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# Management of mydriasis and pain in cataract and intraocular lens surgery: review of current medications and future directions

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**Abstract:** The maintenance of mydriasis and the control of postoperative pain and inflammation are critical to the safety and success of cataract and intraocular lens replacement surgery. Appropriate mydriasis is usually achieved by topical and/or intracameral administration of anticholinergic agents, sympathomimetic agents, or both, with the most commonly used being cyclopentolate, tropicamide, and phenylephrine. Ocular inflammation is common after cataract surgery. Topical steroids and nonsteroidal anti-inflammatory drugs are widely used because they have been proved effective to control postsurgical inflammation and decrease pain. Topical nonsteroidal anti-inflammatory drugs have also been shown to help maintain dilation. However, use of multiple preoperative drops for pupil dilation, inflammation, and pain control have been shown to be time consuming, resulting in delays to the operating room, and they cause dissatisfaction among perioperative personnel; their use can also be associated with systemic side effects. Therefore, ophthalmologists have been in search of new options to streamline this process. This article will review the current medications commonly used for intraoperative mydriasis, as well as pain and inflammation control. In addition, a new combination of ketorolac, an anti-inflammatory agent, and phenylephrine, a mydriatic agent has recently been designed to maintain intraoperative mydriasis and to reduce postoperative pain and irritation from intraocular lens replacement surgery. Two Phase III clinical trials evaluating this combination have demonstrated statistically significant differences when compared to placebo in maintaining intraoperative mydriasis ( $P < 0.00001$ ) and in reducing pain in the early postoperative period ( $P = 0.0002$ ). This medication may be of benefit for use in cataract and lens replacement surgery in the near future.

**Keywords:** ketorolac, phenylephrine, intraocular lens replacement surgery, mydriasis

## Introduction

Appropriate mydriasis and inflammatory control during intraocular lens (IOL) exchange surgery is key to a successful surgical outcome.<sup>1,2</sup> To achieve these aims, a myriad of topical and/or intracameral agents have been used to dilate the pupil and to control postoperative pain and inflammation. Therefore, ophthalmologists have been in search of new options to streamline the process of intraoperative mydriasis and to treat postoperative inflammation. These new therapies include a combination of ketorolac, an anti-inflammatory agent, and phenylephrine, a mydriatic agent. Ketorolac acts as a nonselective cyclooxygenase (COX)-1/COX-2 inhibitor,<sup>3,4</sup> and phenylephrine as an alpha-1 adrenergic receptor agonist.<sup>5,6</sup> These compounds have shown effectiveness in controlling postoperative pain and inflammation and in the maintenance of mydriasis during surgery, respectively.<sup>6-10</sup> Ketorolac has also shown beneficial effects in the maintenance of intraoperative mydriasis; however, there is no consensus on its use as a

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primary mydriatic agent in ophthalmic surgery.<sup>11</sup> OMS302 is a new product developed by Omeros Corporation (Seattle, WA, USA), proprietary PharmacoSurgery™, that is targeted for use during IOL replacement (ILR) surgery, which includes cataract surgery and refractive lens exchange.<sup>12</sup> (None of the authors have or have had any current or past financial interest, support or research participation in Omeros Corporation). The OMS302 combination is designed to maintain intraoperative mydriasis and reduce postoperative pain and inflammation resulting from ILR surgery.

ILR surgery involves replacement of the original lens of the eye with an artificial IOL. This procedure is typically performed to treat cataracts or to correct a refractive error (ie, refractive lens exchange).<sup>13–15</sup> Maintenance of mydriasis is critical to the safety and surgical ease of the procedure.<sup>16</sup> Intraoperative pupil constriction is associated with an increased risk of intraoperative complications, especially in difficult cases, and it can result in prolonged surgical time.<sup>17,18</sup> In addition, the prevention of postoperative pain can improve patient satisfaction with the surgery and the surgeon.<sup>19</sup> OMS302 may be added to a standard irrigation solution used in ILR surgery and it can be delivered intracamerally to maintain mydriasis, to prevent miosis, and to reduce postoperative pain and inflammation.<sup>3</sup>

We will discuss the current status of ILR surgery including the available methods for intraoperative maintenance of mydriasis and the control of postoperative pain and inflammation. Then, we will review the progress and available data from the clinical research trials evaluating OMS302.

