Fluocinolone Implant for Idiopathic Non-Infectious Posterior Uveitis
For decades, corticosteroids have been the standard-of-care, first-line therapy for non-infectious posterior uveitis. In most cases, they are administered by periocular or intravitreal injection or orally.

Only one injectable corticosteroid is FDA approved for the treatment of uveitis (triamcinolone acetonide injectable suspension, Triesence, Alcon), but triamcinolone and other corticosteroids prepared extemporaneously for injection are routinely used for this purpose.* Numerous small studies and reviews of the literature have shown that steroid injections reduce ocular inflammation in patients with uveitis.1-5 However, physicians must be cognizant of their usually short-term duration of action11,12 and the potential for drug- and injection-related side effects such as increased IOP, cataract formation, retinal detachment, endophthalmitis and vitreous hemorrhage.1,3-5

Steroids are the only oral therapy FDA approved for the treatment of noninfectious uveitis. They can reduce ocular inflammation and are used for patients in whom ocular steroid injections do not provide adequate control of posterior segment inflammation. Long-term use of oral corticosteroids, especially when high doses are required, may not be ideal6 because of the potential for the development of cataract and/or increased IOP and serious systemic side effects, including high blood pressure, cardiovascular disease, excessive weight gain, psychiatric disorders, adrenal insufficiency, osteoporosis, osteonecrosis, increased risk of infection, myopathy, hyperglycemia and gastrointestinal problems.7-16

When steroid treatment does not adequately control ocular inflammation or cannot be tolerated by the patient, other immunomodulatory medications are sometimes used. Antimetabolites, T-cell inhibitors, alkylating agents and some drugs in the newer biologics class, e.g., TNF-alpha inhibitors, can provide effective ocular inflammation control but have also been shown to have the potential for severe systemic side effects.17-22 None of these agents has been evaluated for treating ocular inflammation in randomized, controlled trials or approved by the FDA for the treatment of uveitis; most are intended for neurologic, rheumatologic or dermatologic conditions.

Sustained-release ocular drug-delivery devices have been developed to control ocular inflammation and decrease the need for systemic therapy and its subsequent side effects. Two have been approved by the FDA for the treatment of non-infectious posterior uveitis. The first to gain approval, Retisert (fluocinolone acetonide intravitreal implant 0.59 mg, Bausch + Lomb), is surgically implanted into the vitreous and designed to release fluocinolone acetonide for approximately 2.5 years. Retisert is a corticosteroid indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye. (Please see “Important Risk Information for Retisert” on page 3.)

FDA approval of Retisert was based on 34-week results from two multicenter, double-masked, randomized, controlled clinical trials evaluating the safety and efficacy of the implant.23 Subsequently, 3-year follow-up data were published.24 The primary efficacy endpoint in the trials was the rate of recurrence of uveitis in the study eye in the 34 weeks prior to implantation compared with the rate of recurrence 34 weeks, 1 year, 2 years and 3 years after implantation. Retisert significantly reduced recurrence rates.25

The second sustained-delivery device to be FDA approved for treating non-infectious posterior uveitis, Ozurdex (dexamethasone 0.7 mg intravitreal implant, Allergan), is injected into the vitreous using a specially designed applicator. Once in the vitreous, the implant slowly releases dexamethasone and biodegrades into lactic acid and glycolic acid.

Here, I describe a case from my practice that illustrates how Retisert can fit into the treatment armamentarium for patients with non-infectious posterior uveitis and help to achieve treatment goals.

**RETISERT CASE STUDY**

A 60-year-old male, first presented to my office in September 2002. He had been seeing a retinal specialist in another city, who had diagnosed him with non-infectious posterior uveitis.
posterior uveitis in the right eye. The uveitis could not be attributed to any specific ocular or systemic cause. Many cases of noninfectious uveitis are idiopathic.26,27

The patient had recently retired to Austin, Texas, where I practice, and was referred to me for continuing care. While under the care of the first retinal specialist, the patient had been given two periocular injections of triamcinolone, one in November 2001 and one in February 2002. The resulting improvement in ocular inflammation was short-lived following each injection.

