



Dear Healthcare Professional,

Thank you for your unsolicited request for information. Accompanying this letter is the following information you requested on ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg. If we can be of any further assistance, please contact our Medical Information department at 844-445-8843 between the hours of 9:00 AM to 8:00 PM ET (6:00 AM to 5:00 PM PT), Monday through Friday or via email at iluvienmedinfo@anipharma.com.

ILUVIEN is indicated for the treatment of diabetic macular edema (DME) in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure.

ILUVIEN is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

ILUVIEN is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases.

ILUVIEN is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8.

ILUVIEN is contraindicated in patients with known hypersensitivity to any components of this product.

Please see the enclosed ILUVIEN Prescribing Information (PI) for detailed information including Warnings and Precautions and Adverse Reactions as well as the appropriate use of ILUVIEN.

This communication may contain confidential, proprietary, and/or privileged information. It is intended solely for the use of the addressee. If you are not the intended recipient, you are strictly prohibited from disclosing, copying, distributing or using any of this information. If you received this communication in error, please contact the sender immediately and destroy the material in its entirety, whether electronic or hard copy.

Thank you for your inquiry.

Sincerely,

A handwritten signature in black ink that reads "Steve Wu". The signature is written in a cursive, flowing style.

Steve Wu, PharmD
ANI Pharmaceuticals Medical Information

Use of ILUVIEN® in Vitrectomized Eyes

Abstract

- This document provides summary information pertaining to ILUVIEN® (fluocinolone acetonide [FAC] implant) 0.19 mg and its indication for use in the treatment of diabetic macular edema (DME) and treatment of chronic non-infectious uveitis affecting the posterior segment of the eye (NIU-PS)
- Provided in this document are summaries of publications and presentations from Europe and the United States describing functional and anatomical outcomes in patients receiving ILUVIEN following prior vitrectomy

Note that this document is for information purposes only and has been sent as a professional courtesy to provide you with data to assist in making your own practicing decisions. Please refer to the ILUVIEN (fluocinolone acetonide [FAC]) implant USPI for full [Prescribing Information](#) and safety information. ANI Pharmaceuticals does not recommend the use of its products in any manner inconsistent with the FDA-approved labeling. If you have further questions, please contact the Medical Affairs Department at <drugsafety@anipharma.com>.

To report an adverse event for any ANI Pharmaceuticals product, please call 1-800-308-6755 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Email: <drugsafety@anipharma.com>

Introduction

Clinical Background

ILUVIEN is indicated for the treatment of diabetic macular edema (DME) in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure (IOP).¹

ILUVIEN is indicated the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.¹

Composition of ILUVIEN

ILUVIEN is a non-bioerodable intravitreal implant in a drug delivery system containing 0.19 mg FAc, designed to release FAc at an initial rate of 0.25 µg/day and lasting 36 months. Each ILUVIEN consists of a light brown 3.5mm x 0.37mm implant containing 0.19 mg of the active ingredient FAc and the following inactive ingredients: polyimide tube, polyvinyl alcohol, silicone adhesive, and water for injection.¹

Pharmacokinetics

In a human pharmacokinetic study of ILUVIEN, FAc concentrations in plasma were below the lower limit of quantitation of the assay (100 pg/mL) at all post-administration time points from Day 7 through Month 36 following intravitreal administration of a 0.2 mcg/day or 0.5 mcg/day FAc insert.¹

Clinical Pharmacology

ILUVIEN contains the corticosteroid FAc. Corticosteroids inhibit inflammatory responses to a variety of inciting agents including multiple inflammatory cytokines. They inhibit edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. Corticosteroids are thought to act by inhibition of phospholipase A₂ via induction of inhibitory proteins collectively called lipocortins. It is postulated that these proteins control biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting release of the common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A₂.¹

Warnings and Precautions

Intravitreal Injection-related Effects

Intravitreal injections, including those with ILUVIEN, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. For patients with non-infectious uveitis affecting the posterior segment, hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection [see Patient Counseling Information (17)]. Patients may experience temporary blurred vision after injection of the implant.¹

Intraocular Pressure (IOP) Increase

Prolonged use of corticosteroids may result in the development of 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. Intraocular pressure should be routinely monitored during the course of the treatment.¹

