



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](mailto: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.

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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® Intravitreal Implant in Proliferative Diabetic Retinopathy

## 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)
- This document provides summary information about research conducted to assess the effect of ILUVIEN on progression to proliferative diabetic retinopathy (PDR)

**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](http://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).<sup>1</sup>

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

ILUVIEN is not indicated for the treatment of PDR.

### 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.<sup>1</sup>

### 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.<sup>1</sup>

### 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 A<sub>2</sub> 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 A<sub>2</sub>.<sup>1</sup>

Please note, ILUVIEN is not approved by the FDA as safe and effective for the treatment of DR.

## 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.<sup>1</sup>

### **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.<sup>1</sup>

### **Cataracts**

The use of corticosteroids may result in posterior subcapsular cataract formation.<sup>1</sup>

### **Delayed Corneal Wound Healing**

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

### **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.<sup>1</sup>

### **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.<sup>1</sup>

### **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.<sup>1</sup>

### **Fungal Infections**

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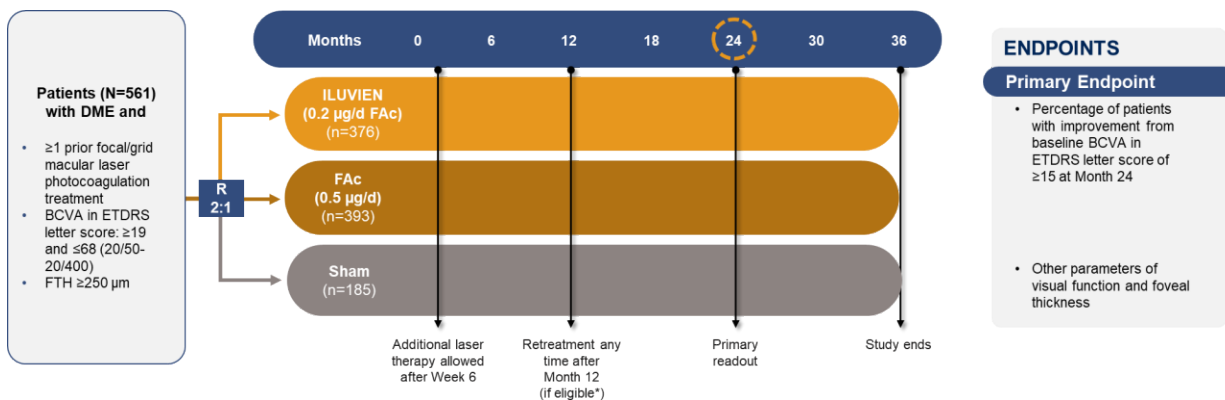
corticosteroid application. Fungus invasion should be suspected in any persistent corneal ulceration where a corticosteroid has been used or is in use. Fungal cultures should be taken when appropriate.<sup>1</sup>

### 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.<sup>1</sup>

### FAME Study: 36-Month Results

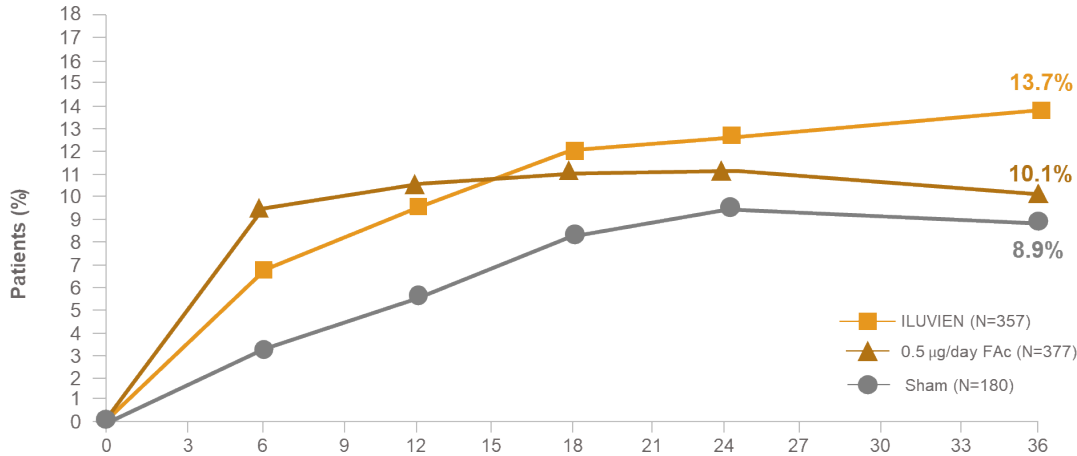
The FAME trials (FAME A and FAME B) were randomized, double-masked, sham injection-controlled, parallel-group, multicenter safety and efficacy studies in subjects with DME despite prior laser treatment.<sup>2</sup> A total of 953 subjects participated in the two studies combined, with subjects randomized in a 2:2:1 ratio to 1 of 3 treatment groups: low-dose ILUVIEN implant (FAc 0.2 µg/day; n=375, high-dose FAc intravitreal implant (FAc 0.5 µg/day; n=393), or sham injection (n=185).<sup>2</sup> Each FAME study consisted of ≥16 visits over a 3-year post-treatment period (Figure 1).<sup>2</sup>



**Figure 1. The FAME Study Design<sup>2</sup>**

\*Patients were eligible for retreatment with their initially assigned study drug after Month 12 if they experienced loss of ≥5 letters in BCVA or an increase in foveal thickness (FTH) ≥50 µm compared with the patient’s best status during the previous 12 months.