## IOL replacement surgery

### Epidemiology

Approximately 30% of the population over 65 years of age in the UK has visually significant cataracts.<sup>20,21</sup> An estimated 17.2% of the United States population, or approximately 20.5 million people over the age of 40 years, will have a cataract in either eye.<sup>20,22</sup> By 2020, this number in the US is expected to rise even further to 30.1 million.<sup>22</sup> Currently, cataracts

are responsible for approximately 60% of Medicare costs associated with vision care.<sup>20</sup> There are an estimated 3.6 million ILR procedures expected in the US this year, and 15 million in developed countries, with a projected annual growth rate of 3%–4%.<sup>3</sup> Most commonly, the indication for ILR surgery is cataract extraction, although refractive lens exchange is a growing segment of the lens replacement market.<sup>13–15</sup> The most frequent indications for removing and replacing a current IOL are IOL dislocation/decentration, incorrect IOL power, glare/optical aberrations, and IOL calcification.<sup>23–27</sup>

## Difficulties/complications of IOL replacement surgery

### Mydriasis in cataract surgery

Appropriate mydriasis during IOL exchange surgery is key to a successful surgical outcome.<sup>1</sup> Impaired visualization through a small pupil increases the chance of tissue damage, retained nuclear material, and vitreous loss.<sup>17,18</sup> Currently, dilation is achieved by topical and/or intracameral administration of anticholinergic agents, sympathomimetic agents, or both, with the most commonly used being cyclopentolate, tropicamide, and phenylephrine.<sup>28–31</sup> Topical mydriatic agents have been used for many years to dilate the pupil before cataract surgery. However, the use of multiple preoperative drops for pupil dilation was shown to be inexact, and this could delay surgery, and cause dissatisfaction among perioperative personnel; moreover, their use is also associated with systemic side effects.<sup>28,29</sup> Adverse ocular and systemic side effects make their use in high-risk patients (for example, hypertensive or elderly patients and children) more of a concern.<sup>30,31</sup> Therefore, ophthalmologists have been in search of new options to streamline the process of intraoperative mydriasis. Available mydriatic agents and their side effects are summarized in Table 1.

### Postoperative pain and inflammation

Ocular inflammation is common after cataract surgery. Untreated inflammation may cause pain, photophobia, and

**Table 1** Mydriatic agents for lens replacement surgery

Medication	Mechanism of dilation	Formulations	Side effects
Phenylephrine	Acts on the iris dilator muscle	2.5%, 5%, 10%	Hypertension, syncope, myocardial infarction, tachycardia, and arrhythmia
Tropicamide	Relaxation of the pupillary sphincter	0.5%, 1.0%	Dry mouth, tachycardia, headache, and allergic reactions
Cyclopentolate	Blocks contraction of the pupillary sphincter muscle	0.5%, 1.0%, 2.0%	Disorientation, dry mouth, incoherent speech, or visual disturbances
Atropine	Blocks contraction of the pupillary sphincter muscle	0.5%, 1.0%	Dry mouth, confusion, ventricular fibrillation, tachycardia, and nausea

other complications such as increased intraocular pressure, posterior capsule opacification, and cystoid macular edema.<sup>32</sup> Topical steroid therapy has been used for many years to control perioperative and postoperative inflammation, but it may inhibit corneal wound healing, increase intraocular pressure, increase the likelihood of infection, and lead to other serious complications.<sup>7,33–35</sup> Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used because they have been proven effective in the control of postsurgical inflammation without the risks of steroid-related side effects.<sup>7,34,36,37</sup> Preoperative treatment with NSAIDs, followed by combined therapy with NSAIDs and steroids postoperatively, has become the standard of care.<sup>36,38</sup>

