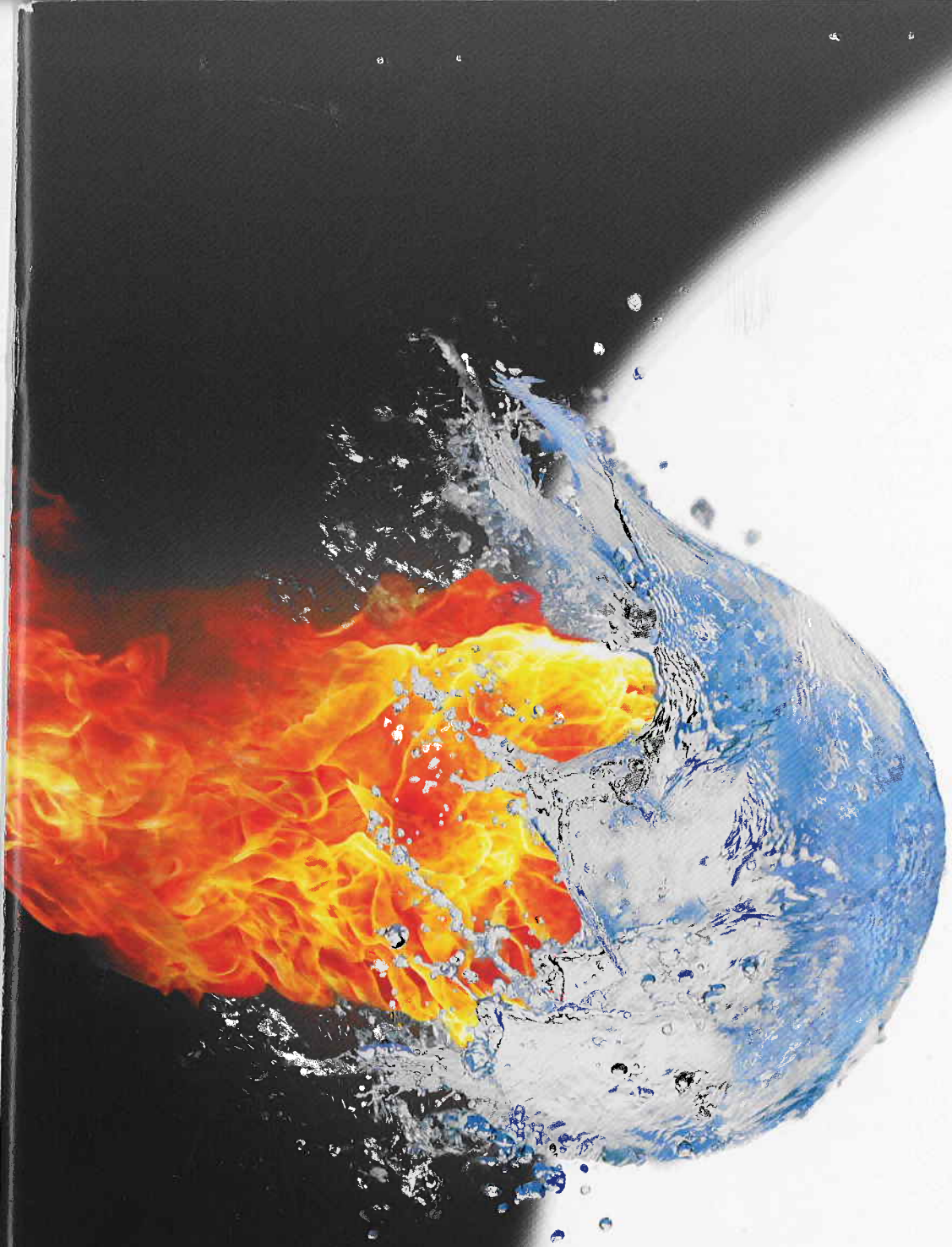
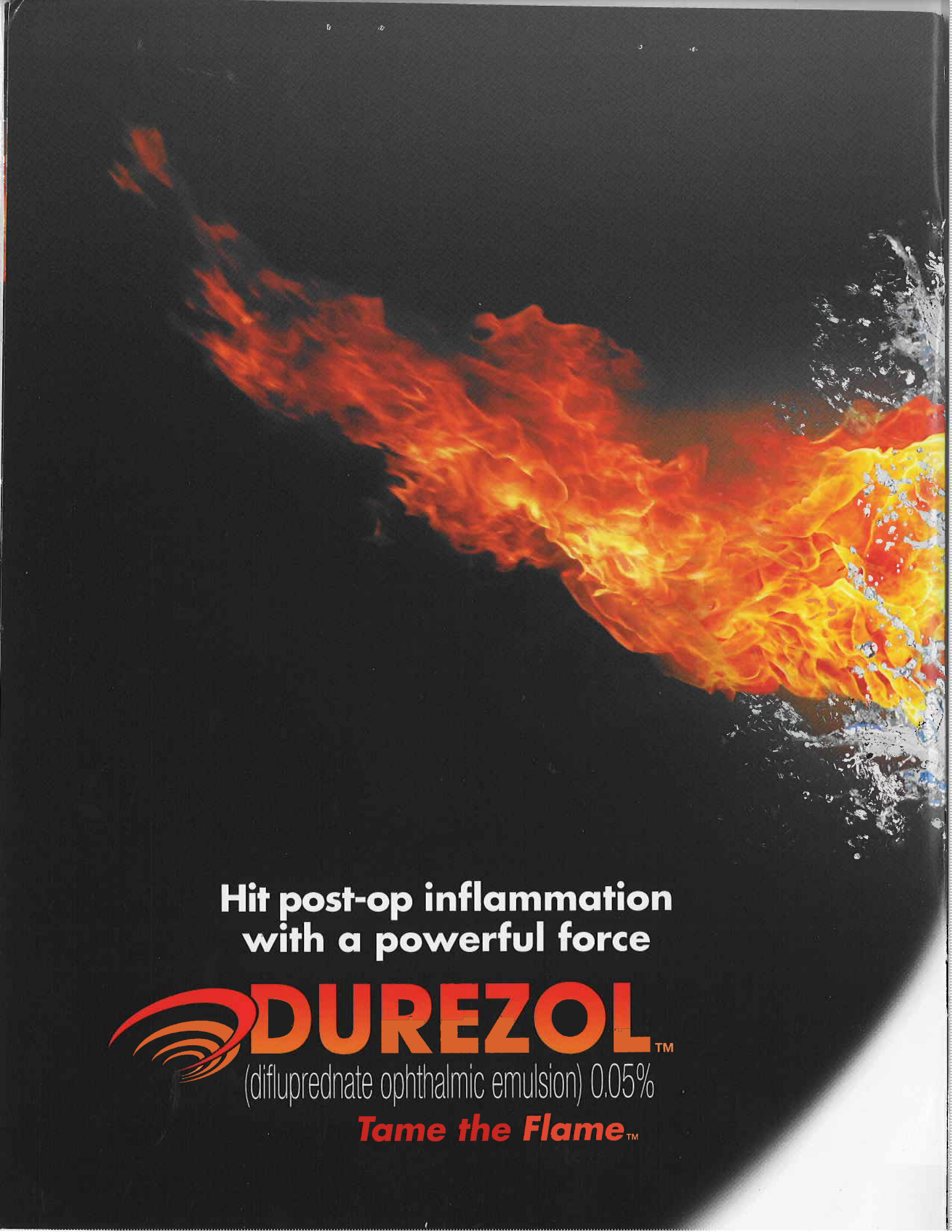