My first examination of the patient confirmed the previous physician’s diagnosis. I did not see any sign of an infectious etiology, and the uveitis did not fit any well-defined type of the disease. It most closely resembled a syndrome that J. Donald Gass, MD, described as idiopathic vitritis.28 The patient’s cornea and anterior chamber inflammation were healthy, but he had a 3-year history of floaters, hazy vision and distortion OD. His visual acuity in the right eye was 20/80, and a posterior subcapsular cataract was present. Fluorescein angiography showed leakage from the disc and macula, suggesting low-grade inflammation. I noted 1+ haze in the vitreous, an epiretinal membrane in the macula and CME. At that time, OCT was not clinically available, so the macular thickening was not quantified. Based on the findings, four factors were contributing to the patient’s decreased vision: uveitis, cataract, epiretinal membrane and CME.

The patient was offered combined surgery as an option to treat both uveitis and the epiretinal membrane by both his previous retinal specialist and me. The patient agreed to proceed with the procedure and surgery was scheduled for December 2002. The patient was pre-treated with a posterior sub-Tenon’s injection of triamcinolone in an attempt to quiet the ocular inflammation prior to surgery. At the time of surgery, an anterior segment surgeon removed the cataract and implanted an IOL. Immediately after, I performed a vitrectomy, removed the epiretinal membrane and injected intravitreal triamcinolone, a commonly used strategy for controlling postoperative inflammation following cataract extraction in patients with uveitis.29

Findings and next steps from key follow-up visits were:
- Four weeks after surgery, no inflammation was present, and visual acuity had improved to 20/40. The patient was somewhat pleased, but also disappointed that his vision did not improve to 20/20 in the operated eye.
- March 18, 2003: OCT, which by this time was in clinical use, showed that CME returned with a macular thickness of 377 µm. A fourth posterior sub-Tenon’s triamcinolone injection was given.
- June 5, 2003: Macular edema increased to 420 µm, and vision decreased from the last visit to 20/60. An intravitreal injection of triamcinolone was given. At a subsequent visit, visual acuity returned to 20/40. In an attempt to maintain visual acuity at that level, topical steroid and topical non-steroidal anti-inflammatory drops were prescribed. At this point, the clinical course of the treatment was unchanged.

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**Important Risk Information for Retisert®**

Surgical placement of RETISERT® (fluocinolone acetonide intravitreal implant 0.59 mg, Bausch + Lomb) is contraindicated in active viral, bacterial, mycobacterial or fungal infections of the eye. Based on clinical trials with RETISERT®, during the 3-year post-implantation period, nearly all phakic eyes are expected to develop cataracts and require cataract surgery.

As with any surgical procedure, there is risk involved. Potential complications accompanying intraocular surgery to place RETISERT® into the vitreous cavity may include, but are not limited to, the following: cataract formation, choroidal detachment, temporary decreased visual acuity, endophthalmitis, hypotony, increased intraocular pressure, exacerbation of intraocular inflammation, retinal detachment, vitreous hemorrhage, vitreous loss, wound complication, wound site erythema and wound dehiscence.

Following implantation of RETISERT®, nearly all patients will experience an immediate and temporary decrease in visual acuity in the implanted eye which lasts for approximately one to four weeks post-operatively.

Use of corticosteroids may result in elevated IOP and/or glaucoma. Based on clinical trials with RETISERT®, within 3 years post-implantation, approximately 77% of patients will require IOP lowering medications to control intraocular pressure and 37% of patients will require filtering procedures to control intraocular pressure.

Patients should be advised to have ophthalmologic follow-up examinations of both eyes at appropriate intervals following implantation of RETISERT®. Physicians should periodically monitor the integrity of the implant by visual inspection.

The most frequently reported ocular adverse events in clinical trials with RETISERT® occurring in 50-90% of patients included: cataract, increased intraocular pressure, procedural complications and eye pain. Thirty five to forty percent (35-40%) of patients reported ocular/conjunctival hyperemia, reduced visual acuity and conjunctival hemorrhage. The most common non-ocular event reported was headache (>33%).

Please see complete information about RETISERT® in the accompanying full prescribing information on pages 7 and 8.
patient’s condition was similar to what is seen in Irvine-Gass syndrome, i.e., CME following cataract surgery, which is typically treated with these topical agents. Many of the available topical steroid and NSAID drops are specifically indicated for the reduction of ocular inflammation following cataract surgery, and it is generally accepted that their effectiveness against CME can be synergistic. With use of the drops, the patient’s visual acuity was maintained at 20/40 for more than a year.

