious side effects such as posterior synechiae, pupillary block, severe iritis, and macular oedema.[5,6] NEVANAC® 0.1% is indicated for the prevention and treatment of postoperative pain and inflammation associated with cataract surgery.[7] Thus, controlling and treating ocular inflammation is an essential part of cataract surgery. After surgical trauma occurs, phospholipase A2 is activated and converts phospholipids into arachidonic acid, which is then converted into prostaglandins by cyclooxygenase enzymes (COX-1 and COX-2) (Figure 3).[11] Prostaglandins are an important class of inflammatory mediators which, in the eye, act on iris smooth muscle and are largely responsible for the subsequent miosis, increased vasodilation, pain, redness, and loss of visual acuity.[12,13] A more insidious and dangerous consequence of inflammation is permanent vision loss as a result of cystoid macular oedema (CMO), which can occur 4 to 12 weeks after cataract surgery.[14,15] Thus, the inhibition of prostaglandins has beneficial effects on intraocular inflammation.

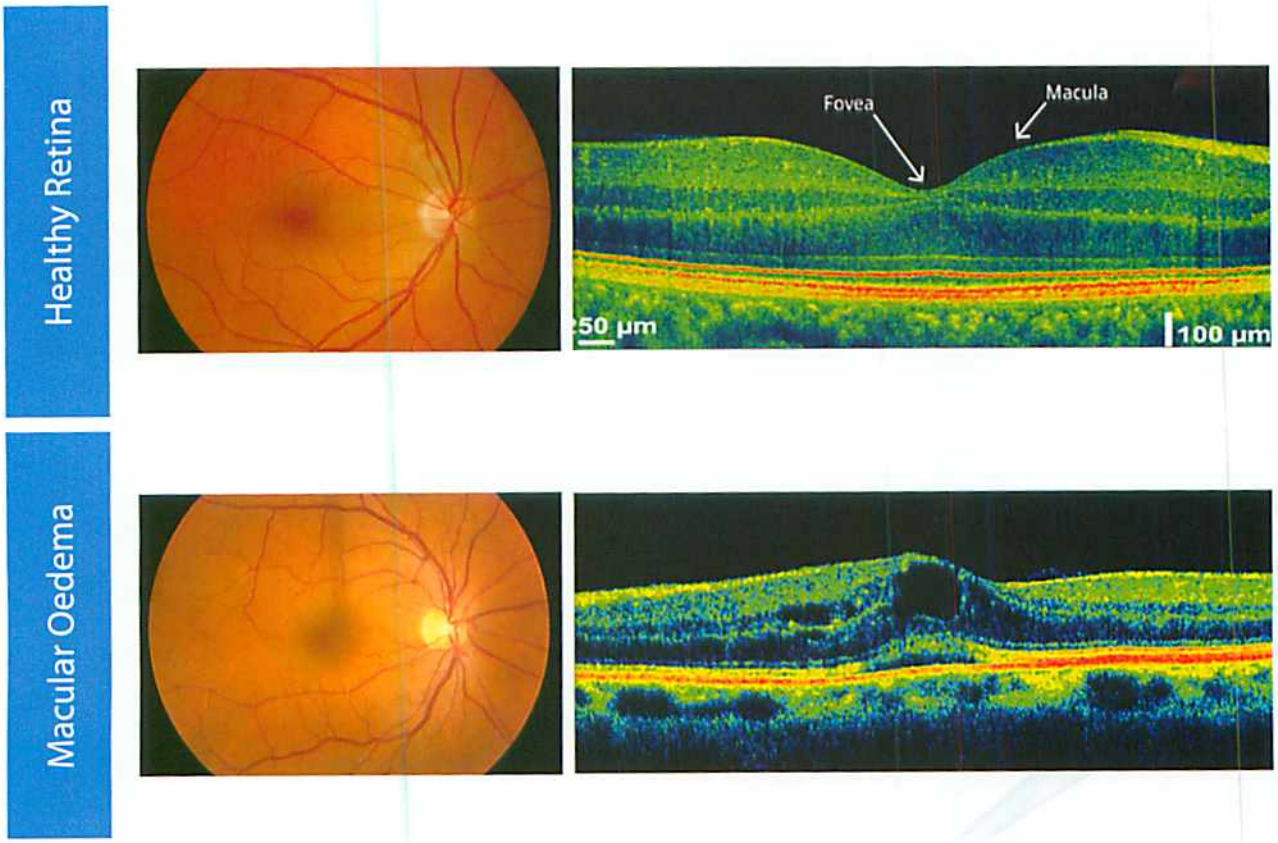
Presently there are two main classes of medications available to clinicians for management of inflammation: **corticosteroids** and **NSAIDs**.[5] Corticosteroids act early in the inflammatory cascade to inhibit phospholipase A2. NSAIDs, on the other hand, act later in the cascade to prevent the conversion of arachidonic acid to prostaglandins by inhibiting the action of cyclooxygenase enzymes (COX-1 and COX-2).[5]

Macular Oedema Underdiagnosis, Higher Prevalence in Diabetics Compared to Nondiabetic Patients[16]

Macular oedema is considered one of the most common reasons of poor visual outcome after cataract surgery, and it can occur even after successful, uncomplicated cataract surgery.[5] It is a swelling or thickening of the eye's macula and occurs when blood vessels in the retina leak fluids (Figure 4).[7]

When this occurs, the macula, which is responsible for detailed central vision, may not function properly leading to mild or even severe vision decrease.[7,8] In the majority of cases, the oedema is transient. However, in some cases it is chronic, and patients will have lasting cystic changes in the macula, with permanent visual loss.[17]

FIGURE 4:
Fundus and optical coherence tomography (OCT) images of a healthy subject and a subject with macular oedema.