Cataracts

The use of corticosteroids may result in posterior subcapsular cataract formation.¹

Delayed Corneal Wound Healing

The use of corticosteroids after cataract surgery may delay healing and increase the incidence of bleb formation.¹

Corneal and Scleral Melting

Various ocular diseases and long-term use of topical corticosteroids have been known to cause corneal and scleral thinning. Use of ophthalmic corticosteroids in the presence of thin corneal or scleral tissue may lead to perforation of the globe.¹

Bacterial Infections

Prolonged use of corticosteroids may suppress the host immune response and thus increase the hazard of secondary ocular infections. Acute purulent or parasitic infections of the eye may be masked or activity enhanced by the presence of corticosteroid medication. If signs and symptoms fail to improve after 2 days, the patient should be reevaluated.¹

Viral Infections

Use of ocular corticosteroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution; frequent slit lamp microscopy is recommended.¹

Fungal Infections

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local corticosteroid application. Fungus invasion should be suspected in any persistent corneal ulceration where a corticosteroid has been used or is in use. Fungal cultures should be taken when appropriate.¹

Risk of Implant Migration

Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.¹

Incidence of Vitrectomy in FAME Studies

The FAME trials were randomized, double-masked, sham-injection–controlled studies to assess the efficacy and safety of ILUVIEN in patients with persistent DME despite prior macular laser treatment.² In the FAME trials, patients with a prior history of vitrectomy were excluded from enrollment.² However, during the trial, 24 patients treated with the ILUVIEN implant underwent vitrectomy.³ An assessment comparing retinal thickness before and after showed no evidence of reduced efficacy.³ When comparing the retinal thickness reduction in patients who underwent vitrectomy to those randomized to ILUVIEN but did not undergo the procedure, no difference was observed that would indicate a loss of effect.³ Additionally, there were no reports of implant damage due to vitrectomy in these patients.³

A PubMed literature search up to December 2024 using the terms “fluocinolone acetonide,” “intravitreal implant,” “fluocinolone acetonide intravitreal implant,” “ILUVIEN,” and “vitreotomy,” or “vitrectomized eyes,” was conducted, excluding case reports with N≤2 eyes. The following publications were identified to be of interest and are summarized to describe outcomes in patients with DME receiving ILUVIEN with vitrectomized and non-vitrectomized eyes.

A Retrospective Analysis of Patients With Vitrectomized vs Non-Vitrectomized Eyes Treated With ILUVIEN for DME

In a retrospective analysis based in Portugal, Pessoa and colleagues compared the functional and anatomical outcomes after administration of the ILUVIEN implant among vitrectomized vs non-vitrectomized eyes with chronic diabetic macular edema. Among 43 eyes, all patients were treated with a single ILUVIEN implant and followed for a mean of 8.5 months (median, 6.0 months; range 1-21 months). Patients were divided into 2 groups: 24 eyes having undergone pars plana vitrectomy prior to ILUVIEN implantation (Group 1) and 19 eyes that had not been vitrectomized (Group 2).⁴

Mean change in BCVA at the last observation point vs baseline was significantly improved by $+16.9 \pm 3.39$ (mean \pm SE) letters in Group 1 ($P < 0.001$) and improved by $+8.2 \pm 4.62$ letters in Group 2 ($P = 0.092$) (Figure 1). Mean change in CSFT was -217.7 ± 40.8 μm and -155.6 ± 43.4 μm in Group 1 and Group 2, respectively, with no statistically significant difference observed between groups (Figure 2).⁴