Hit post-op inflammation with a powerful force

DUREZOL™

(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™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Introducing the first and only powerful steroid with proven pain relief[1,2]

Powerful anti-inflammatory efficacy to clear cells and flare[1]

First and only steroid proven to reduce pain[1]

Emulsion formulation with no shaking required[2]

Demonstrated safety profile[2]

BAK-free[2]

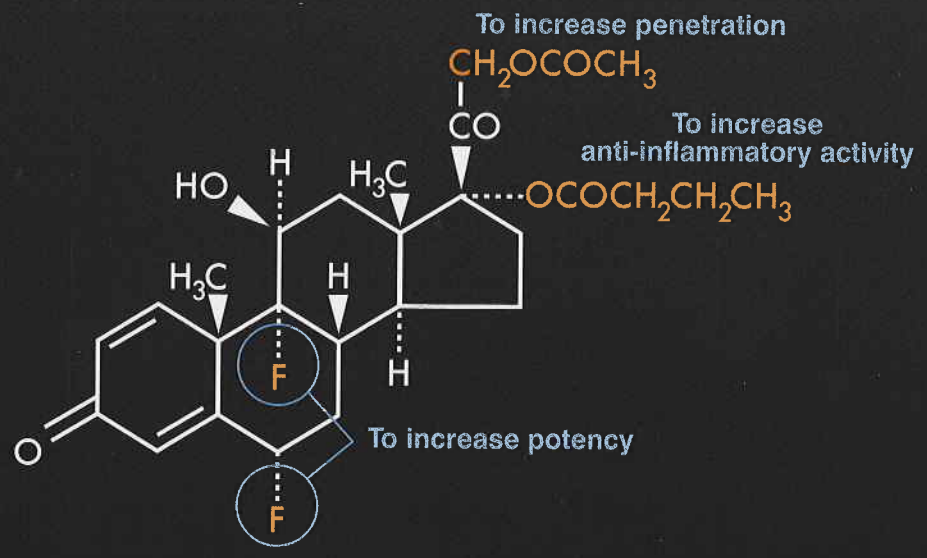
Please see page 14 for Important Safety Information.

BAK=benzalkonium chloride

DESIGNED FOR PATIENTS

Engineered to optimize power and penetration[1,3-5]

- Fluorination at the C6- and C9-positions to increase potency of the molecule
- Substitution of the hydroxyl group with acetic acid at C21 to increase lipophilicity and epithelial penetration
- Replacement of the hydroxyl group with butyric acid at C17 to increase anti-inflammatory activity



- Acts at the site of initial application
  - —Rapidly penetrates cornea and acts upon glucocorticoid receptors in the iris/ciliary body[6-8]
- Active metabolite resides in ocular tissues with limited penetration into nonocular tissues, resulting in little or no systemic effect[2,8]

DUREZOL™

(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™

Formulated for patient comfort[2]

- Emulsion formulation with no shaking required
- Durezol is a BAK-free product

Facilitating patient access

- Copay assistance card to reduce patient financial burden
- Patient assistance program to help qualified patients

Please see page 14 for Important Safety Information.

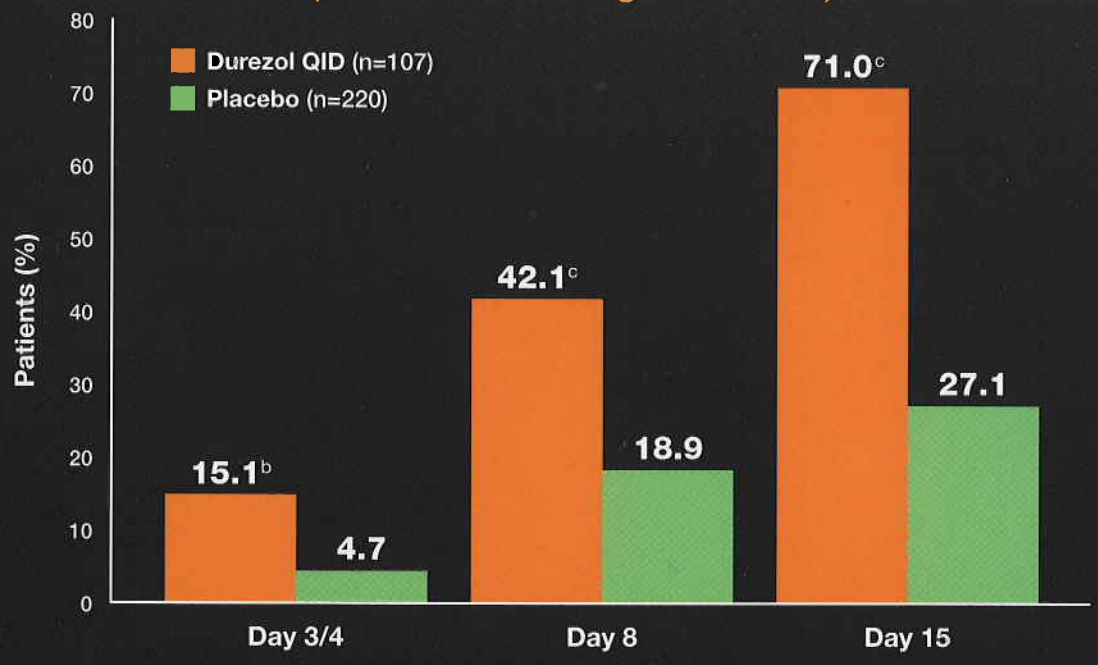
In clinical studies of patients with an anterior chamber cell count of ≥11 cells ***one day post surgery***[1]*...*