## Use of analgesic/mydriatic agents in IOL replacement surgery

### Topical

Pharmacologic mydriasis can be achieved using a number of different topical agents. Phenylephrine is an adrenergic stimulant that acts on the iris dilator muscle. Its mydriatic effects have been known for some time.<sup>9,39,40</sup> There are different concentrations of phenylephrine and some studies have shown an increase in the effectiveness of dilation at higher concentrations.<sup>10,42</sup> However, higher concentrations have also been associated with more systemic side effects.<sup>30,41–43</sup> Side effects are mostly cardiovascular reactions, primarily seen in the high-risk populations such as among the elderly, hypertensive patients, and children, and these effects include a marked increase in blood pressure, myocardial infarction, arrhythmia, syncope, and tachycardia.<sup>44</sup>

Acetylcholine antagonists, such as tropicamide, allow for relaxation of the iris sphincter.<sup>45</sup> A common regimen for cataract surgery, as mentioned previously, includes phenylephrine and tropicamide with or without cyclopentolate. Topical tropicamide has been shown to cause nonocular reactions including dry mouth, allergic reactions, headache, and tachycardia.<sup>44,46</sup> Other muscarinic antagonists include cyclopentolate and atropine. Atropine is not as regularly used due to its long-lasting effects and given that evidence shows that there is not an increase in the mydriatic effect with the addition of atropine to the standard regimens.<sup>47</sup>

A new topical ocular insert, Mydriaser<sup>®</sup> (Spectrum Thea Pharmaceuticals Limited, Cheshire, UK) has also been evaluated for its efficacy and safety in its use for cataract surgery.<sup>48</sup> It is a small, oblong, cylinder-shaped insert that includes 0.28 mg of tropicamide and 5.4 mg of phenylephrine hydrochloride. It is placed in the inferior fornix of the eye

undergoing surgery. There was no statistically significant difference in the pupil diameter during surgery in patients using Mydriaser<sup>®</sup> versus those who received conventional topical dilating eye drops (tropicamide 1%, phenylephrine 10%, and cyclopentolate 1%).<sup>48</sup> However, pupil size was restored to normal much more quickly (when evaluated at 24 hours) with Mydriaser<sup>®</sup> compared to conventional therapy. This effect is likely related to the lack of cyclopentolate in the insert, which is known for its long-lasting pupillary effects.<sup>48</sup> Importantly, this insert needs to be in place 60 minutes prior to surgery; however, it does provide the advantage of not having to instill multiple rounds of eye drops.<sup>48</sup>

The preoperative use of NSAIDs has also been shown to be effective in maintaining mydriasis during cataract surgery.<sup>1</sup> Miosis during cataract surgery is thought to be partly related to an increase in the concentration of prostaglandins.<sup>49</sup> NSAIDs work by their ability to inhibit COX, which ultimately decreases the production of prostaglandins.<sup>50</sup> In addition, steroids are known to block the release of arachidonic acid, which is also a precursor for prostaglandin synthesis.<sup>51</sup> Options include, but are not limited to, ketorolac, nepafenac, flurbiprofen, and prednisolone. There is evidence that preoperative NSAIDs and/or steroid drops are effective in maintaining intraoperative mydriasis as compared to no other additional preoperative eye drops.<sup>1,52,53</sup>

Additionally, both NSAIDs and steroids are included in many perioperative drop regimens. Often, patients are maintained on an NSAID and a steroid drop for 2–4 weeks after cataract surgery for postoperative inflammation and pain control.<sup>51</sup> Nepafenac, a topical NSAID, is often used starting 1 day prior to cataract surgery and continued for the first 2 weeks in the postoperative period. It is an inhibitor of COX-1/COX-2 and has shown efficacy in controlling pain and inflammation associated with cataract surgery.<sup>54–56</sup> Normally, the nepafenac 0.1% ophthalmic suspension is used three times daily; however, a new once-daily 0.3% formulation has been shown to be noninferior to nepafenac 0.1% in controlling inflammation and pain.<sup>57</sup> Other available NSAIDs are presented in Table 2.