Oct. 26, 2004: By the time of this visit, the patient’s ocular inflammation had recurred. OCT showed macular thickening to 428 µm as well as the development of subretinal fluid (Figure 1). Vision declined to 20/60. A fifth triamcinolone injection was given (sub-Tenon’s), and oral acetazolamide was prescribed. Systemic carbonic anhydrase inhibitors, used off-label, have been shown to be of some benefit for reducing subretinal fluid.30

Dec. 23, 2004: Fluorescein angiography showed early and diffuse cystic leakage in the macula and disc (Figures 2a and 2b). A sixth sub-Tenon’s triamcinolone injection was given. For the next 9 months, vision was stable at 20/40.

Sept. 20, 2005. Visual acuity was 20/40, but OCT showed recurrent serous detachment of the macula and macular thickness of 324 µm.

By this point in the patient’s treatment, it was clear his condition was chronic. The Standardization of Uveitis Nomenclature (SUN) Working Group defined “chronic” uveitis as persistent and characterized by prompt relapse (less than 3 months) after discontinuation of therapy.31 None of the treatments that we tried were providing the desired continuous control of the ocular inflammation. We had not been able to improve his visual acuity to better than 20/40 and sometimes it would drop below that level. I preferred not to initiate systemic steroid or other immunomodulatory therapy, and risk the potential side effects, because the inflammation in this particular case was only in one eye, and the patient did not have an underlying condition that required either of those therapies. Also, approximately 5 months prior to his September 2005 visit, the FDA had approved the Retisert implant, giving us an alternative treatment to consider. I participated in the Retisert clinical trials and had seen some good results in the patients I treated.

The patient was a good candidate for Retisert because his non-infectious posterior uveitis was chronic, and:

• ocular disease, rather than a systemic condition, was driving treatment decisions
periocular and intravitreal steroid injections had improved his condition for short periods, but continuous control of ocular inflammation had not yet been achieved.  
- periocular and intravitreal steroid injections had not increased his IOP.  
- he had no glaucomatous nerve damage.

Weighing these factors against the potential risks of the Retisert implantation procedure and the known side effects of sustained-release ocular steroids, including cataract (the patient had already undergone cataract removal OD) and increased IOP, (See “Important Risk Information for Retisert,” on page 3), I recommended Retisert.32 After discussing the potential benefits and risks with the patient, he elected to proceed.

I implanted a Retisert on Nov. 2, 2005. Given that the eye had previously undergone a vitrectomy, I placed a transconjunctival 25-gauge infusion cannula during surgery to help maintain a safe pressure. Per my usual protocol, the patient returned for follow-up every 2–3 months for the first year post-implantation. Since the eye remained quiet, I extended the time between follow-up visits to every 3–4 months during the second year.

After implantation, the patient experienced gradual and steady improvement in visual acuity. He did not experience elevated IOP and did not require any treatment other than Retisert for the uveitis. Visual acuity was 20/20 and macular thickness was normal at 203 through 2009 (Figures 3a and 3b).

In the clinical trials which eventually led to FDA approval, two versions of the implant, 0.59-mg and 2.1-mg, were evaluated. Only efficacy data on the 0.59-mg implant were considered, and approval was based on 34-week results.4 The primary efficacy endpoint in the studies was the rate of recurrence of uveitis in the study eye in the 34 weeks prior to implantation compared with the rate of recurrence 34 weeks, 1 year, 2 years and 3 years after implantation. In two randomized, double-masked, multicenter, controlled clinical trials, 224 patients received a 0.59-mg Retisert implant, which significantly reduced recurrence rates. (See “Uveitis Recurrence Rates” chart for specific results.)

Additional secondary endpoints of the 3-year clinical trials showed that 23% of eyes that received the 0.59-mg implant had improved visual acuity (gain of ≥3 lines) compared with 6% of fellow non-implanted eyes.24 In addition, at 1 year after implantation in the 0.59-mg group, reduction in the area of CME was seen in 86% of eyes. At 3 years after implantation, the area of CME was decreased in 73% of eyes. Mean area of CME decreased from 33 mm² to 7 mm² from screening to 34 weeks after implantation.