PROVEN POST-OP POWER

Significant reduction in cells and flare[1,a]

- 71.0% of patients receiving Durezol experienced ocular inflammation clearing as defined by cell count ≤5 and grade 0 flare at Day 15 (*P*<.0001 vs placebo)
  - —Grade 0 flare defined as none

Patients with clearing of ocular inflammation
(cell count ≤5 and grade 0 flare)



[b]*P*<.05
[c]*P*<.0001

At Day 0[d]
- Mean anterior chamber cell count of 24.0 (Durezol) and 22.5 (placebo)
- Mean anterior chamber flare grade of 1.5 (Durezol) and 1.4 (placebo)

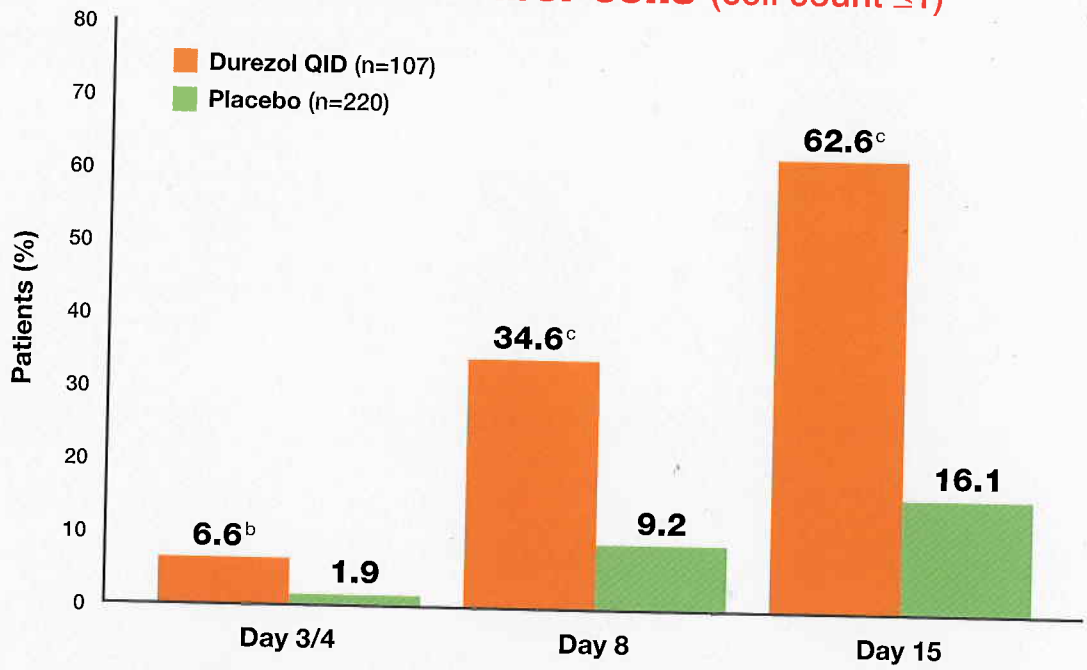
DUREZOL™
(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™

Significant clearing of anterior chamber cells[1,a]

- 62.6% of patients receiving Durezol experienced a clearing (cell count ≤1) of anterior chamber cells at Day 15 ($P<.0001$ vs placebo)

Patients with clearing of anterior chamber cells (cell count ≤1)



[b]$P<.05$
[c]$P<.0001$

At Day 0[d] • Mean anterior chamber cell count of 24.0 (Durezol) and 22.5 (placebo)

Please see page 14 for Important Safety Information.

[a]Results from a pooled analysis of two Phase 3, Pivotal, US multicenter, randomized, clinical studies in patients treated for inflammation and pain following ocular surgery. All data based on last observation carried forward (LOCF) analysis.[1]

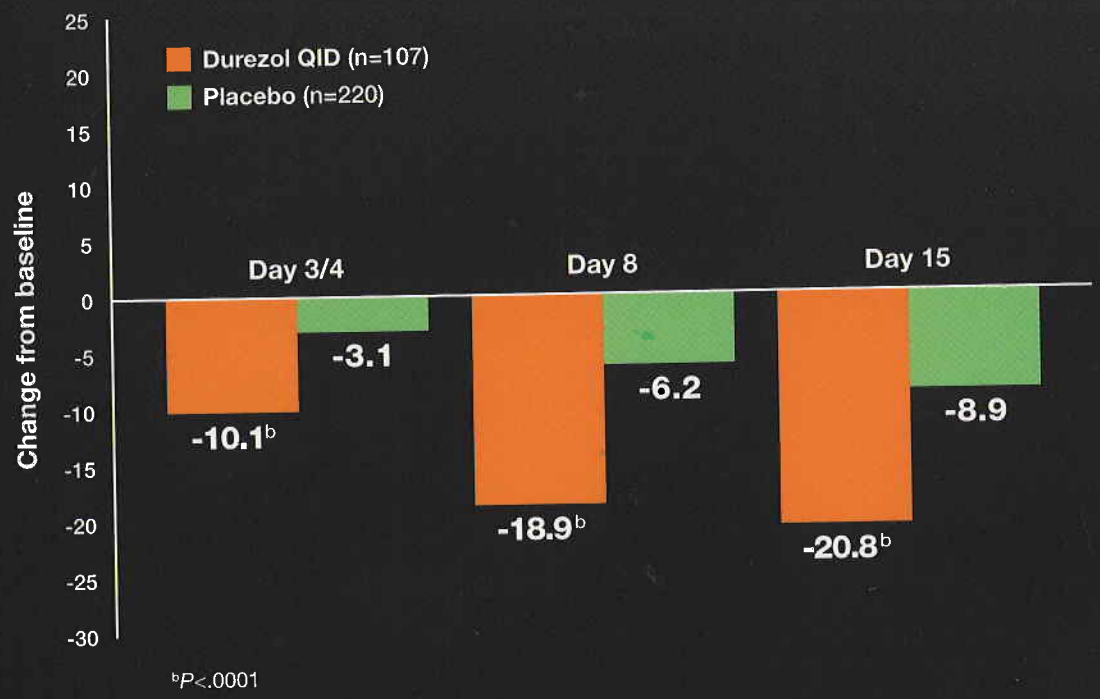
[d]Day of surgery.

