HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OMIDRIA® safely and effectively. See full prescribing information for OMIDRIA.

OMIDRIA® (phenylephrine and ketorolac injection) 1% / 0.3%
Initial U.S. Approval: 2014

INDICATIONS AND USAGE

OMIDRIA is an alpha 1-adrenergic receptor agonist and nonselective cyclooxygenase inhibitor indicated for:

- Maintaining pupil size by preventing intraoperative miosis (1)
- Reducing postoperative pain (1)

OMIDRIA is added to an irrigation solution used during cataract surgery or intraocular lens replacement.

DOSAGE AND ADMINISTRATION

OMIDRIA must be diluted prior to use. For administration to patients undergoing cataract surgery or intraocular lens replacement, 4 mL of OMIDRIA is diluted in 500 mL of ophthalmic irrigating solution. Irrigation solution is to be used as needed for the surgical procedure. (2)

DOSAGE FORMS AND STRENGTHS

OMIDRIA is a sterile solution concentrate containing 1% w/v of phenylephrine and 0.3% w/v ketorolac in a single-patient-use vial. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

Systemic exposure of phenylephrine may cause elevations in blood pressure. (5.1)

ADVERSE REACTIONS

The most common reported adverse reactions at 2-24% are eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Omeros Corporation at 1-844-OMEROS1 or *www.omidria.com* or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

See 17 for PATIENT COUNSELING INFORMATION

Revised: June 2015

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION:

1 INDICATIONS AND USAGE

Omidria® is added to an ophthalmic irrigation solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

2 DOSAGE AND ADMINISTRATION

Omidria must be diluted prior to intraocular use. For administration to patients undergoing cataract surgery or intraocular lens replacement, 4 mL of Omidria is diluted in 500 mL of ophthalmic irrigation solution. Irrigation solution is to be used as needed for the surgical procedure.

The storage period for the diluted product is not more than 4 hours at room temperature or 24 hours under refrigerated conditions.

Do not use if the solution is cloudy or if it contains particulate matter.

3 DOSAGE FORMS AND STRENGTHS

Omidria is a sterile solution concentrate containing 10.16 mg/mL (1% w/v) of phenylephrine and 2.88 mg/mL (0.3% w/v) of ketorolac in a single-patient-use vial.

4 CONTRAINDICATIONS

Omidria is contraindicated in patients with a known hypersensitivity to any of its ingredients.

5 WARNINGS AND PRECAUTIONS

5.1 Elevated Blood Pressure

Systemic exposure of phenylephrine can cause elevations in blood pressure.

5.2 Cross-Sensitivity or Hypersensitivity

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other non-steroidal anti-inflammatories (NSAIDs). There have been reports of bronchospasm or exacerbation of asthma associated with the use of ketorolac in patients who either have a known hypersensitivity to aspirin/NSAIDs or a past medical history of asthma. Therefore, use Omidria with caution in individuals who have previously exhibited sensitivities to these drugs.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to the rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Table 1 shows frequently reported ocular adverse reactions with an incidence of ≥ 2% of subjects as seen in the combined clinical trial results from three randomized, placebo-controlled studies.

Table 1: Ocular Adverse Reactions Reported by ≥ 2% of Subjects

MedDRA Preferred Term	Placebo (N=462)	Omidria (N=459)
	n (%)	n (%)
Ocular Events		
Anterior Chamber Inflammation	102 (22%)	111 (24%)
Intraocular Pressure Increased	15 (3%)	20 (4%)
Posterior Capsule Opacification	16 (4%)	18 (4%)
Eye Irritation	6 (1%)	9 (2%)
Foreign Body Sensation in Eyes	11 (2%)	8 (2%)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C

Animal reproduction studies have not been conducted with Omidria or phenylephrine. It is also not known whether Omidria can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Omidria should be used in pregnant women only if clearly needed.

Ketorolac, administered during organogenesis, was not teratogenic in rabbits or rats at oral doses of 3.6 mg/kg/day and 10 mg/kg/day, respectively. These doses produced systemic exposure that is 1150 times and 4960 times the plasma exposure (based on C_{max}) at the recommended human ophthalmic dose (RHOD), respectively. When administered to rats after Day 17 of gestation at oral doses up to 1.5 mg/kg/day (740 times the plasma exposure at the RHOD), ketorolac produced dystocia and increased pup mortality.

Clinical Considerations:

Premature closure of the ductus arteriosus in the fetus has occurred with third trimester use of oral and injectable NSAIDs. Detectable ketorolac plasma concentrations are available following ocular Omidria administration [*see Clinical Pharmacology (12.3)*]. The use of Omidria during late pregnancy should be avoided.