### Intracameral mydriatics

Intracameral mydriatics were introduced in 2003, and the original compound included a preservative-free mixture of cyclopentolate 0.1%, phenylephrine 1.5%, and lidocaine 1%.<sup>29</sup> Cyclopentolate later demonstrated no additional mydriatic effects to phenylephrine 1.5% when administered together with lidocaine.<sup>58</sup> It has also been established that the addition of epinephrine to the

**Table 2** Available nonsteroidal anti-inflammatory drugs

Drug	Formulations	Preparation	FDA approved
Indomethacin	1%	Indole	Available outside of the US
Flurbiprofen	0.03%	Water-soluble phenylalkanoic acid	Approved for intraoperative use during cataract surgery for the inhibition of miosis
Suprofen	1%	Water-soluble phenylalkanoic acid	Approved for intraoperative use during cataract surgery for the inhibition of miosis
Ketorolac tromethamine	0.5%	Water-soluble phenylalkanoic acid	Postoperative inflammation and pain control
Diclofenac	1%	Water-soluble phenylalkanoic acid	Minimize inflammation related to cataract surgery
Bromfenac	0.09%	Water-soluble phenylalkanoic acid	Postoperative inflammation
Nepafenac	0.1%	Prodrug arylacetic acid	Pain and inflammation associated with cataract surgery

**Abbreviation:** FDA, Food and Drug Administration.

irrigating solution is not necessary when intracameral mydriatics are being used.<sup>59</sup> Intracameral mydriatics have been shown to provide sufficient pupil dilation without causing measurable ocular side effects or influencing the phacoemulsification procedure negatively, as compared to topical mydriatics.<sup>29,60,61</sup>

One of the early randomized, controlled studies of intracameral injections<sup>29</sup> evaluated 60 patients who received either intracameral injection of mydriatics in phacoemulsification cataract surgery versus conventional topical therapy. One group received topical mydriatics comprised of three drops of cyclopentolate 1% and phenylephrine 1%, which were given 15 minutes apart, and 150  $\mu$ L of intracameral lidocaine hydrochloride 1%. The other group received intracameral mydriatics including 150  $\mu$ L of cyclopentolate 0.1%, phenylephrine 1.5%, and lidocaine hydrochloride 1% with placebo eye drops. The patients with intracameral mydriatics achieved rapid results with 95% $\pm$ 3% (standard deviation) of the final value of mydriasis within 20 seconds. Intracameral mydriatics were effective and safe as well. However, the pupils tended to be slightly smaller than in the topical group (mean 6.7 $\pm$ 1.0 mm versus 7.7 $\pm$ 1.0 mm;  $P$ <0.001), but the pupils did not contract intraoperatively.

Over time, other intracameral combinations were studied, and it was found that similar levels of effectiveness could be achieved with fewer medications in the formulation.<sup>29,60,61</sup> A study evaluated intraoperative mydriasis in 31 consecutive eyes scheduled for phacoemulsification cataract extraction and IOL implantation using an intracameral injection of 0.2–0.3 mL of preservative-free 1% lidocaine without any additional preoperative or intraoperative mydriatics.<sup>62</sup> The mean pupil diameter after intracameral lidocaine was significantly greater than the baseline pupil size, and it increased by 4.39 $\pm$ 0.53 mm. The pupil dilation was found to be satisfactory, persistent, and stable throughout the duration of the cataract surgery.<sup>62</sup> Previously, Cionni et al<sup>63</sup> used lidocaine 1% as a single intracameral mydriatic agent with the addition of

epinephrine to the irrigation fluid, and it showed adequate dilation for cataract surgery in 12 patients.