Please see Important Risk Information for Retisert on page 3.
implantation. The area of CME remained statistically significantly lower than baseline at the 1-, 2- and 3-year post-implantation visits.

I typically do not remove an initial Retisert implant when the drug is depleted; I do however see these patients every 6 or 12 months to ensure the implant is not causing any problems. The patient described here is now 69 years old and seeing an eye doctor every 6 to 12 months is recommended.

Although this patient did not experience any problems related to wound closure after Retisert implantation, I have since changed my Retisert suture strategy to bolster prevention of such problems over the long-term. I still use the recommended 8-0 propylene suture to secure the implant to the sclera, but before placing the recommended single 9-0 propylene suture on each side, I now often use 7-0 Vicryl absorbable sutures to tightly close the incision. This creates tighter wound closure without the risks of extra permanent sutures, such as conjunctival erosion, exposure or infection.

The more recently approved sustained-release steroid implant Ozurdex may also alter my treatment protocol in certain cases. For example, Ozurdex, which is designed to release steroid for less time than Retisert, may sufficiently treat non-infectious posterior uveitis characterized by mild inflammation (but resistant to steroid injections) without exposing the eye to several years of drug.

FORWARD PROGRESS

In my opinion, the case I have presented here is an excellent illustration of how Retisert can be a useful addition to our treatment options for non-infectious posterior uveitis. The implant allowed us to achieve long-term remission of uveal inflammation for this patient without the use of any systemic therapy or ongoing need for local therapy.

Please see Important Risk Information for Retisert on page 3.
Bausch & Lomb
Resitert
(fluocinolone acetonide intravitreal implant) 0.59 mg
STERILE

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use RETISERT safely and effectively. See full prescribing information for RETISERT. RETISERT (fluocinolone acetonide intravitreal implant) 0.59mg Initial U.S. Approval: 1963

INDICATIONS AND USAGE
RETISERT is a corticosteroid indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye (1)

DOSAGE AND ADMINISTRATION
RETISERT is surgically implanted into the posterior segment of the affected eye through a pars plana incision. (2.1)

RETISERT is designed to release fluocinolone acetonide at a nominal initial rate of 0.6 µg/day, decreasing over the first month to a steady state between 0.3-0.4 µg/day over approximately 30 months. (2.1)

Dose should be maintained at all times prior to and during the surgical implantation procedure. (2.2)

DOSE FORMS AND STRENGTHS
0.59 mg fluocinolone acetonide intravitreal implant.

CONTRAINDICATIONS
Surgical placement of RETISERT is contraindicated in active viral, bacterial, mycobacterial and fungal infections of ocular structures. (4.1)

WARNINGs AND PRECAUTIONS
Cataract formation: Nearly all phakic patients are expected to develop cataracts and require cataract surgery. (5.1)

Endophthalmitis: Late onset endophthalmitis has been observed. (5.2)

Increase in intraocular pressure: Use of corticosteroids may result in increased IOP and/or glaucoma. (5.3)

IOP lowering medications were required in >75% of patients; filtering surgeries were required in >35% of patients. (6.1)

Separation of implant components: Physicians should periodically monitor the integrity of the implant by visual inspection. (5.4)

ADVERSE REACTIONS
Ocular adverse events included procedural complications, and eye pain (<5%). Thirty-five percent of patients reported ocular/conjunctival hyperemia, reduced visual acuity, and conjunctival hemorrhage. (6.1)

The most common non-ocular event reported was headache (>3%). (6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb at 1-800-323-0000 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION

Revised March 2009

6.2 Clinical Trials Experience - Non-Ocular Events
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8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
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17. PATIENT COUNSELING INFORMATION

Sections or subsections omitted from the full prescribing information are not listed.
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience - Occular Events

The available safety data includes exposure to RETISERT in patients with chronic noninfectious uveitis affecting the posterior segment in two multicenter controlled clinical trials. Patients were randomized to dosages regimens of 0.59 mg or 2.1 mg implants. The most frequently reported ocular adverse events were cataract, increased intraocular pressure, procedural complication, and eye pain. These events occurred in approximately 50 - 90% of patients. Cataract includes aggravated cataract, and posterior capsular opacification. Procedural complications includes post-op complication, post-op wound site erythema, and wound dehiscence.