8.3 Nursing Mothers

Because many drugs are excreted in human milk, caution should be exercised when Omidria is administered to nursing women.

8.4 Pediatric Use

Safety and effectiveness of Omidria in pediatric patients below the age of 18 years have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and adult patients.

10 OVERDOSAGE

Systemic overdosage of phenylephrine may cause a rise in blood pressure. It may also cause headache, anxiety, nausea, vomiting, and ventricular arrhythmias. Supportive care is recommended.

11 DESCRIPTION

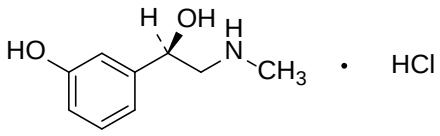
Omidria is a sterile aqueous solution concentrate containing the α_1-adrenergic receptor agonist phenylephrine HCl and the nonsteroidal anti-inflammatory ketorolac tromethamine.

The descriptions and structural formulae are:

Phenylephrine Hydrochloride Drug Substance:

Common Name: phenylephrine hydrochloride
Chemical Name: (-)-*m*-Hydroxy-α-[(methylamino)methyl]benzyl alcohol hydrochloride
Molecular Formula: $C_9H_{13}NO_2 \cdot HCl$
Molecular Weight: 203.67 g/mole

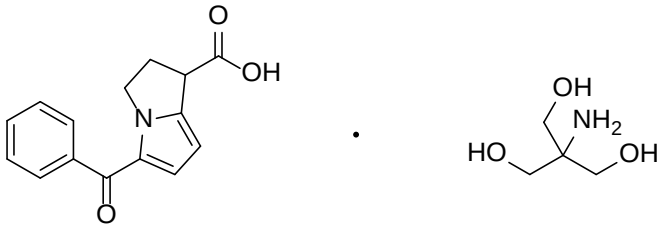
Figure 1: Chemical Structure for Phenylephrine HCl



Ketorolac Tromethamine Drug Substance:

Common Name: ketorolac tromethamine
Chemical Name: (±)-5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid : 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1)
Molecular Formula: $C_{15}H_{13}NO_3 \cdot C_4H_{11}NO_3$
Molecular Weight: 376.40 g/mole

Figure 2: Chemical Structure for Ketorolac Tromethamine



Omidria is a clear, colorless to slightly yellow, sterile solution concentrate with a pH of approximately 6.3.

Each vial of Omidria contains:

Actives: phenylephrine hydrochloride 12.4 mg/mL equivalent to 10.16 mg/mL of phenylephrine and ketorolac tromethamine 4.24 mg/mL equivalent to 2.88 mg/mL of ketorolac.

Inactives: citric acid monohydrate; sodium citrate dihydrate; water for injection; may include sodium hydroxide and/or hydrochloric acid for pH adjustment.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The two active pharmaceutical ingredients (API) in Omidria, phenylephrine and ketorolac, act to maintain pupil size by preventing intraoperative miosis, and reducing postoperative pain.

Phenylephrine is an α_1-adrenergic receptor agonist and, in the eye, acts as a mydriatic agent by contracting the radial muscle of the iris. Ketorolac is a nonsteroidal anti-inflammatory that inhibits both cyclooxygenase enzymes (COX-1 and COX-2), resulting in a decrease in tissue concentrations of prostaglandins to reduce pain due to surgical trauma. Ketorolac, by inhibiting prostaglandin synthesis secondary to ocular surgical insult or direct mechanical stimulation of the iris, also prevents surgically induced miosis.

12.3 Pharmacokinetics

In a pharmacokinetic study evaluating Omidria, systemic exposure to both phenylephrine and ketorolac was low or undetectable.

A single-dose of Omidria as part of the irrigation solution was administered in 14 patients during lens replacement surgery. The volume of irrigation solution used during surgery ranged between 150 mL to 300 mL (median 212.5 mL). Detectable phenylephrine plasma concentrations were observed in one of 14 subjects (range 1.2 to 1.4 ng/mL) during the first two hours after the initiation of Omidria administration. The observed phenylephrine plasma concentrations could not be distinguished from the preoperative administration of phenylephrine 2.5% ophthalmic solution prior to exposure to Omidria.

Ketorolac plasma concentrations were detected in 10 of 14 subjects (range 1.0 to 4.2 ng/mL) during the first 8 hours after the initiation of Omidria administration. The maximum ketorolac concentration was 15 ng/mL at 24 hours after the initiation of Omidria administration, which may have been due to application of postoperative ketorolac ophthalmic solution.