Intracameral lidocaine has also been shown to relieve intraoperative discomfort related to iris movement or manipulation.<sup>64,65</sup> The amount of 0.1–0.5 mL of unpreserved lidocaine can be injected into the anterior chamber for intraoperative pain control. Combined topical and intracameral anesthesia is well tolerated and it is effective in maintaining a low pain score during cataract surgery in most patients (approximately 76% of patients).<sup>66</sup> Intracameral triamcinolone acetonide has also shown effectiveness in the prevention of postoperative anterior chamber inflammation in patients undergoing phacoemulsification<sup>67</sup> and phacotrabeculectomy.<sup>67,68</sup>

The intracameral method has also been suggested to improve the operating conditions in more complicated cataract surgeries, including those with intraoperative floppy iris syndrome, by stabilizing the iris during surgery.<sup>69–72</sup> A recent study<sup>72</sup> evaluated the efficacy of intracameral phenylephrine on 42 patients receiving tamsulosin and undergoing cataract surgery. Intracameral phenylephrine was found to be highly effective for prophylaxis of floppy iris syndrome by reversing intraoperative floppy iris, restoring iris rigidity and causing the pupil to return to its normal preoperative size.<sup>72</sup>

## Mechanical

If the necessary pupil dilation cannot be achieved with medications alone, then alternative mechanical devices are available for dilation assistance. The next step in pupil dilation involves mechanical stretching of the pupil.<sup>73</sup> Other options include iris retainers, which are devices developed to hold the iris in an enlarged state, or physical cutting of the iris sphincter.<sup>73</sup> Adjunct devices for pupil expansion include nylon iris hooks, the Beehler pupil dilator (MORIA SA, Antony, France), and pupillary rings, including the Perfect Pupil (Milvella Limited, North Sydney, NSW, Australia), the Graether 2000 pupil-expander system

(Eagle Vision, Inc., Memphis, TN, USA), the Malyugin Ring® (MicroSurgical Technology, Redmond, WA, USA), and the Morcher pupil dilator (Morcher, Stuttgart, Germany).<sup>17,74–77</sup>

## Efficacy of phenylephrine and ketorolac on intraoperative mydriasis and postoperative pain control

Phenylephrine is a selective alpha-1 adrenergic receptor agonist, which has mydriatic effects on the iris.<sup>9,39,40</sup> It has shown success both topically and intracamerally in maintaining mydriasis during cataract surgery.<sup>9,10,29,70</sup> Several concentrations of phenylephrine have been evaluated and several studies have shown an increase in effectiveness of pupil dilation with higher concentrations.<sup>10,40</sup> However, other studies differ in their conclusions. One study found that 2.5% phenylephrine is as effective as 10% phenylephrine in the maintenance of mydriasis during both extracapsular and phacoemulsification cataract extraction when used in conjunction with cyclopentolate.<sup>78</sup> Importantly, with the use of a lower concentration of phenylephrine, there is a lower risk of systemic side effects.

Phenylephrine has been combined with a number of other topical drops to evaluate improvements in dilation and maintenance of dilation during cataract surgery. Most commonly, phenylephrine is combined with tropicamide. The use of tropicamide 1.0% and phenylephrine 2.5% proved to be an effective preoperative regimen for mydriasis in phacoemulsification, and it showed improved dilation compared to lower concentrations of tropicamide 0.5% and phenylephrine 0.5% with equal safety profiles.<sup>8</sup>

Ketorolac has been approved in the US for treatment of postoperative pain and inflammation after cataract surgery. Ketorolac has been used successfully in the alleviation of ocular inflammation and pain, the prevention and treatment of postoperative cystoid macular edema, and the prevention of intraoperative miosis.<sup>7,79–80</sup> Use of twice-daily ketorolac 0.45% for 16 days beginning 1 day before surgery resulted in a greater percentage of patients with an ocular inflammatory score of 0 on day 14 (52.5% compared to 26.5% in the vehicle group) and a greater number of patients with a pain score of 0 on day 1 postoperatively (72.4% versus 39.7%, respectively).<sup>79</sup> Topically, it is available in 0.4%, 0.5%, and 0.45% concentrations (ACULAR LS®, ACULAR®, and ACUVAIL®; Allergan, Inc., Irvine, CA, USA). It was first used at a concentration of 0.5% for the treatment of conjunctivitis and pain; however, lower concentrations have since become available, and the preservatives have also been changed to

assist in patient comfort upon instillation. Ketorolac 0.45% was found to be superior in its ability to inhibit prostaglandin E2 compared to nepafenac 0.1% and bromfenac 0.09%, which are used in patients undergoing phacoemulsification. Prostaglandin E2 is a mediator of inflammatory signals within the COX pathway and it can also enhance the constrictor action of the iris sphincter through mechanisms that are not dependent on cholinergic receptors.<sup>81–83</sup> Ketorolac tromethamine 0.5% was also better than prednisolone acetate 1% solutions in preventing surgically-induced miosis.<sup>11</sup>