REDUCE INFLAMMATION & PAIN

Significant reduction in cell count[1,a]

- Durezol offered significant anterior chamber cell count reduction from baseline of 20.8 vs 8.9 with placebo at Day 15 ($P<.0001$)

Mean reduction from baseline in anterior chamber cell count



[b]$P<.0001$

At Day 0[c] • Mean anterior chamber cell count of 24.0 (Durezol) and 22.5 (placebo)

DUREZOL™

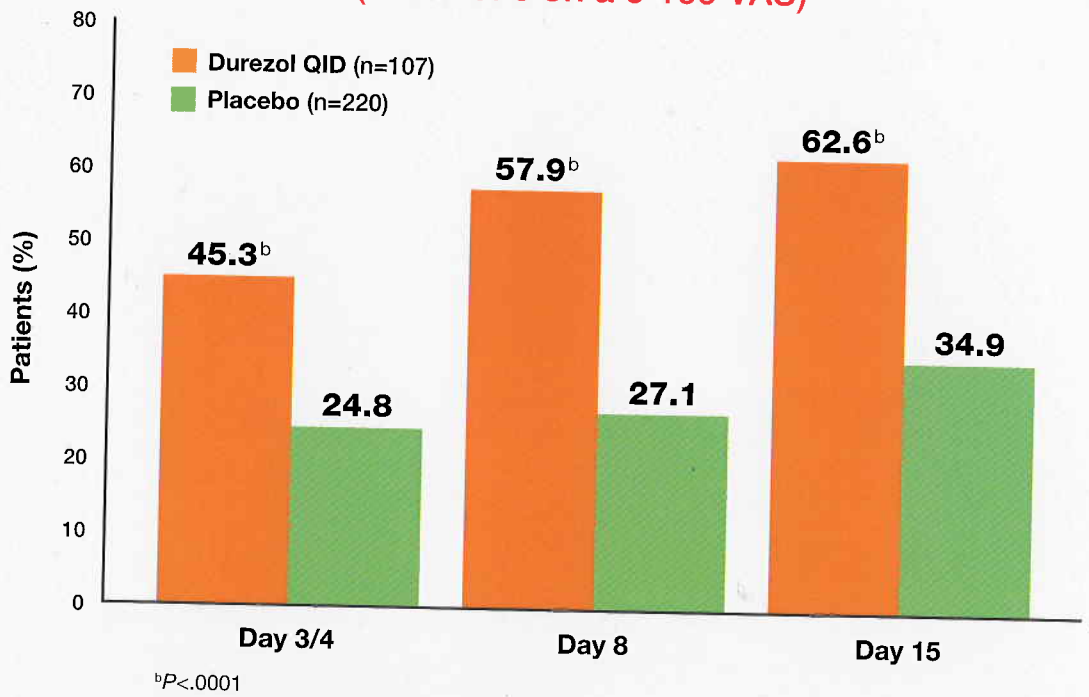
(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™

The first steroid proven to reduce pain[1,a]

- With Durezol, significantly more patients were pain free (score of 0 on a 0 to 100 VAS) at Day 15
  —62.6% with Durezol vs 34.9% with placebo ($P<.0001$)

Patients free from pain
(score of 0 on a 0-100 VAS)



[b]$P<.0001$

Significant reduction in photophobia

- Significantly more patients were photophobia free (score of 0 on a 0 to 100 VAS) with Durezol vs placebo at Day 15 (54.2% vs 25.7%, respectively; $P<.0001$)

At Day 0[c] • Mean photophobia scores were 22.0 (Durezol) and 24.6 (placebo)

Please see page 14 for Important Safety Information.

[a]Results from a pooled analysis of two Phase 3, Pivotal, US multicenter, randomized, clinical studies in patients treated for inflammation and pain following ocular surgery. All data based on LOCF analysis.[1]
[c]Day of surgery.
VAS=visual analog scale

In a clinical study of patients receiving Durezol QID starting ***one day prior to surgery***[9]...

ANTI-INFLAMMATORY POWER

Demonstrated efficacy in managing inflammation[9,a]

- 81.3% of patients receiving Durezol achieved clearing of ocular inflammation vs 25.0% of placebo patients at Day 14 ($P<.0001$)

Patients with clearing of ocular inflammation

(cell count ≤5 and grade 0 flare)

[b]$P<.05$
[c]$P<.0001$

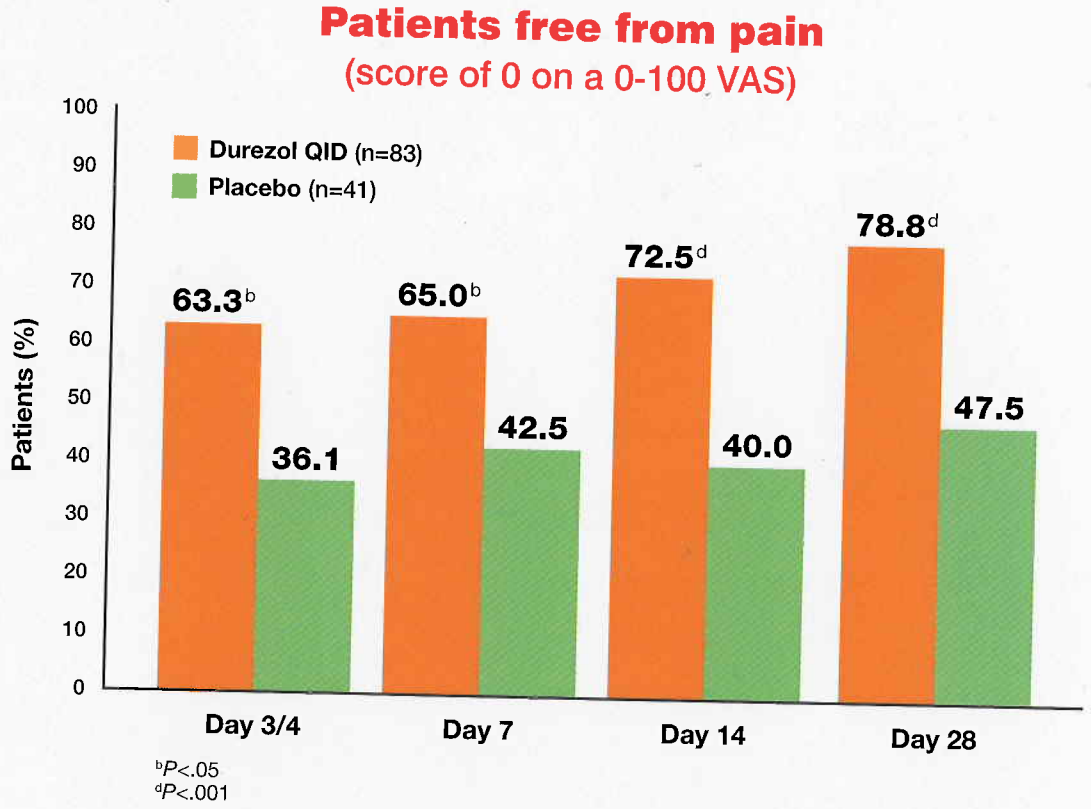
DUREZOL™

(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™

Significantly more patients free from pain[9,a]