Macular Oedema Underdiagnosis, Higher Prevalence in Diabetics Compared to Nondiabetic Patients[16]

(continued)

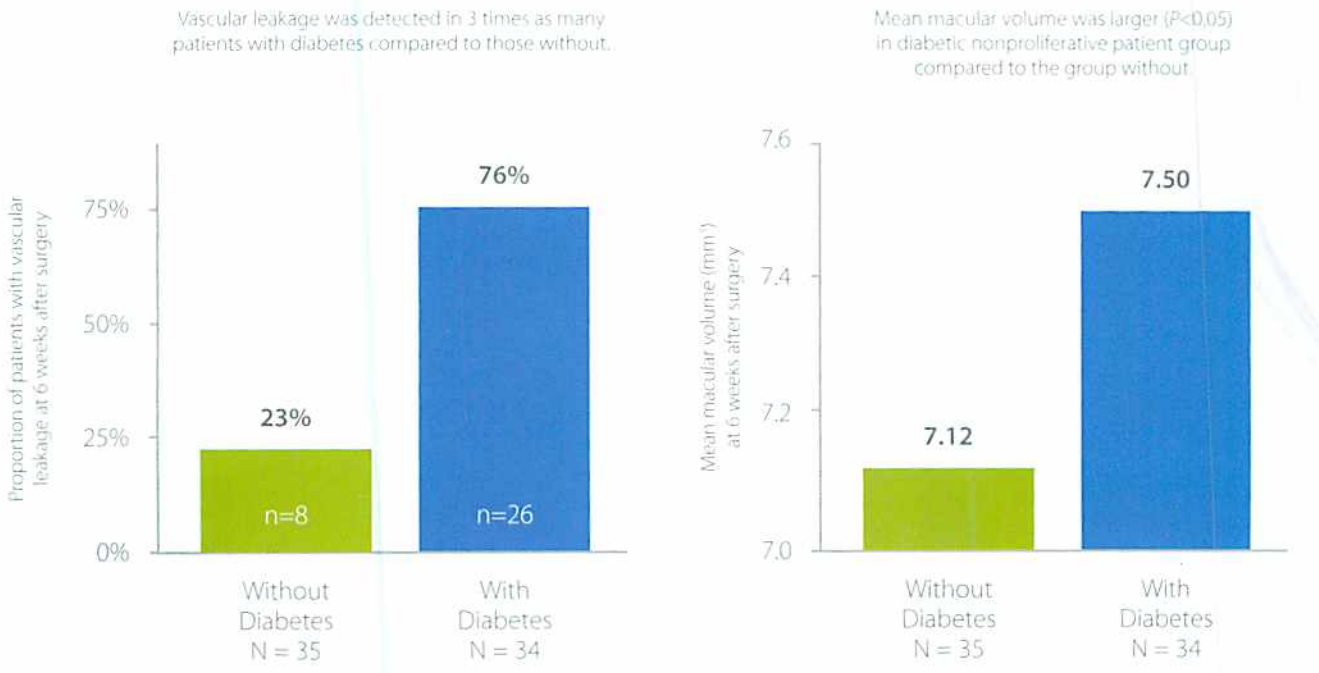
When macular oedema is associated with a decrease in visual acuity, it is classified as clinically significant macular oedema.[17] However, macular oedema can present without visual acuity changes, as characterised by fluorescein angiography or optical coherence tomography (OCT). Until recently, assessment of macular thickness was subjective, relying on slit-lamp stereoscopic biomicroscopy of the fundus.[18] With the advent of OCT, a more reliable and objective assessment became available to clinicians.[18] OCT creates a cross-sectional image of the retina by capturing reflected light from retinal structures.[19] It can show three basic structural changes of the retina: retinal swelling, cystoid oedema, and serious retinal detachment.[19] Additional advantages include its ability to monitor response to treatment by laser, intravitreal pharmacotherapies, and surgery.[20] CMO can be seen clearly on OCT as multiple circular cystic spaces in the retina, indicating intraretinal oedema.[20] OCT measurements are now used in many clinical studies of CMO treatment as critical endpoints.[16,21]