Given the success of these two medications with cataract surgery, the thought of combining the two for use in intraoperative administration was implemented. The two medications would work synergistically in the establishment and maintenance of pupillary dilation and would prevent/control postoperative pain and inflammation to improve patient comfort and satisfaction.

## Early research on ketorolac/phenylephrine or OMS302

A number of the early clinical trials have reported success in the use of OMS302 in the maintenance of pupillary dilation during cataract surgery and in the prevention of postoperative pain and inflammation.<sup>84–87</sup> In a Phase IIB study, 223 subjects undergoing cataract extraction with lens replacement were randomized to receive treatment with one of the following: balanced salt solution only (vehicle); phenylephrine; ketorolac; or OMS302.<sup>84</sup>

Results from this study were announced in 2011 by Omeros Corporation. They reported that OMS302 and phenylephrine demonstrated significant improvement in the maintenance of intraoperative mydriasis, compared with vehicle and ketorolac alone ( $P < 0.00001$  for both comparisons).<sup>84</sup> They found that pupil diameter steadily decreased throughout the surgical procedure in both the vehicle and ketorolac groups, and vehicle and ketorolac use resulted in pupillary constriction greater than 4 mm from baseline. More than 20% of subjects in the vehicle-controlled group experienced a decrease in pupillary diameter of 2.5 mm or more during surgery. In contrast, only 4.4% of OMS302-treated subjects experienced this level of pupillary constriction.<sup>84</sup>

In addition, they found patients treated with OMS302 or ketorolac alone had significantly less pain in the early postoperative period than patients who received vehicle or phenylephrine alone ( $P < 0.05$  for both comparisons). Moderate to severe pain was reported by 17% of vehicle-treated subjects. They reported that OMS302 was safe and well-tolerated by the patient population.<sup>84</sup>

In the first Phase III trial, including over 400 participants, Omeros reported that OMS302 demonstrated statistically significant superiority over placebo in the maintenance of intraoperative mydriasis and a reduction of postoperative pain (both  $P < 0.00001$ ).<sup>87</sup>

Safety data were collected until postoperative day 90. The results from the first Phase III clinical trial were presented at the American Academy of Ophthalmology Meeting in Chicago, November 2012.<sup>89,90</sup> It was a 405-subject randomized, double-blind, and placebo-controlled study in which all patients received preoperative mydriatics and anesthetics. The investigators found that OMS302 was delivered intracamerally in balanced salt solution during the IOL replacement surgery. OMS302 was superior to placebo in maintaining mydriasis ( $P < 0.0001$ ) and preventing pain ( $P < 0.0001$ ). Fewer OMS302-treated subjects experienced a pupil diameter  $< 6$  mm at cortical clean up ( $P < 0.0001$ ) or moderate-to-severe pain ( $P = 0.006$ ), and more patients were pain-free ( $P = 0.011$ ). Adverse events were similar between the two groups. Therefore, their conclusion was that OMS302 significantly maintained mydriasis, prevented miosis, and decreased postoperative pain.<sup>90</sup> Additionally, a second trial was designed and initiated to evaluate the same efficacy and safety measures as the earlier Phase IIB and Phase III clinical trials.<sup>85</sup> In November 2012, Omeros Corporation announced that OMS302 met the coprimary efficacy end points in this second pivotal Phase III clinical trial by demonstrating statistically significant differences in the maintenance of intraoperative mydriasis ( $P < 0.00001$ ) and in the reduction of pain in the early postoperative period ( $P = 0.0002$ ) between OMS302 and placebo.<sup>85,88</sup> Pupil constriction of at least 3 mm was common in control patients, while constriction  $> 1$  mm was uncommon in OMS302-treated patients. Safety data were collected until postoperative day 90. OMS302 was reported to be well-tolerated in this Phase III clinical trial.<sup>85</sup> The incidence of adverse events was similar between the two treatment groups. Additionally, the adverse event profile was comparable to those seen in prior OMS302 clinical trials.<sup>84,87</sup>