- 72.5% of patients receiving Durezol were pain free (score of 0 on a 0 to 100 VAS) compared with 40.0% of patients receiving placebo at Day 14 (*P*=.0006)



Please see page 14 for Important Safety Information.

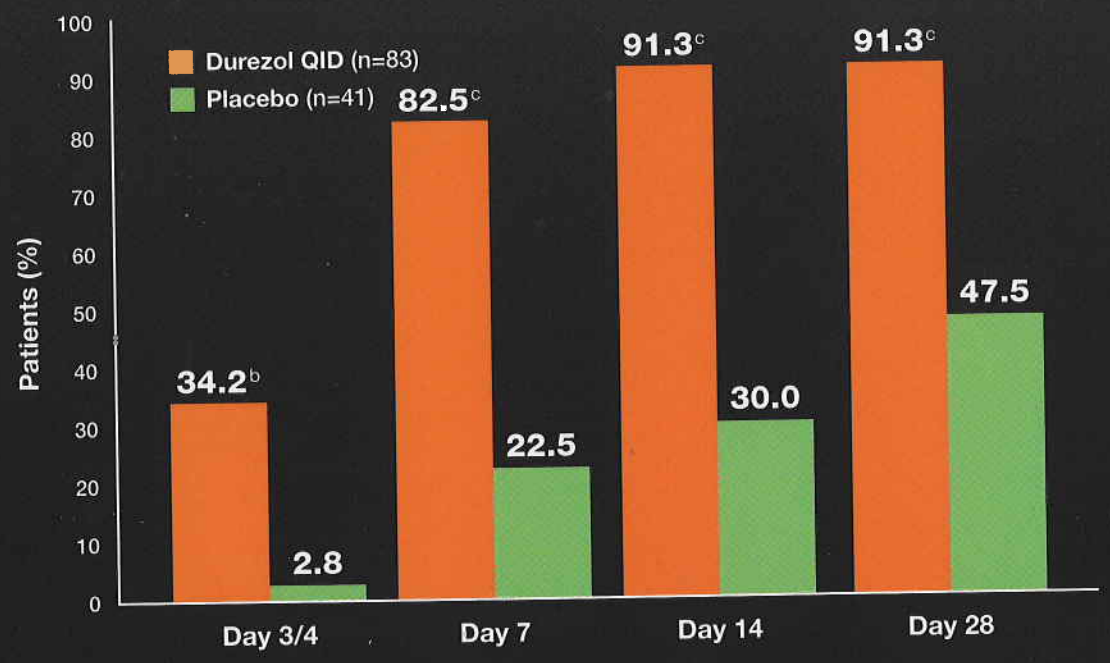
[a]Results from a Phase 3 multicenter, randomized, double-masked, placebo-controlled study of the safety and efficacy of difluprednate administered 4 times daily in the management of inflammation following ocular surgery. All data based on LOCF analysis.[9]

DEMONSTRATED EFFICACY

Power to reduce inflammation[9,a]

- 91.3% of patients receiving Durezol achieved a cell count ≤5 vs 30.0% with placebo at Day 14 (*P*<.0001)

Patients with clearing of anterior chamber cells (≤5 cells)



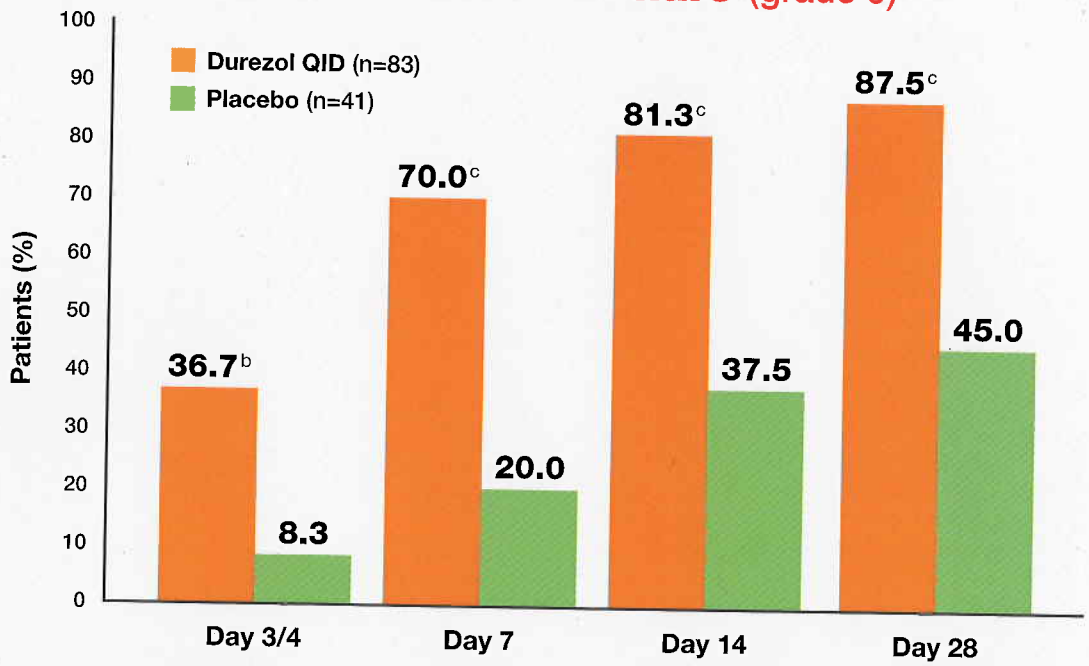
[b]*P*<.05
[c]*P*<.0001

DUREZOL™
(difluprednate ophthalmic emulsion) 0.05%
Tame the Flame™

Significant clearing of anterior chamber flare[9,a]

- 81.3% of patients receiving Durezol experienced a clearing of anterior chamber flare (grade 0) vs 37.5% with placebo at Day 14 ($P<.0001$)
  - —Grade 0 flare defined as complete absence

Patients with clearing of anterior chamber flare (grade 0)



[b]$P<.05$
[c]$P<.0001$

Please see page 14 for Important Safety Information.