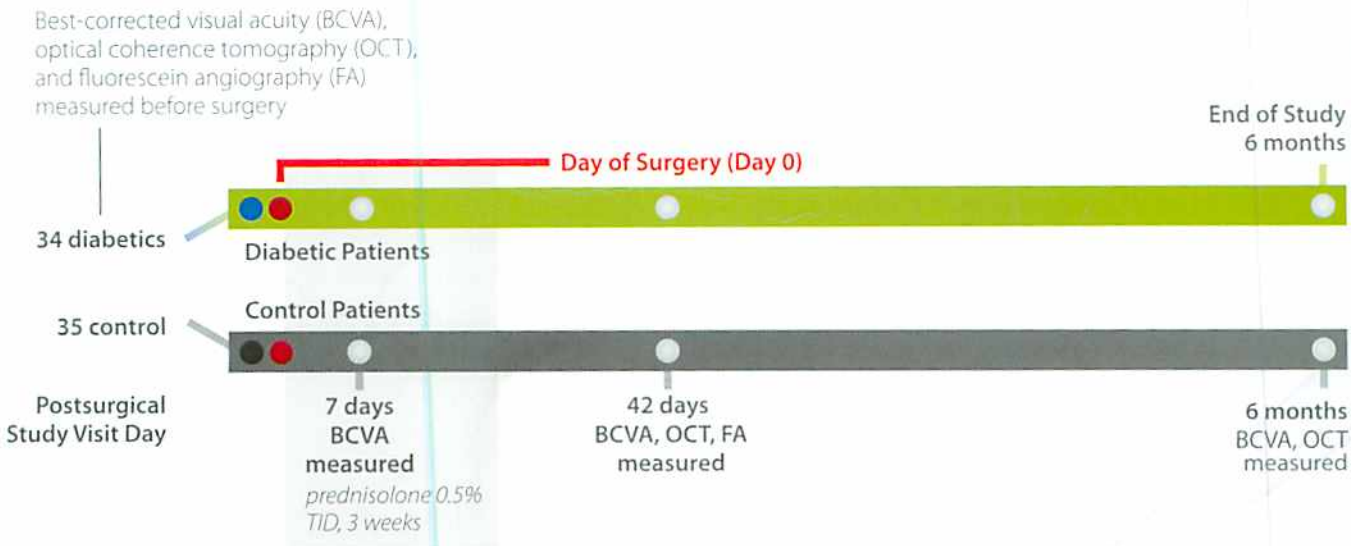
Because many patients may not be monitored for macular oedema with biomicroscopic examinations and only after visual acuity changes, macular oedema may be underdiagnosed. For example, the rate of clinically significant macular oedema has an estimated prevalence of 1% to 6%.[21,22] By contrast, macular oedema characterised by fluorescein angiogram or OCT shows macular oedema rates of 9% to 20%.[17,22] Therefore, macular oedema may occur more frequently than reported.

In diabetic patients, the development of CMO after cataract surgery is a frequent and complex problem. Patients with diabetes mellitus develop cataracts at an earlier age and 2 to 5 times more frequently than nondiabetic patients (Figure 5).[8] Although increased CMO prevalence in diabetic patients after cataract surgery is widely recognised, the true incidence has not been clearly determined in literature, and thus, it has a reported range from 31% to 81%.[16,17] CMO is an important consequence of cataract surgery and its prevention is essential, particularly in higher-risk patients such as those with diabetes.[8]

FIGURE 5:
Increased prevalence of vascular leakage in diabetic patients.[17]

A higher proportion of diabetic patients developed vascular leakage and had significantly higher mean macular volume than nondiabetic control subjects at 6 weeks post cataract surgery.[17]





If CME developed, patients were prescribed diclofenac 0.1% three times daily over 3 weeks.

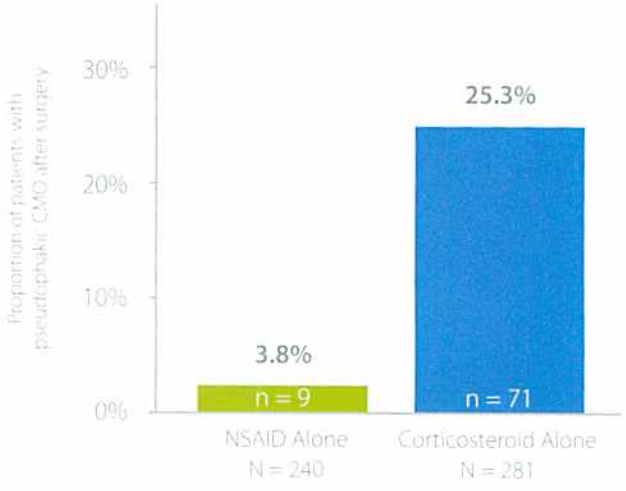
Despite the many years that CMO has been treated by clinicians, clear guidelines on how to manage CMO are not established. Currently, there is a large array of management options for CMO care. Typically treatment for CMO includes a steroid eye drop, NSAID eye drop, intravitreal steroid injection, or anti-vascular endothelial growth factor (VEGF) injection.[22] However, recent studies suggest that NSAID use may be an important consideration in CMO treatment.[5]

Role Of NSAIDs And Underutilization in Current Regimens (Current Guidelines)

A systematic review combined the results of 6 studies to investigate the formation of pseudophakic cystoid macular oedema in patients treated with NSAIDs alone or corticosteroids alone (Figure 6).[5] Four of the 6 studies evaluated the presence of CMO by fluorescein angiography at 5 weeks after cataract surgery, and 2 studies evaluated CMO by OCT at 1 month after cataract surgery. The results showed that NSAID use had an approximately 6.5-fold lower prevalence of CMO than corticosteroid when used alone. In a paper published by Kessel et al in 2014, the results of 15 randomised trials were combined in a meta-analysis that showed that the prevalence of pseudophakic cystoid macular edema at 1 month after uncomplicated cataract surgery was higher in patients treated with steroids, 25.3%, vs patients treated with NSAIDs, 3.8%.[5] The study found no indication that the use of topical NSAIDs was associated with a higher risk of adverse events than topical steroids nor was there any difference in visual outcome. Overall, the authors of the study recommend using topical NSAIDs after cataract surgery to prevent inflammation and the risk of developing macular oedema following cataract surgery.[5]