Based on clinical trials with RETISERT, during the 3-year post-implantation period, nearly all phakic eyes are expected to develop cataracts and require cataract surgery. IOP lowering medications to lower intraocular pressure were required in approximately 77% of patients; filtering surgeries were required to control intraocular pressure in 37% of patients. Ocular adverse events occurring in approximately 10 - 40% of patients in decreasing order of incidence were ocular/conjunctival hyperemia, reduced visual acuity, glaucoma, conjunctival hemorrhage, blurred vision, abnormal sensation in the eye, eye irritation, maculopathy, vitreous floaters, hyptonus, pruritus, ptosis, increased tearing, vitreous hemorrhage, dry eye, eyelid edema, macula edema and visual disturbance. Ocular adverse events occurring in approximately 5 - 9% of patients in decreasing order of incidence were eye discharge, photophobia, blepharitis, corneal edema, iris adhesions, choroidal detachment, diplopia, eye swelling, retinal detachment, photopsia, retinal hemorrhage and lypheoma.

6.2 Clinical Trials Experience - Non-Ocular Events

The most frequently reported non-ocular adverse event was headache (33%). Other non-ocular adverse events occurring in approximately 5-20% of patients in decreasing order of incidence were nasopharyngitis, rhinitis, sinusitis, dizziness, pyrosis, upper respiratory tract infection, influenza, vomiting, naso, cough, back pain, limb pain, and rash.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy

Pregnancy Category C

No adequate animal reproduction studies have been conducted with fluconolone acetone. Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Fluconolone acetone when administered subcutaneously at a dose of 0.13 mg/kg/day (approximately 10,000 times the daily clinical dose of RETISERT), during days 2 to 18 of pregnancy in the rabbit, induced abortion at the end of the third and at the beginning of the fourth gestational week. When administered subcutaneously to rats and rabbits during gestation at a maternal toxic dose of 50 mg/kg/day (approximately 4,000 times the clinical dose of RETISERT), fluconolone acetone caused abortion and malformations in a few surviving fetuses. There are no adequate and well-controlled studies in pregnant women. RETISERT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

It is not known whether ocular administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production and produce untoward effects. Caution should be exercised when RETISERT is implanted in a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients below the age of 12 years have not been established.

8.5 Geriatric Use

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

11 DESCRIPTION

RETISERT® (Fluconolone acetone intraocular implant) 0.59 mg is a sterile implant designed to release Fluconolone acetone locally to the posterior segment of the eye at a nominal initial rate of 0.6 mg/day, decreasing over the first month to a steady state between 0.3-0.4 mg/day over approximately 30 months. The drug substance is the synthetic corticosteroid Fluconolone acetone, represented by the following structural formula:

CH3 C6H5 COO H

**C** H5 F0 Mol. Wt. 462.50

Chemical Name: Prednisolone-1,4-dione 3,20-dione, 6,9-difluoro-11,12-dihydroxy-16,17-[(1-methyl-ethylenedioxy)benzoyl]-(6a,11b,16a):

Fluconolone acetone is a white crystalline powder, insoluble in water, and solubile in methylene. It has a melting point of 265-266°C.

Each RETISERT® consists of a tablet containing 0.59 mg of the active ingredients, Fluconolone Acetone, USP and the following inactives: microcrystalline cellulose, polyvinyl alcohol, and magnesium stearate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism Of Action

Corticosteroids inhibit the inflammatory response to a variety of inciting agents and probably delay or slow healing. They inhibit the edema, fibrin deposition, capillary dilation, leukocyte migration, monocyte proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation.

There is no generally accepted explanation for the mechanism of action of oculi corticosteroids. However, corticosteroids are thought to act by the induction of phospholipase A2, 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 A2. Corticosteroids are capable of producing a rise in intraocular pressure.