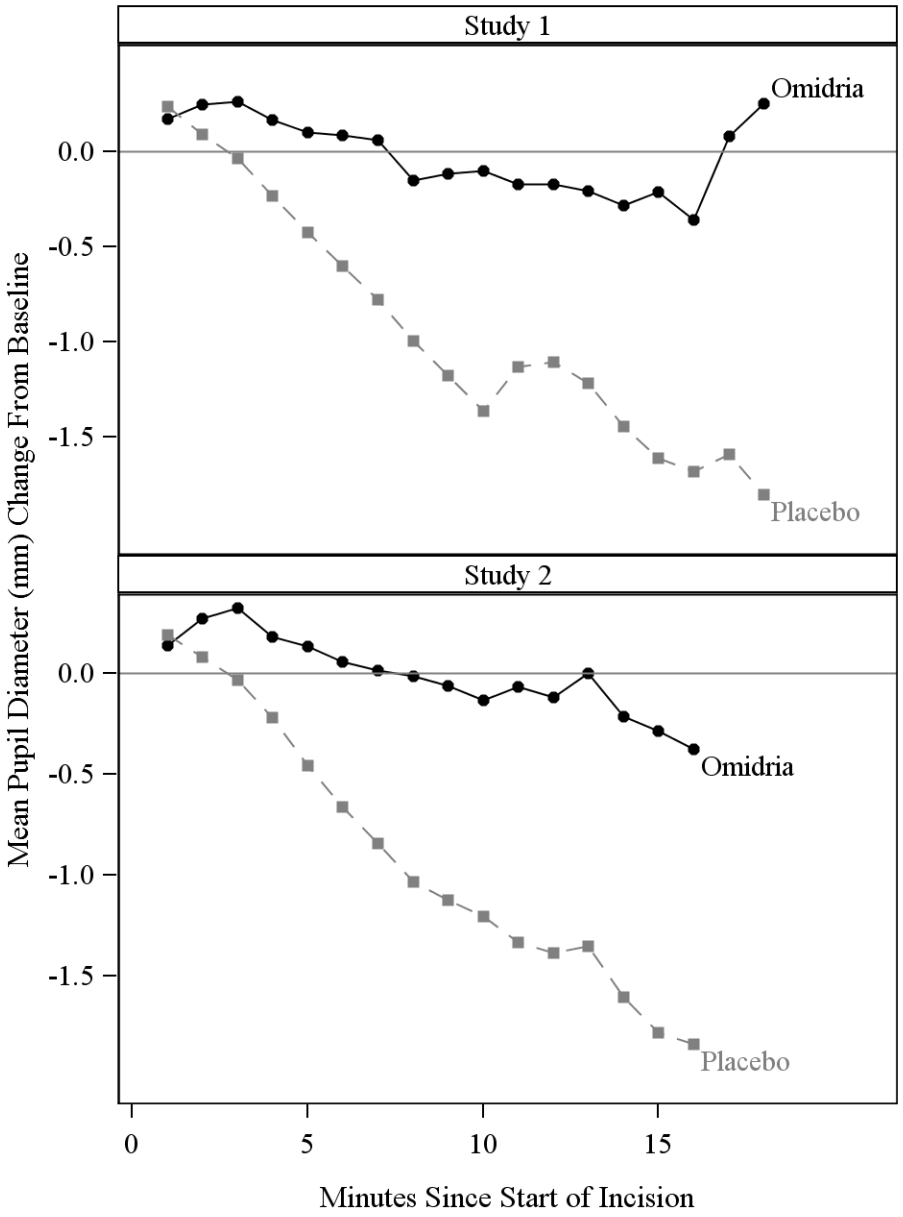
14 CLINICAL STUDIES

The efficacy and safety of Omidria were evaluated in two Phase 3, randomized, multicenter, double-masked, placebo-controlled clinical trials in 808 adult subjects undergoing cataract surgery or intraocular lens replacement.

Subjects were randomized to either Omidria or placebo. Subjects were treated with preoperative topical mydriatic and anesthetic agents. Pupil diameter was measured throughout the surgical procedure. Postoperative pain was evaluated by self-administered 0-100 mm visual analog scales (VAS).

Mydriasis was maintained in the Omidria-treated groups while the placebo-treated groups experienced progressive constriction.