FIGURE 6:

In a paper published by Kessel et al in 2014, the results of 15 randomised trials were combined in a meta-analysis that showed that the prevalence of pseudophakic cystoid macular edema at 1 month after uncomplicated cataract surgery was higher in patients treated with steroids, 25.3%, vs patients treated with NSAIDs, 3.8%.[5]



Furthermore, NSAIDs have an important role in preventing postoperative pain and inflammation, which can impact patient comfort and satisfaction.[3] One study showed that 37% of patients reported postoperative ocular pain in the recovery room after the cataract procedure, while pain during and after cataract surgery was a major reason for lower patient satisfaction in regards to cataract care.[23] NSAIDs are becoming a major part of many proposed guidelines for cataract care in the United States. In fact, a recent American Academy of Ophthalmology survey found that 75% of respondents prescribe NSAIDs for all cataract patients.[24] However, this shift to increased NSAID use has not yet occurred in the European Union.

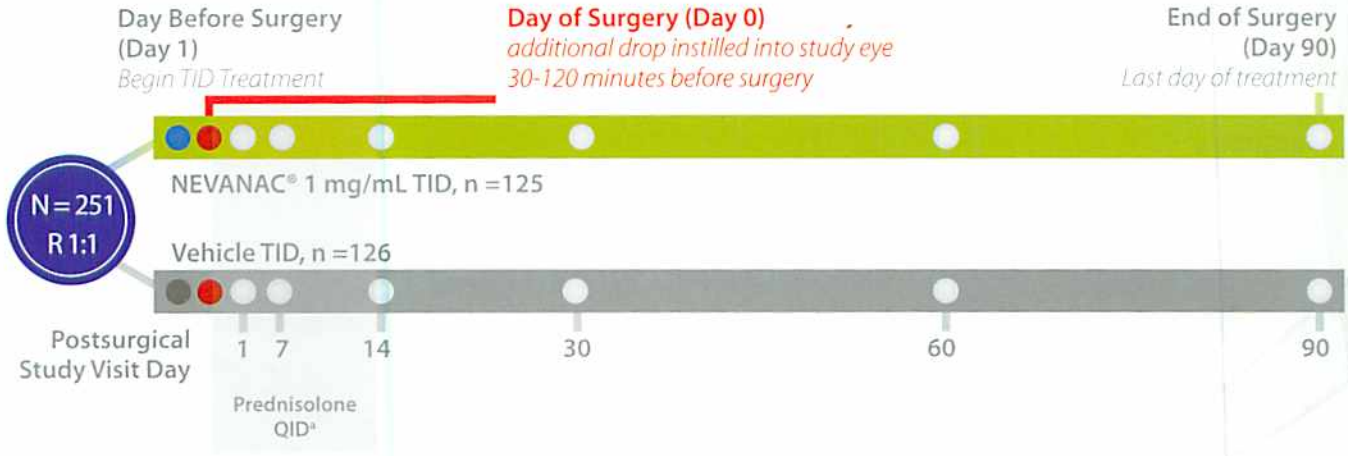
In the European Union, guidelines can differ by hospital, country, and even from physician to physician. The majority of European countries do not currently follow a guideline or standard treatment regimen post cataract surgery. The guidelines proposed by physicians from both the United States and Europe recommend using preoperative and postoperative NSAIDs.[9] Furthermore, NSAID use and duration should be increased for high-risk patients, such as diabetics. For example, some physicians may use NSAIDs for a short period of time postoperatively. However, macular oedema development typically occurs 4 to 12 weeks after cataract surgery.[25] Therefore, to have the greatest effect, diabetic patients should be treated for up to 60 days with NSAIDs postoperatively to prevent the risk of macular oedema following cataract surgery.

NSAID regimens are not being followed by all physicians in the EU, but evidence suggests that it may be time to incorporate them. NSAID use is important because NSAIDs improve patient experience by reducing postoperative pain and inflammation. Furthermore, the diabetic patient population is quickly growing, and since diabetics develop cataracts more frequently and are more prone to macular oedema, it is essential to use NSAIDs prophylactically to prevent macular oedema in diabetic patients.[1]

NEVANAC® for Reduction in the Risk of Postoperative Macular Oedema Associated With Cataract Surgery in Diabetic Adult Patients

The only NSAID currently approved for the reduction of risk for postoperative macular oedema associated with cataract surgery in diabetic adult patients is NEVANAC® (nepafenac ophthalmic suspension, 0.1%). NEVANAC® is also indicated in adults for prevention and treatment of postoperative pain and inflammation associated with cataract surgery.

FIGURE 7:
Study design employed by Singh et al to test the efficacy and safety of nepafenac, 1 mg/mL, in the prevention of postsurgical macular oedema in diabetic patients.[25]



Note: The dose of NEVANAC® is 1 drop in the conjunctival sac of the affected eye(s) 3 times daily, beginning 1 day prior to cataract surgery, continued on the day of surgery and up to 60 days of the postoperative period as directed by the clinician.