[a]Results from a Phase 3 multicenter, randomized, double-masked, placebo-controlled study of the safety and efficacy of difluprednate administered 4 times daily in the management of inflammation following ocular surgery. All data based on LOCF analysis.[9]

PROVEN SAFETY PROFILE

Low incidence of IOP rise in Phase 3 Pivotal trials[6,a]

- 97.2% of patients experienced no clinically relevant effects on IOP
  - —2.8% of patients experienced a criterion increase in IOP with Durezol compared to 0.9% with placebo
  - —IOP criterion increase defined as an observed value of ≥21 mmHg and a change from baseline of ≥10 mmHg

Mean IOP in Phase 3 Pivotal trials

- Mean IOP remained similar to baseline measures in Phase 3 Pivotal trials through Day 29

DUREZOL™

(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™

Duration of treatment in Phase 3 Pivotal trials[6,a]

- 92.5% of patients were exposed to Durezol for ≥19 days
  - —Mean duration of exposure to Durezol was 27 days

Important Safety Information[2]

- Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.
- Ocular adverse reactions occurring in 5–15% of subjects in clinical studies with Durezol included corneal edema, ciliary and conjunctival hyperemia, eye pain, photophobia, posterior capsule opacification, anterior chamber cells, anterior chamber flare, conjunctival edema, and blepharitis. Other ocular adverse reactions occurring in 1–5% of subjects included reduced visual acuity, punctate keratitis, eye inflammation, and iritis. Ocular adverse events occurring in <1% of subjects included application site discomfort or irritation, corneal pigmentation and striae, episcleritis, eye pruritis, eyelid irritation and crusting, foreign body sensation, increased lacrimation, macular edema, scleral hyperemia, and uveitis. Most of these events may have been the consequence of the surgical procedure.

Please see full prescribing information.

[a]Results from a pooled analysis of two Phase 3, Pivotal, US multicenter, randomized, clinical studies in patients treated for inflammation and pain following ocular surgery. All data based on LOCF analysis.[1]

IOP=intraocular pressure

References: 1. Data on file, Sirion Therapeutics, Inc. **2.** Durezol Prescribing Information. Sirion Therapeutics, Inc. 2008. **3.** Bikowski J. The position not the presence of the halogen in corticosteroids influences potency and side effects. http://findarticles.com/p/articles/mi_m0PDG/is_2_5/ai_n16085948/print. Accessed April 29, 2008. **4.** Gysler A, Lange K, Korting HC, Schäfer-Korting M. Prednicarbate biotransformation in human foreskin keratinocytes and fibroblasts. *Pharm Res*. 1997;14(6):793-797. **5.** Hammer S, Spika I, Sippl W, et al. Glucocorticoid receptor interactions with glucocorticoids: evaluation by molecular modeling and functional analysis of glucocorticoid receptor mutants. *Steroids*. 2003;68:329-339. **6.** Data on file, Sirion Therapeutics, Inc. **7.** Inoue J, Yamaguchi M, Sakaki H, et al. Preclinical pharmacokinetics of difluprednate ophthalmic emulsion. Poster presented at the 2007 Annual Meeting of the Association for Research in Vision and Ophthalmology; May 6-10, 2007; Fort Lauderdale, FL. **8.** Tajika T, Shirasaki Y, Kimura M, et al. Ocular distribution and metabolism after instillation of difluprednate ophthalmic emulsion in rabbits. Poster presented at the 2007 Annual Meeting of the Association for Research in Vision and Ophthalmology; May 6-10, 2007; Fort Lauderdale, FL. **9.** Data on file, Sirion Therapeutics, Inc.

Introducing the first and only powerful steroid with proven pain relief[1,2]

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First and only steroid proven to reduce pain[1]

Emulsion formulation with no shaking required[2]

Demonstrated safety profile[2]

BAK-free[2]

Please see page 14 for Important Safety Information.

REPRESENTATIVE USE ONLY. NOT TO BE LEFT WITH PHYSICIANS.

Hit post-op inflammation with a powerful force

DUREZOL™

(difluprednate ophthalmic emulsion) 0.05%

Tame the Flame™

For more information, please visit our website at **durezol.com**

SIRiON Therapeutics

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The first and only powerful steroid with proven pain relief[1,2]