12.3 Pharmacokinetics

In a subset of patients who received the intravitreal implant, and had blood samples taken at various times (weeks 1, 4 and 16) after implantation, plasma levels of fluconolone acetone were below the limit of detection (0.2 mg/ml) at all times. Aqueous and vitreous humor samples were assayed for fluorocine acetone in a further subset of patients. While detectable concentrations of fluorocine acetone were seen throughout the observation interval (up to 34 months), the concentrations were highly variable, ranging from below the limit of detection (0.2 mg/ml) to 589 mg/ml.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment Of Fertility

Long-term animal studies have not been performed on RETISERT to evaluate the carcinogenic potential or the effect on fertility of fluorocine acetone. Fluconolone acetone was not genotoxic in vitro in the Ames test, the mouse lymphoma TK assay, or in vivo the bone marrow micronucleus assay.

14 CLINICAL STUDIES

In two randomized, double-masked, multicenter controlled clinical trials, 224 patients with chronic (a one year or greater history) non-infectious uveits affecting the posterior segment of both or one eyes were randomized to receive a 0.59 mg RETISERT. The primary efficacy endpoint in both trials was the rate of recurrence of uveits affecting the posterior segment of the study eye in the 34 week pre-implantation period compared to the rate of recurrence in the 34 week post-implantation period. Uveits recurrence rates at 1, 2, and 3 years post-implantation were also compared to the 34 week pre-implantation period.

Detailed results are shown in Table 1 below:

<table>
<thead>
<tr>
<th>TIME POINT</th>
<th>STUDY 1</th>
<th>STUDY 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>34 Weeks Pre-implantation</td>
<td>58 (37.3%)</td>
<td>46 (39.7%)</td>
</tr>
<tr>
<td>34 Weeks Post-implantation</td>
<td>2 (1.8%)</td>
<td>15 (12.9%)</td>
</tr>
<tr>
<td>1 Year Post-implantation</td>
<td>4 (3.7%)</td>
<td>15 (12.9%)</td>
</tr>
<tr>
<td>2 Years Post-implantation</td>
<td>11 (10.2%)</td>
<td>16 (13.8%)</td>
</tr>
<tr>
<td>3 Years Post-implantation</td>
<td>22 (20.9%)</td>
<td>20 (17.2%)</td>
</tr>
<tr>
<td>3 Years' Post-implantation</td>
<td>33 (30.6%)</td>
<td>28 (24.1%)</td>
</tr>
</tbody>
</table>

* Recurrence of uveits for all post-implantation time points was compared to the 34 weeks pre-implantation time point.

** p-value = 0.01 from McNemar’s test.

* Results presented include imputed recurrences. Recurrences were imputed when a subject was not seen within 10 weeks of their final scheduled visit.

16 HOW SUPPLIED/STORAGE AND HANDLING

The implant consists of a tablet encased in a silicone elastomer cup containing a release orifice and a polyvinyl alcohol membrane positioned between the tablet and the orifice. The silicone elastomer cup assembly is attached to a polyvinyl alcohol suture tab with silicone adhesive. Each RETISERT® is approximately 3 mm x 2 mm x 5 mm.

Each implant is stored in a clear polyethylene case within a foil pouch within a Tyvek peelable overwrap. Each packaged implant is provided in a carton which includes the package insert.

NDC 24208-416-01

Storage: Store in the original container at 15° - 25°C (59° - 77°F). Protect from freezing.

17 PATIENT COUNSELING INFORMATION

Patients should be advised to have ophthalmologic follow-up examinations of both eyes at appropriate intervals following implantation of RETISERT.

As with any surgical procedure, there is risk involved. Potential complications accompanying intravitreal surgery to place RETISERT into the vitreous cavity may include, but are not limited to, the following: cataract formation, choroidal detachment, temporary decreased visual acuity, endophthalmitis, hypotony, increased intraocular pressure, exacerbation of intraocular inflammation, retinal detachment, vitreous hemorrhage, vitreous loss, and wound dehiscence.

Following implantation of RETISERT, nearly all patients will experience an immediate and temporary decrease in visual acuity in the implanted eye which lasts for approximately one to four weeks post-operatively.

Based on clinical trials with RETISERT, within 3 years post-implantation, approximately 77% of patients will require IOP lowering medications to control intraocular pressure and 37% of patients will require filtering procedures to control intraocular pressure. (see 6.1 Clinical Trials Experience - Ocular Events section).

Based on clinical trials with RETISERT, during the 3-year post-implantation period, nearly all phakic eyes are expected to develop cataracts and require cataract surgery.

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