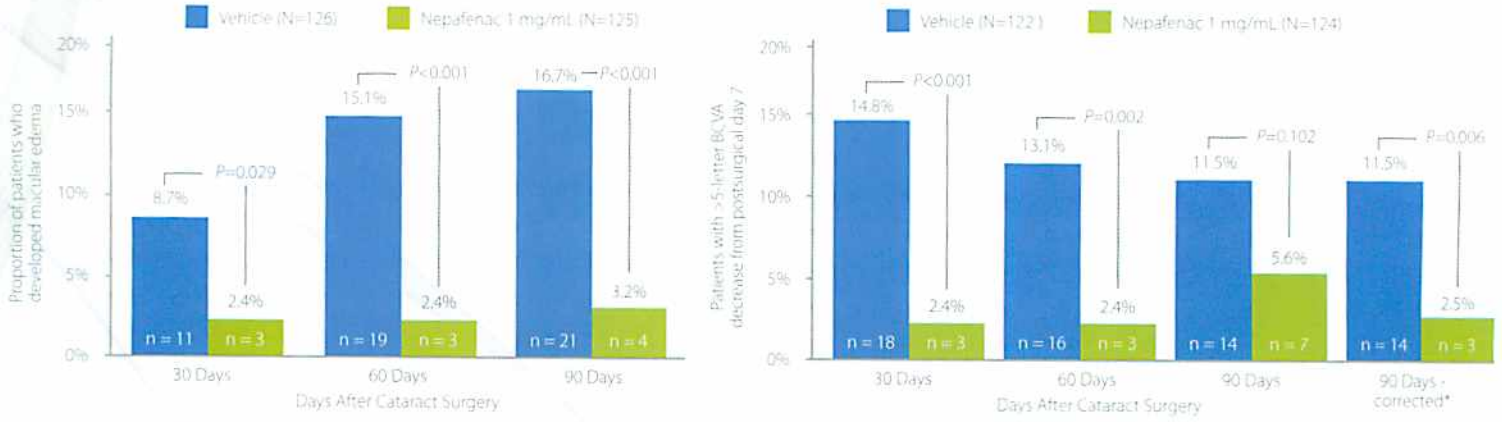
[a]Prednisolone (Omniped®) QID allowed for 2 weeks after surgery or longer if considered necessary to treat anterior segment inflammation.

NEVANAC® for Reduction in the Risk of Postoperative Macular Oedema Associated With Cataract Surgery in Diabetic Adult Patients *(continued)*

Singh et al conducted the pivotal clinical studies testing the efficacy of prophylactic nepafenac 1 mg/mL use to prevent macular oedema in diabetic patients.[25] This multicenter, randomised, double-masked, vehicle-controlled phase 3 study was designed to test the efficacy and safety of a 90-day course of nepafenac, 1 mg/mL, for prevention of macular oedema associated with cataract surgery in diabetic patients. A total of 251 diabetic patients were randomised 1:1 to receive nepafenac or vehicle treatment beginning 1 day before surgery and continuing up to 90 days postoperatively (Figure 7). CMO was defined as an increase of 30% or more in central subfield macular thickness relative to the pre-surgical baseline measurement. The results of the study determined that a significantly greater percentage of patients in the vehicle group developed macular oedema than in the nepafenac group at day 30 (8.7% vs 2.4%; *P*=0.029), at day 60 (15.1% vs 2.4%; *P*<0.001), and at day 90 (16.7% vs 3.2%; *P*<0.001) (Figure 8). Nepafenac also led to a significant decrease in the percentage of patients with >5-letter loss in best-corrected visual acuity (BCVA) compared with vehicle at day 90 post surgery (2.5% vs 11.5%; *P*=0.006). Furthermore, mean macular thickness and mean macular volume were significantly lower in patients treated with nepafenac than with vehicle from day 14 to day 90 (Figure 9). Finally, nepafenac treatment also led to a statistically significant increase in the proportion of patients with a gain of >15 lines BCVA after day 7. A total of 56.8% of nepafenac-treated patients compared with 41.9% of vehicle-treated patients displayed >15 lines BCVA gain (*P*=0.019).

FIGURE 8:

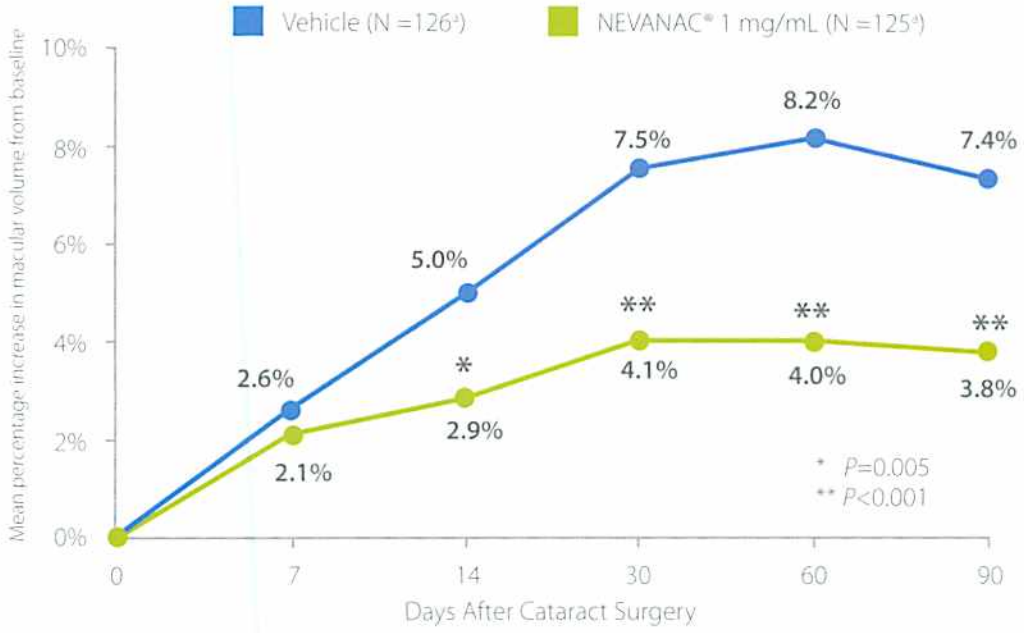
The Singh study demonstrated significantly lower rates of macular oedema and greater visual acuity in patients receiving nepafenac than those receiving vehicle for 60 days after cataract surgery.[25]

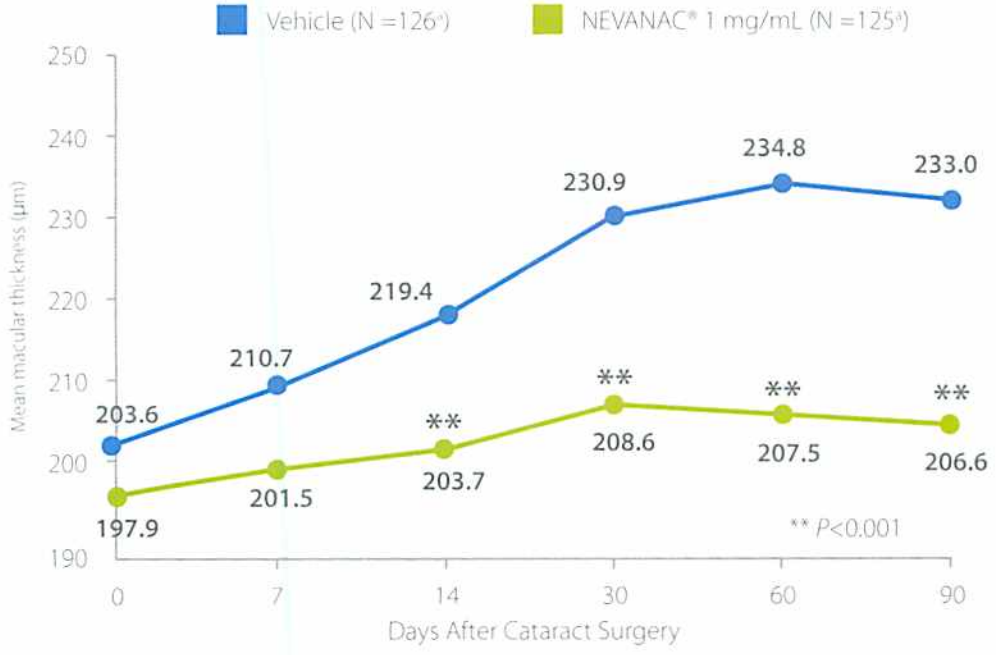


*Corrected data excludes 4 patients in nepafenac group with BCVA losses unrelated to macular oedema: 2 posterior capsular opacification, 1 clinically significant superficial punctate keratitis, 1 vitreous haemorrhage; no patients in vehicle group had confounding reasons for BCVA loss.

FIGURE 9:

Nepafenac treatment following cataract surgery in diabetic patients led to a statistically significant reduction in macular thickness and macular volume from day 14 through day 90, while vehicle treatment did not.[25]





[a]Vehicle group sample size was 124 at day 7 and 125 at day 14; Nepafenac group sample size was 121 at day 7. These graphs were adapted from Singh et al.[25]

This pivotal clinical study led to approval of NEVANAC® for the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients.

The Aim of Clinicians Should Be to Prevent Rather Than Treat Macular Oedema in Diabetic Patients After Cataract Surgery

One goal for clinicians should be to limit inflammation, which can be accomplished by proper preparation, successful surgery, and a successful postoperative therapeutic regimen.[9] NSAIDs should be used in the prevention of the risk of macular oedema in diabetic patients. Unfortunately, rather than preventing the risk of macular oedema in the diabetic population with integration of an NSAID, clinicians often wait until macular oedema develops before addressing it. Preventing the risk of macular oedema in this population may avoid many of the visual effects associated with this condition. Evidence suggests that diabetic patients have higher basal levels of inflammatory mediators and are more susceptible to macular oedema following cataract surgery.[3] In this high-risk patient population, NSAIDs should be used for a longer period of time than in nondiabetic patients. The standard length of time a patient is on an NSAID is low (approximately a few weeks); diabetic patients should be treated for up to 60 days in order to reduce the risk of the development of macular oedema. Prolonged NSAID use, up to 60 days after cataract surgery, may have enhanced efficacy in preventing macular oedema and improving visual outcomes in diabetic patients.