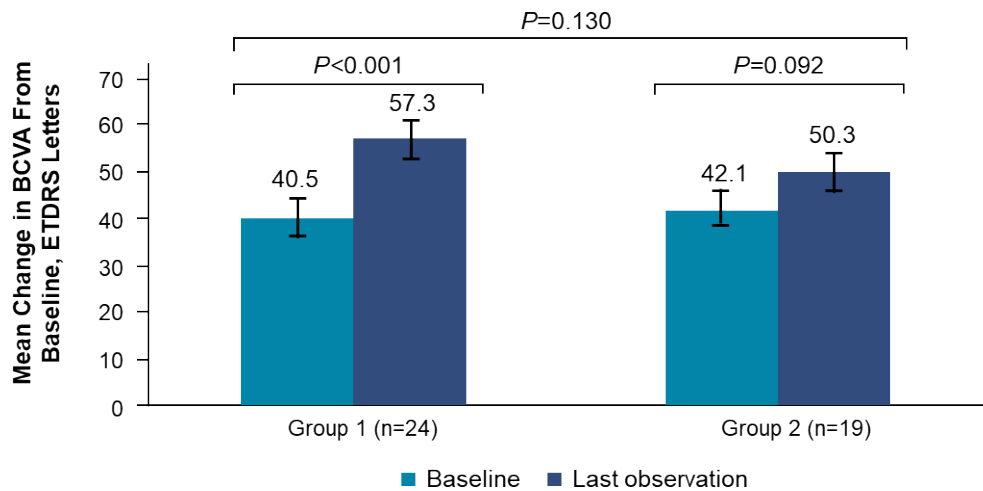


Figure 1. Mean Change in BCVA in Vitrectomized Eyes (Group 1) and Non-Vitrectomized Eyes (Group 2)

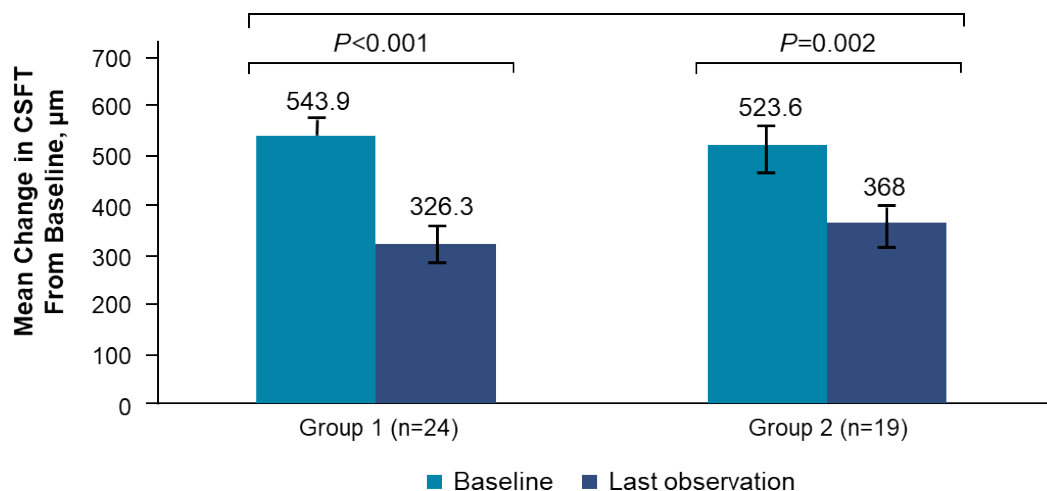


Figure 2. Mean Change in CSFT in Vitrectomized Eyes (Group 1) and Non-Vitrectomized Eyes (Group 2)

The mean change in IOP relative to baseline was $+1.6 \pm 0.7$ mmHg in Group 1 and $+0.8 \pm 1.3$ mmHg in Group 2; with no significant difference observed between groups. Limitations of this analysis include the retrospective nature of the data, small cohort size, and variable follow up between patients.⁴

A Comparative, Retrospective, Observational Study Assessing Patients Treated with Iluvien for DME With and Without PPV

In a single-center, comparative, retrospective, observational study based in London, UK, La Mantia and colleagues reported 12-month outcomes of ILUVIEN-treated patients with chronic DME (n=23 eyes) that included both pars plana vitrectomized (PPV) and non-PPV subjects. Best corrected visual acuity (BCVA) and central macular thickness were recorded at multiple time points including baseline, 1, 4, and 12 months. Approximately 7 PPV and 16 non-PPV eyes were included in the study. The main indication for PPV was vitreous hemorrhage, followed by epiretinal membrane and tractional retinal detachment. Mean BCVA gain in the PPV group at 12 months was 0.24 logMAR compared with 0.17 logMAR in the non-PPV group. Mean improvement in CMT in the PPV group from baseline to 12 months was 60 μm compared with 72 μm in the non-PPV group. Kruskal-Wallis tests did not demonstrate a difference in mean ranks for BCVA or CMT over the study period. Mean/median BCVA and CMT are provided in the table below. IOP lowering drops were prescribed for some patients following implant placement; none required surgical treatment to reduce IOP after ILUVIEN. Minimal change in visual acuity and macular thickness were observed in eyes that had undergone PPV; however, better visual outcomes and reductions in macular thickness were observed in eyes that had not undergone PPV. Limitations of the study included small sample size and retrospective design.⁵