In November of 2013, the combined results of the two Phase III clinical trials (both including  $> 400$  participants) were presented as a scientific poster at the American Academy of Ophthalmology Annual Meeting in New Orleans.<sup>91</sup> The results showed that OMS302 maintained a necessary pupil diameter throughout the IOL replacement procedure, while the placebo group showed progressive constriction ( $P < 0.00001$ ). Fewer OMS302-treated patients ( $< 3\%$ ) compared to placebo-treated patients ( $> 27\%$ )

experienced  $\geq 2.5$  mm pupillary constriction, representing a 50% decrease in the operative field ( $P < 0.001$ ) during the surgery.<sup>92</sup> Larger randomized clinical trials are warranted to provide evidence of the safety profile and efficacy of this formulation, OMS302, of its goal of maintaining mydriasis and preventing pain associated with IOL replacement surgery.

## Current ongoing research on the medication

### Approvals in Europe and the US for use in ophthalmic surgery

The US Food and Drug Administration (FDA) has accepted a proposed brand name for OMS302, Omidria™ (Omeros Corporation). The acceptance of the proprietary brand name by the FDA is subject to the agency's final determination prior to any approval of the product's new drug application and market launch, expected in 2014. Omeros Corporation previously provided the trademark application for Omidria™ from the United States Patent and Trademark Office (Alexandria, VA, USA). The company also submitted the brand name, Omidria™, to the European Medicines Agency, with a decision anticipated soon. Omeros Corporation also recently registered Omidria™ as a European Community Trade Mark. Finally, Omeros Corporation has also received permission by the FDA to study OMS302 in the pediatric population undergoing primary cataract extraction, and the results will likely be available in the postmarketing period.<sup>93</sup>

### Clinical trials ongoing or completed

There are four clinical trials<sup>84-87</sup> listed in Clinicaltrials.gov (see Table 3). Omeros Corporation has recently presented the most currently available results at the American Academy of Ophthalmology Annual Meeting in 2013;<sup>91</sup> however, the final official results and the report's submission to a peer-reviewed journal are still pending.

## Conclusion

Appropriate mydriasis and inflammatory control during intraocular lens exchange surgery is key to a successful surgical outcome.<sup>1,2</sup> To achieve these, a myriad of topical and/or intracameral agents have been used to dilate the pupil and to control postoperative pain and inflammation, as we have reviewed. A prospective new therapy, OMS302, is a combination of ketorolac, an anti-inflammatory agent, and phenylephrine, a mydriatic agent. At this time, the available evidence in peer-reviewed literature for this new agent is limited. We believe larger studies testing the efficacy and

**Table 3** Clinical trials pending published results

Clinical trial	Title	Phase	Status	Trial identifier
1	Safety, efficacy and pharmacokinetics of OMS302 in subjects undergoing intraocular lens replacement with phacoemulsification (OMS302-ILR-004) <sup>86</sup>	III	Completed, pending published results	NCT01579565
2	Safety and efficacy of OMS302 in subjects undergoing intraocular lens replacement with phacoemulsification (OMS302-ILR-003) <sup>78</sup>	III	Completed, pending published results	NCT01454063
3	Exploratory study of OMS302 injection in subjects undergoing unilateral cataract extraction by phacoemulsification <sup>87</sup>	I/II	Completed, pending published results	NCT00721695
4	Safety and efficacy of OMS302 in subjects undergoing unilateral cataract extraction with lens replacement (CELR) <sup>85</sup>	II	Completed, pending published results	NCT01193127

safety profile of this new formulation are warranted to provide more evidence that supports its use.

## Disclosure

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