An important consideration for patients and clinicians is medication adherence. Patients often discontinue medication when they feel their symptoms have subsided, but CMO may develop 4 to 12 weeks after cataract surgery.[10] Therefore, one additional consideration with the extended use of NSAIDs in diabetic patients includes patient education. Diabetic patients must be aware of the importance of continuing their medication for the entire prescribed regimen in order to properly prevent macular oedema due to their increased risk for developing this condition.[6]

Therefore, an important next step in cataract surgery is physician and patient understanding of the importance of prolonged NSAID use. If diabetic patients are convinced of the benefits of the extended use of NSAIDs to prevent macular oedema, they will be more likely to adhere to this treatment regimen. This awareness will likely arise through physicians informing patients about the importance of full use of NSAIDs to improve outcomes.

Conclusions

NSAID use has become a mainstay in cataract management in the United States, but the integration of NSAIDs in Europe is not as widespread. NSAIDs are potent anti-inflammatory compounds that can improve surgical outcomes by managing postoperative pain and inflammation and may reduce the incidence of macular oedema in diabetic patients.[1] European physicians, who currently do not routinely prescribe NSAIDs, particularly in high-risk diabetic patients, should consider adding these agents to their regimens.

Despite successful and uncomplicated cataract surgery, macular oedema may still develop. It is a common cause of poor patient experience and decreased vision and is more common in the diabetic patient population. The postoperative use of NSAIDs for up to 60 days

can reduce the risk of macular oedema development in diabetic patients, and the benefits of prophylactic NSAID use are well established and supported by clinical studies. This marks an appropriate time for European clinicians to adopt clear guidelines to prevent CMO instead of treating it after it has developed.

NEVANAC® (nepafenac ophthalmic solution, 0.1%) is indicated for the reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients. Adding an extended NEVANAC® 0.1% regimen for diabetic patients following cataract surgery for up to 60 days can help to reduce the risk of macular oedema development, which may improve vision outcomes and patient satisfaction.

NEVANAC® 1 mg/mL Prescribing Information

(Refer to full Summary of Product Characteristics (SmPC) before prescribing)
1 ml of NEVANAC® suspension contains 1 mg nepafenac, benzalkonium chloride 0.05 mg.

INDICATION(S):
Prevention and treatment of postoperative pain and inflammation associated with cataract surgery. Reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients. Posology and method of administration.

Adults, including the elderly: For the prevention and treatment of pain and inflammation, 1 drop in the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and up to 21 days of the postoperative period, as directed by the clinician. An additional drop should be administered 30 to 120 minutes prior to surgery. For the reduction in the risk of macular oedema associated with cataract surgery in diabetic patients, 1 drop in the affected eye(s) 3 times daily beginning 1 day prior to cataract surgery, continued on the day of surgery and up to 60 days of the postoperative period, as directed by the clinician. An additional drop should be administered 30 to 120 minutes prior to surgery. Children and adolescents: Not recommended. Hepatic and renal impairment: No dose adjustment warranted. Contra-indications: Hypersensitivity to nepafenac, any of the excipients, or to other nonsteroidal anti-inflammatory drugs (NSAIDs); and in patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or other NSAIDs. Warnings and precautions: Do not inject or swallow. Instruct patients to avoid sunlight during treatment. Use of topical NSAIDs may result in keratitis, in some susceptible patients, continued use may be sight threatening. Topical NSAIDs may slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems. Topical NSAIDs should be used with caution in patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases, rheumatoid arthritis, or repeat ocular surgeries within a short period of time. These patients may be at increased risk for corneal adverse reactions which may become sight threatening. Prolonged use of topical NSAIDs may increase patient risk for occurrence and severity of corneal adverse reactions. Ophthalmic NSAIDs may cause increased bleeding of ocular tissues (including hyphaemas) in conjunction with ocular surgery. Use NEVANAC with caution in patients with known bleeding tendencies or who are receiving other medicinal products which may prolong bleeding time. Concomitant use of prostaglandin analogues and NEVANAC is not recommended. Benzalkonium chloride may cause keratopathy and irritation and is known to discolour soft contact lenses. Contact lens wear is not recommended during the postoperative

period following cataract surgery. Patients should be advised not to wear contact lenses during treatment with NEVANAC. Close monitoring is required with frequent or prolonged use. An acute ocular infection may be masked by the topical use of anti-inflammatory medicines. NSAIDs do not have any antimicrobial properties. In case of ocular infection, their use with anti-infectives should be undertaken with care. Cross-sensitivity: Potential exists for cross-sensitivity of nepafenac to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs. Interactions: In vitro studies have demonstrated a very low potential for interaction with other medicinal products and protein binding interactions. Pregnancy and lactation: Pregnancy: not recommended during pregnancy and in women of childbearing potential not using contraception. Lactation: Can be used during lactation. Effects on ability to drive and use machines: If blurred vision occurs wait until the vision clears before driving or using machinery. Undesirable effects: Common: Punctate keratitis. Frequency not known: Dizziness, impaired corneal healing, corneal scar, reduced visual acuity, eye irritation, eye swelling, blood pressure increased. Serious: Keratitis, choroidal effusion, corneal epithelium defect, corneal opacity. Prescribers should consult the SmPC in relation to other side effects. Overdose: No experience of overdose with ocular use. Application of >1 drop/eye is unlikely to lead to unwanted side effects. Practically no risk of adverse effects due to accidental oral ingestion. Incompatibilities: Not applicable. Special Precautions for Storage: Do not store above 30°C. Legal Category: POM. Package Quantities and Basic NHS Costs: 5ml £14.92. MA Number(s): EU/1/07/433/001. Further information available from the MA Holder: Alcon Laboratories (UK) Ltd, Frimley Business Park, Frimley Camberley, Surrey, GU16 7SR United Kingdom. Date of preparation: 20 May 2013 (V9). Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Alcon Medical Information. Tel: 0871 376 1402. Email: GB.ADR@alcon.com