Parameters	BCVA (logMAR)				CMT (μm)			
	N	Mean	Median	Range	n	Mean	Median	Range
PPV								
Pre-injection	7	0.96	0.60	0.50-2.40	7	459	483	242-713
1 month	6	0.78	0.75	0.44-1.12	7	447	475	307-554
4 months	7	0.81	0.80	0.36-1.60	7	414	372	305-631
12 months	7	0.72	0.74	0.26-1.20	7	399	397	236-631
Non-PPV								
Pre-injection	16	0.67	0.65	0.30-1.22	16	416	430	235-584
1 month	14	0.60	0.59	0.14-1.32	15	380	341	232-652
4 months	13	0.44	0.40	0.10-1.30	13	343	316	215-483
12 months	16	0.51	0.42	0.00-1.10	16	344	317	222-732

Table 1. Mean/Median BCVA and CMT Pre-ILUVIEN and Post-ILUVIEN Implant Insertion in Vitrectomized and Non-Vitrectomized Eyes

PPV, pars plana vitrectomy; BCVA, best corrected visual acuity; CMT, central macular thickness.

A Retrospective Audit Study Assessing Patients Treated with a Single ILUVIEN Implant for DME With and Without PPV

At ARVO 2017, Koch and colleagues presented a retrospective, monocentric audit of data on 33 eyes (n=25 patients) treated with a single ILUVIEN implant. Thirty-two eyes had undergone previous PPV. ILUVIEN was administered after suboptimal response to prior DME therapies, which included ranibizumab (n=19), dexamethasone (n=12), panretinal photocoagulation (n=19), and focal laser (n=7). After ILUVIEN implantation, no other therapies were given. During a mean follow-up of 6.7 months, treatment with ILUVIEN therapy showed a mean improvement in visual acuity from baseline of 5.1 Early Treatment of Diabetic Retinopathy Study (ETDRS) letters. Of note, visual acuity improved by an average of 3.8 ETDRS letters in eyes with previous suboptimal response to dexamethasone. Visual acuity was improved or maintained in 72.7% of eyes. Cataract extraction was performed in six of 13 eyes that were phakic at baseline. IOP elevation to 30 mmHg in a single eye was treated successfully with a trabeculectomy.⁶ In another seven patients, moderate IOP increases were treated successfully with topical therapies.⁴

Multinational Retrospective Case Series of Patients With DME Treated With ILUVIEN After PPV

Meireles and colleagues described the first multinational (UK, France, Portugal, and Germany) multicenter case series (26 eyes, 25 patients) publication to retrospectively assess safety and efficacy of a single ILUVIEN implant in patients with DME and a PPV. Prior intravitreal therapies included anti-VEGF (mean, 3.8 injections) and steroids (mean, 1.9 injections). The ILUVIEN implant was injected an average of 24.2 months after PPV and the mean duration of follow-up after injection was 8.5 months. PPV was performed in these eyes primarily for abnormalities of vitreoretinal interface, followed by proliferative diabetic retinopathy and vitreous hemorrhage.⁷

The mean change in BCVA in PPV eyes was +11.7 ETDRS letters compared to baseline (range, -19 to +40 letters; $P<0.0004$) (Figure 3). Mean change in central foveal thickness (CFT) in PPV eyes was -233.5 μm compared to baseline (range, -678 to 274 μm ; $P<0.0001$) (Figure 4). Study results showed a mean gain in visual acuity of >2 ETDRS lines and a mean 43% decrease in CRT vs baseline.⁷