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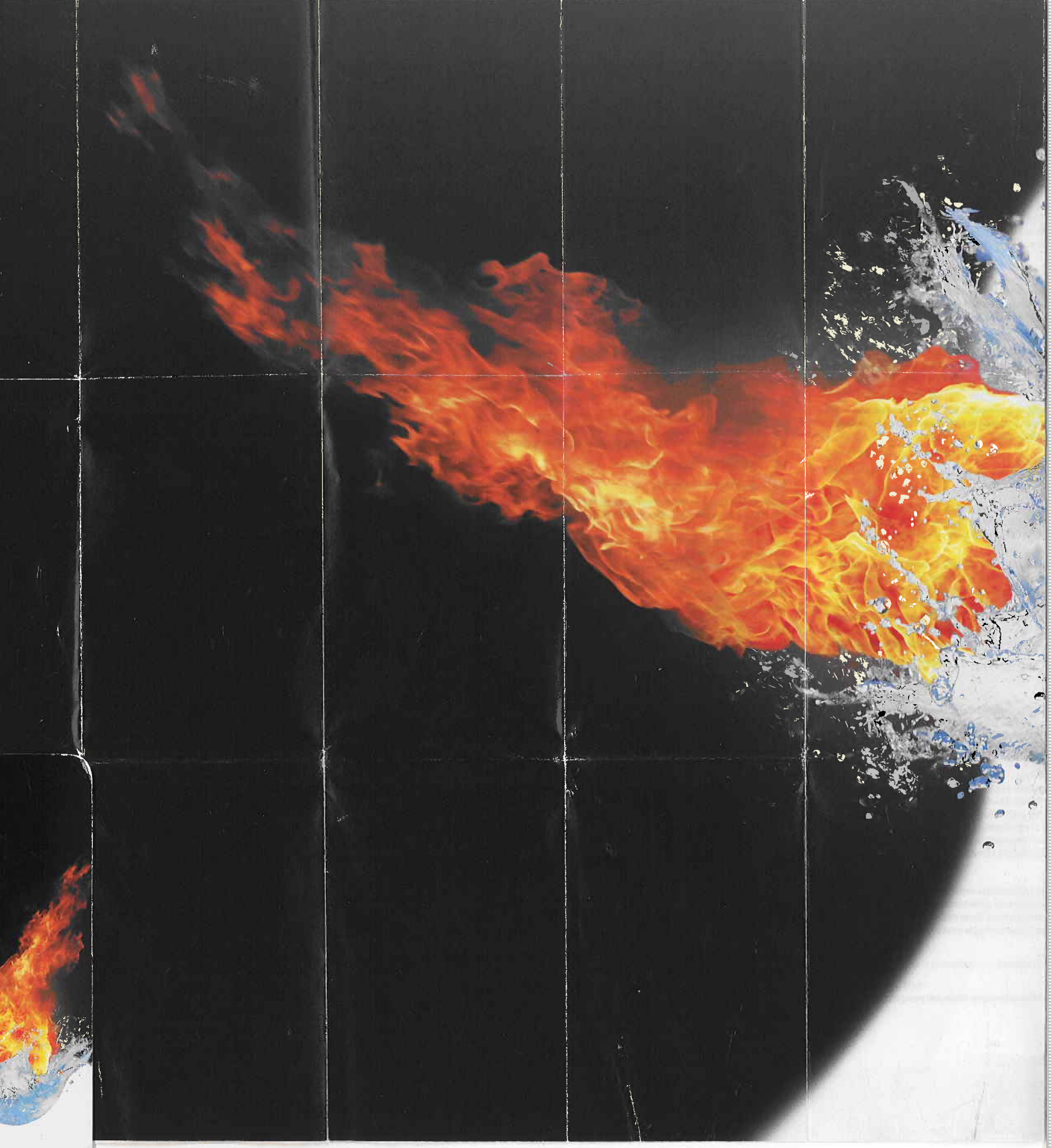
Please see full prescribing information enclosed.

NDC 42826-601-05



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BAK-free[2]

NDC 42826-601-05

Please see full prescribing information for Important Safety Information.

References: 1. Data on file, Sirion Therapeutics, Inc. **2.** Durezol Prescribing Information. Sirion Therapeutics, Inc. 2008.

BAK=benzalkonium chloride

For more information, please visit our website at **durezol.com**

SIRiON Therapeutics

The first and only powerful steroid with proven pain relief[1,2]

DUREZOL™ (difluprednate ophthalmic emulsion) 0.05%

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NDC 42826-601-05

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US patent 5156898 Z-CARD® North America, NYC.
CARD 212-797-3450 www.zcardna.com Job no. C696

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all of the information needed to use Durezol™ safely and effectively. See full prescribing information for Durezol.

DUREZOL™
(difluprednate ophthalmic emulsion) 0.05%
Initial U.S. approval: 2008

Based on full prescribing information, revised September 2008.

INDICATIONS AND USAGE

Durezol is a topical corticosteroid that is indicated for the treatment of inflammation and pain associated with ocular surgery. **(1)**

DOSAGE AND ADMINISTRATION

Instill one drop into the conjunctival sac of the affected eye(s) 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period, followed by 2 times daily for a week and then a taper based on the response. **(2)**

DOSAGE FORMS AND STRENGTHS

Durezol contains 0.05% difluprednate, as a sterile preserved ophthalmic emulsion for topical ophthalmic use only. **(3)**

CONTRAINDICATIONS

Durezol, as with other ophthalmic corticosteroids, is contraindicated in most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures. **(4)**

WARNINGS AND PRECAUTIONS

- Intraocular pressure (IOP) increase–Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored. **(5.1)**
- Cataracts–Use of corticosteroids may result in posterior subcapsular cataract formation. **(5.2)**
- Delayed healing–The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order beyond 28 days should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining. **(5.3)**
- Bacterial infections–Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated. **(5.4)**
- Viral infections–Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). **(5.5)**
- Fungal infections–Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. **(5.6)**

To report SUSPECTED ADVERSE REACTIONS, contact Sirion Therapeutics at 1-866-4SIRION (1-866-474-7466) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

FULL PRESCRIBING INFORMATION: CONTENTS*

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2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 IOP Increase
5.2 Cataracts
5.3 Delayed Healing
5.4 Bacterial Infections
5.5 Viral Infections
5.6 Fungal Infections
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*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Durezol (difluprednate ophthalmic emulsion) 0.05%, a topical corticosteroid, is indicated for the treatment of inflammation and pain associated with ocular surgery.

2 DOSAGE AND ADMINISTRATION

Instill one drop into the conjunctival sac of the affected eye(s) 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period, followed by 2 times daily for a week and then a taper based on the response.

3 DOSAGE FORMS AND STRENGTHS

Durezol contains 0.05% difluprednate as a sterile preserved emulsion for topical ophthalmic administration.

4 CONTRAINDICATIONS

The use of Durezol, as with other ophthalmic corticosteroids, is contraindicated in most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures.

5 WARNINGS AND PRECAUTIONS

5.1 IOP Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

5.2 Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

Introducing the first and only powerful steroid with proven pain relief[1,2]

5.3 Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order beyond 28 days should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

5.4 Bacterial Infections

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

5.5 Viral Infections

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

5.6 Fungal Infections

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

5.7 Topical Ophthalmic Use Only

Durezol is not indicated for intraocular administration.

6 ADVERSE REACTIONS

Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

Ocular adverse reactions occurring in 5–15% of subjects in clinical studies with Durezol included corneal edema, ciliary and conjunctival hyperemia, eye pain, photophobia, posterior capsule opacification, anterior chamber cells, anterior chamber flare, conjunctival edema, and blepharitis. Other ocular adverse reactions occurring in 1–5% of subjects included reduced visual acuity, punctate keratitis, eye inflammation, and iritis. Ocular adverse events occurring in <1% of subjects included application site discomfort or irritation, corneal pigmentation and striae, episcleritis, eye pruritis, eyelid irritation and crusting, foreign body sensation, increased lacrimation, macular edema, scleral hyperemia, and uveitis. Most of these events may have been the consequence of the surgical procedure.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects

Pregnancy Category C. Difluprednate has been shown to be embryotoxic (decrease in embryonic body weight and a delay in embryonic ossification) and teratogenic (cleft palate and skeletal anomalies) when administered subcutaneously to rabbits during organogenesis at a dose of 1–10 µg/kg/day. The no-observed-effect-level (NOEL) for these effects was 1 µg/kg/day, and 10 µg/kg/day was considered to be a teratogenic dose that was concurrently found in the toxic dose range for fetuses and pregnant females. Treatment of rats with 10 µg/kg/day subcutaneously during organogenesis did not result in any reproductive toxicity, nor was it maternally toxic. At 100 µg/kg/day after subcutaneous administration in rats, there was a decrease in fetal weights and delay in ossification, and effects on weight gain in the pregnant females. It is difficult to extrapolate these doses of difluprednate to maximum daily human doses of Durezol, since Durezol is administered topically with minimal systemic absorption, and difluprednate blood levels were not measured in the reproductive animal studies. However, since use of difluprednate during human pregnancy has not been evaluated and cannot rule out the possibility of harm, Durezol should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

8.3 Nursing Mothers

It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Durezol is administered to a nursing woman.