REFERENCES:

1. NEVANAC [package insert]. Surrey, United Kingdom: Alcon Laboratories (UK) Ltd; 2014. **2.** World Health Organization (2010). Prevention of Blindness and Visual Impairment. Priority eye diseases—Cataract. Retrieved on 11/07/2014 from: http://www.who.int/blindness/causes/priority/en/index1.html. **3.** Allen D, Vasavada A. Cataract and surgery for cataract. *BMJ*. 2006;333(7559):128-132. **4.** Kim SJ, Flach AJ, Jampol LM. Nonsteroidal anti-inflammatory drugs in ophthalmology. *Surv Ophthalmol*. 2010;55(2):108-133. **5.** 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. **6.** Javadi M, Zarei-ghanavati S. Cataracts in diabetic patients: a review article. *J Ophthalmic Vis Res*. 2008;3(1):52-65. **7.** Tsilimbaris MK, Toka C. Macular edema and cataract surgery. In: *Cataract Surgery*. 2009:323-326. **8.** Alio JL, Bodaghi B, Tassignon M. Guidelines for managing post-cataract surgery inflammation: can we reach a consensus? *Ophthalmology Times Europe*. 2008:1-12. **9.** Lafortune G, Balestat G, Durand A. Comparing activities and performance of the hospital sector in Europe: how many surgical procedures performed as inpatient and day cases? 2012;1-80. **10.** American Academy of Ophthalmology Cataract and Anterior Segment Panel. Preferred Practice Pattern® Guidelines. Cataract in the adult eye. San Francisco, CA: American Academy of Ophthalmology; 2011. Available at www.aao.com/ppp. **11.** Holland EJ, Chan CC, Goldman DA, Henderson BA. The impact of cataract surgery stress on ocular inflammation and refractive cataract outcomes. *Eyeworld*. 2013;(suppl):1-4. **12.** Donnenfeld ED. Current use of non-steroidal anti-inflammatory drugs in the treatment of ocular inflammation related to cataract surgery. *European Ophthalmic Rev*. 2012;6(3):173-177. **13.** Schoenberger SD, Kim SJ, Sheng J, Rezaei KA, Lalezary M, Cherney E. Increased prostaglandin E2 (PGE2) levels in proliferative diabetic retinopathy, and correlation with VEGF and inflammatory cytokines. *Invest Ophthalmol Vis Sci*. 2012;53(9):5906-5911. **14.** Walter K. NSAIDs alone after cataract surgery—a better choice. 2014:48-50. **15.** O'hEineachain R. CME after cataract surgery. Retrieved on 11/07/2014 from http://www.eurotimes.org/node/1225. **16.** Kim SJ, Equi R, Bressler NM. Analysis of macular edema after cataract surgery in patients with diabetes using optical coherence tomography. *Ophthalmology*. 2007;114(5):881-889. **17.** Eriksson U, Alm A, Bjarnhall G, Granstam E, Matsson AW. Macular edema and visual outcome following cataract surgery in patients with diabetic retinopathy and controls. *Graefes Arch Clin Exp Ophthalmol*. 2011;249(3):349-359. **18.** Maalej A, Chelma W, Asma K, Riadh R, Salem G. Optical coherence tomography for diabetic macular edema: early diagnosis, classification and quantitative assessment. *J Clin Exp Ophthalmol*. 2012;(S2:004):1-6. **19.** Mavrikakis E. Macular edema in diabetes workup. Retrieved on 11/19/2014 from http://emedicine.medscape.com/article/1224138-workup. **20.** Baldaro E, Novais E, Prodocimo LM, Sallum JMF. Spectral-domain optical coherence tomography for macular edema. *Scientific World Journal*. 2014;(doi:10.1155/2014/191847. **21.** Pereira I, Utine CA, Ozturker C, et al. Evaluation of macular changes after uncomplicated phacoemulsification surgery by optical coherence tomography. *Curr Eye Res*. 2007;32(3):241-247. **22.** Rotsos TG, Moschos MM. Cystoid macular edema. *Clin Ophthalmol*. 2008;2(4):919-930. **23.** Fung D, Cohen MM, Stewart S, Davies A. What determines patient satisfaction with cataract care under topical local anesthesia and monitored sedation in a community hospital setting? *Anesth Analg*. 2005;100(6):1644-1650. **24.** Stuart A. *Invest Ophthalmol Vis Sci*. 2007;48:E-Abstract 5464. **25.** Singh R, Alpern L, Jaffe GJ, et al. Evaluation of nepafenac in prevention of macular edema following cataract surgery in patients with diabetic retinopathy. *Clin Ophthalmol*. 2012:1259-1269.

Alcon®
a Novartis company