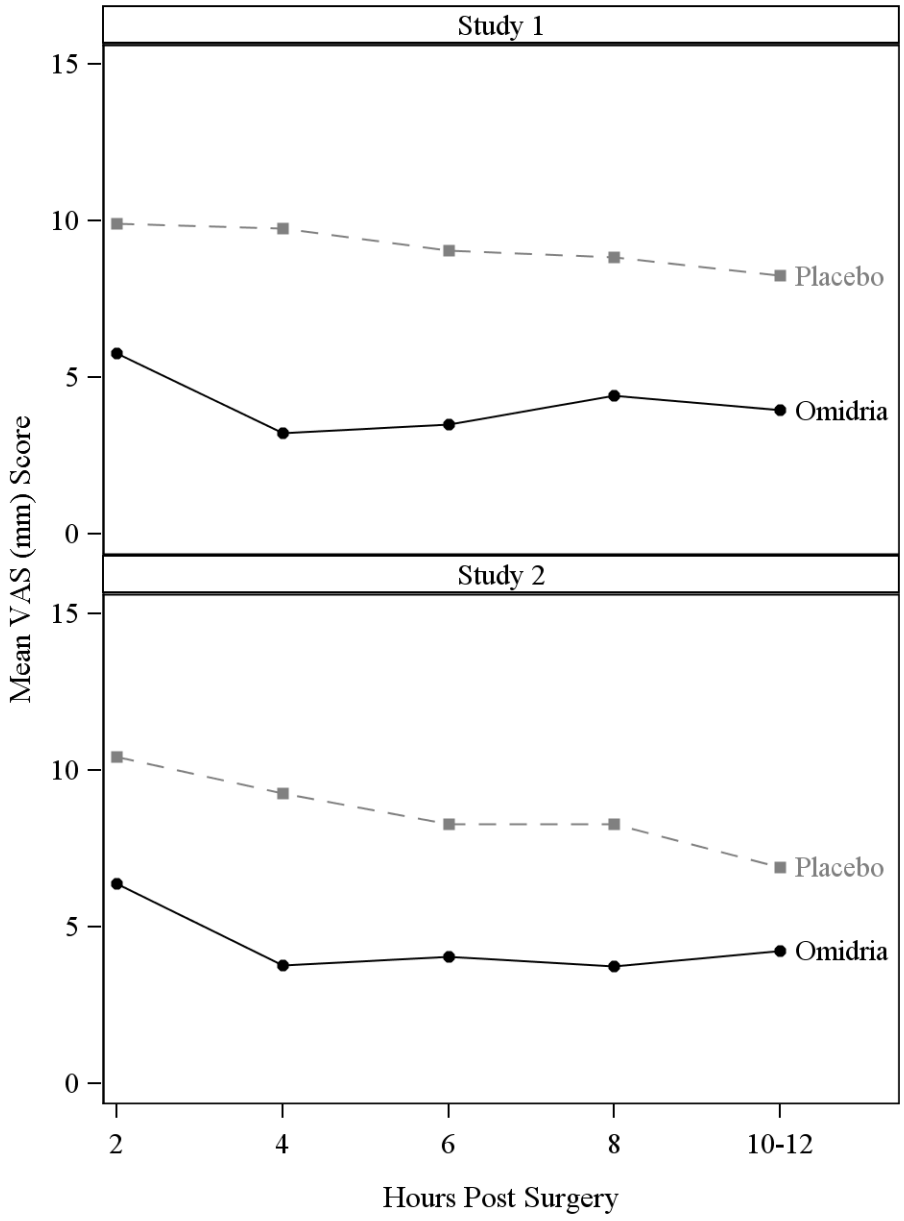
Figure 3: Intraoperative Pupil Diameter (mm) Change-from-Baseline



At the end of cortical clean-up, 23% of placebo-treated subjects and 4% of Omidria-treated subjects had a pupil diameter less than 6 mm ($p < 0.01$).

Pain during the initial 10-12 hours postoperatively was statistically significantly less in the Omidria-treated groups than in the placebo-treated groups.

Figure 4: Postoperative Mean Visual Analog Scale (VAS) Scores for Pain



During the 10-12 hours postoperatively, 26% of Omidria-treated subjects reported no pain (VAS = 0 at all timepoints) while 17% of placebo-treated subjects reported no pain ($p < 0.01$).

16 HOW SUPPLIED/STORAGE AND HANDLING

Omidria is supplied as a sterile solution concentrate in a clear, 5-mL glass, single-patient-use vial containing 4 mL of sterile solution.

Omidria is supplied in a multi-pack containing:

4 single-patient-use vials: NDC 62225-600-04 or

10 single-patient-use vials: NDC 62225-600-10

Storage: Store at 20˚ to 25˚C (68˚ to 77˚F). Protect from light.

17 PATIENT COUNSELING INFORMATION

Inform patients that they may experience sensitivity to light.

Omeros Corporation

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