8.4 Pediatric Use

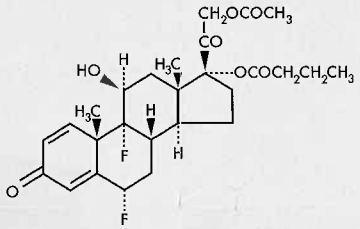
Safety and effectiveness in pediatric patients has not been established.

8.5 Geriatric Use

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

11 DESCRIPTION

Durezol (difluprednate ophthalmic emulsion) 0.05% is a sterile, topical anti-inflammatory corticosteroid for ophthalmic use. The chemical name is 6α,9-difluoro-11β,17,21-trihydroxypregna-1,4-diene-3,20-dione 21-acetate 17-butyrate (CAS number 23674-86-4). Difluprednate is represented by the following structural formula:



Difluprednate has a molecular weight of 508.56, and the empirical formula is $C_{27}H_{34}F_2O_7$.

Each mL contains: ACTIVE: difluprednate 0.5 mg (0.05%) INACTIVE: boric acid, castor oil, glycerin, polysorbate 80, purified water, sodium acetate, sodium EDTA, and sodium hydroxide (to adjust the pH to 5.2 to 5.8). The emulsion is essentially isotonic with a tonicity of 304 to 411 mOsm/kg. PRESERVATIVE: sorbic acid 0.1%.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Corticosteroids inhibit the inflammatory response to a variety of inciting agents that may delay or slow healing. They inhibit edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. There is no generally accepted explanation for the mechanism of action of ocular corticosteroids. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Difluprednate is structurally similar to other corticosteroids.

12.3 Pharmacokinetics

Difluprednate undergoes deacetylation in vivo to 6α,9-difluoroprednisolone 17-butyrate (DFB), an active metabolite of difluprednate.

Clinical pharmacokinetic studies of difluprednate after repeat ocular instillation of 2 drops of difluprednate (0.01% or 0.05%) QID for 7 days showed that DFB levels in blood were below the quantification limit (50 ng/mL) at all time points for all subjects, indicating the systemic absorption of difluprednate after ocular instillation of Durezol is limited.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Difluprednate was not genotoxic in vitro in the Ames test, and in cultured mammalian cells CHL/IU (a fibroblastic cell line derived from the lungs of newborn female Chinese hamsters). An in vivo micronucleus test of difluprednate in mice was also negative. Treatment of male and female rats with subcutaneous difluprednate up to 10 µg/kg/day prior to and during mating did not impair fertility in either gender. Long term studies have not been conducted to evaluate the carcinogenic potential of difluprednate.

13.2 Animal Toxicology and/or Pharmacology

In multiple studies performed in rodents and non-rodents, subchronic and chronic toxicity tests of difluprednate showed systemic effects such as suppression of body weight gain; a decrease in lymphocyte count; atrophy of the lymphatic glands and adrenal gland; and for local effects, thinning of the skin; all of which were due to the pharmacologic action of the molecule and are well known glucocorticosteroid effects. Most, if not all of these effects were reversible after drug withdrawal. The NOEL for the subchronic and chronic toxicity tests were consistent between species and ranged from 1–1.25 µg/kg per day.

For more information, please visit

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DUREZOL™

(difluprednate ophthalmic emulsion) 0.05%

14 CLINICAL STUDIES

14.1 Postoperative Ocular Inflammation and Pain

Clinical efficacy was evaluated in 2 randomized, double-masked, placebo-controlled trials in which subjects with an anterior chamber cell grade ≥ "2" (a cell count of 11 or higher) after cataract surgery were assigned to Durezol or placebo (vehicle) following surgery. One drop of Durezol or vehicle was self instilled either 2 (BID) or 4 (QID) times per day for 14 days, beginning the day after surgery. The presence of complete clearing (a cell count of 0) was assessed at 8 days and 15 days post-surgery using a slit lamp binocular microscope. In the intent-to-treat analyses of both studies, a significant benefit was seen in the QID Durezol-treated group in ocular inflammation and reduction of pain when compared with placebo. The consolidated clinical trial results are provided below.

Ocular Inflammation and Pain Endpoints (Studies Pooled)

	Durezol QID (n=107)		Vehicle (n=220)	
Day	8	15	8	15
Anterior Chamber cell clearing (% subjects)	**24** (22%)*	**44** (41%)*	**17** (7%)	**25** (11%)
Pain free (% subjects)	**62** (58%)*	**67** (63%)*	**59** (27%)	**76** (35%)

* Statistically significantly better than vehicle, $P<0.01$

16 HOW SUPPLIED/STORAGE AND HANDLING

Durezol (difluprednate ophthalmic emulsion) 0.05% is a sterile, aqueous topical ophthalmic emulsion supplied in an opaque plastic bottle with a controlled drop tip and a pink cap in the following size:

5 mL in a 5 mL bottle (NDC 42826-601-05)

Storage

Store at 15-25°C (59-77°F). Do not freeze. Protect from light. When not in use keep the bottles in the protective carton.

17 PATIENT COUNSELING INFORMATION

This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the emulsion. If pain develops or if redness, itching, or inflammation becomes aggravated, the patient should be advised to consult a physician. As with all ophthalmic preparations containing a preservative, patients should be advised not to wear contact lenses when using Durezol.

SIRiON Therapeutics

Manufactured for: Sirion Therapeutics, Inc., Tampa, FL 33619
By: Catalent Pharma Solutions, Inc., Woodstock, IL 60098

US PATENT 6,114,319

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