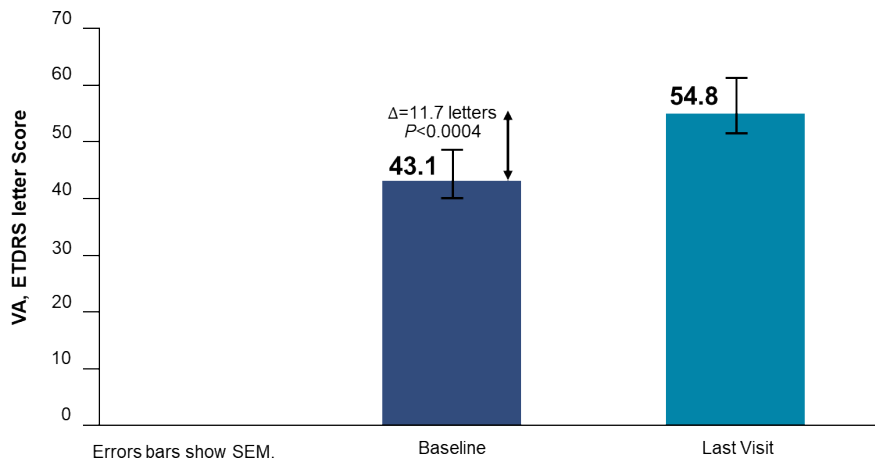


Figure 3. Change in Visual Acuity (ETDRS Letters) From Baseline to the Last Visit

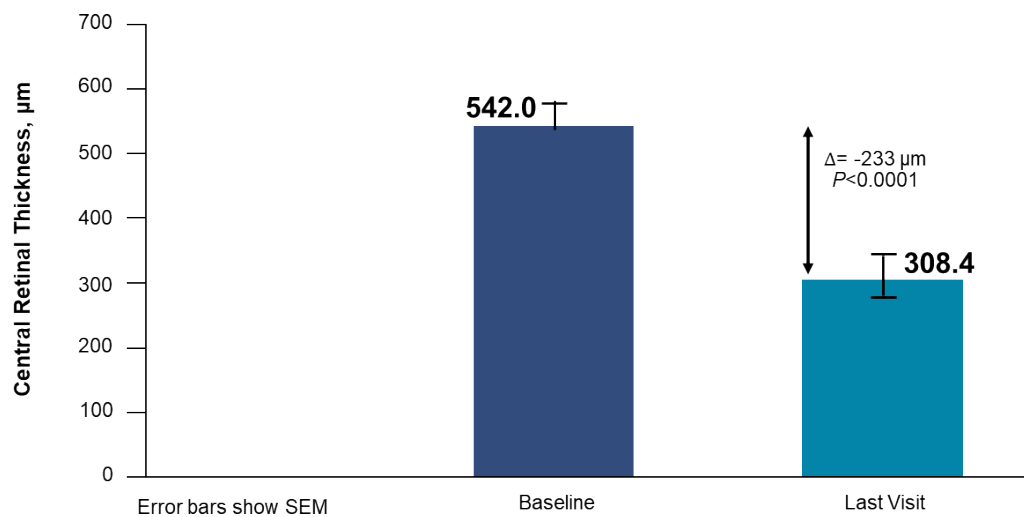


Figure 4. Change in Central Retinal Thickness (CRT) From Baseline to the Last Visit

Safety findings showed a mean change of +1.4 mmHg in IOP vs baseline (range, -9 to +8 mmHg; $P=0.0090$) at the last visit. Eight eyes initiated or continued IOP-lowering medications and none required IOP-lowering surgery. Implant migration occurred in 2 eyes with a previous capsular tear. The authors concluded that caution is required in vitrectomized eyes where there is a disruption in the posterior capsule.⁷

Multi-Centre UK-Based Retrospective Study of Patients with DME Treated with ILUVIEN Who Underwent Prior Vitrectomy

In a multi-center, United Kingdom based retrospective study, the efficacy and safety of ILUVIEN was evaluated in 22 patients with DME over a 3 month period. A total of 5 eyes had undergone vitrectomy prior to the administration of the ILUVIEN implant. In this subcohort, visual acuity improved by + 7.2 letters (range: 0 to +14), and CRT reduced by 176.8 (range: -714 to +385) compared to baseline. Four of the 5 eyes showed both a reduction in CRT and improved visual acuity relative to baseline. However, one patient experienced a reduction in CRT (-345) without any gain in visual acuity. During the short follow up period, only one eye required IOP lowering medication (baseline mean IOP was 16.9 mmHg with a mean change of 0.3 mmHg (SD: ± 3.1 ; range: -7 to +5) at Month 3).⁸

References

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