Assessment of DR based on the Early Treatment Diabetic Retinopathy Study (ETDRS) Multistep Eye Scale of Diabetic Retinopathy was not a primary endpoint of the FAME trials; however, it was reviewed among the secondary endpoints (Figure 2). At Month 36, the percentage of patients with ≥2-step improvement in the ETDRS DR scale in the sham treatment group (8.9%) was smaller than the percentage of patients treated with ILUVIEN (low dose FAc) (13.7%) and similar to the percentage in the high dose FAc group (10.1%). There were no statistically significant differences observed between groups. To note, the high-dose FAc insert only released active drug for approximately 24 months, whereas the ILUVIEN insert released drug for approximately 36 months but retreatment was not allowed after Month 33.<sup>2</sup>



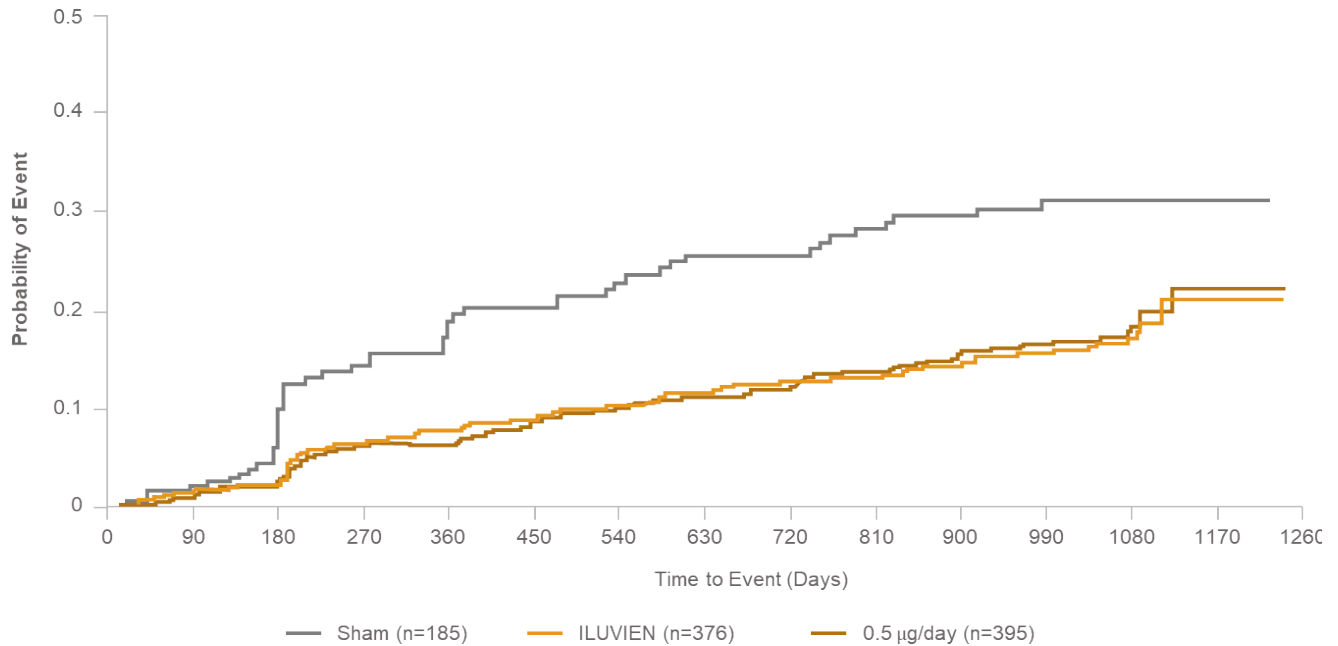
**Figure 2. Percentage of Patients With a  $\geq 2$ -Step Improvement in ETDRS Diabetic Retinopathy Severity Score<sup>2</sup>**

#### Effects on Progression to PDR: Post Hoc Analysis of FAME

Wykoff and colleagues conducted a post hoc analysis of FAME to assess the effect of ILUVIEN on progression to PDR and regression of DR.<sup>3</sup> At baseline, approximately 60% of patients were graded as nonproliferative diabetic retinopathy (NPDR), while 40% were graded as proliferative diabetic retinopathy (PDR).<sup>3</sup>

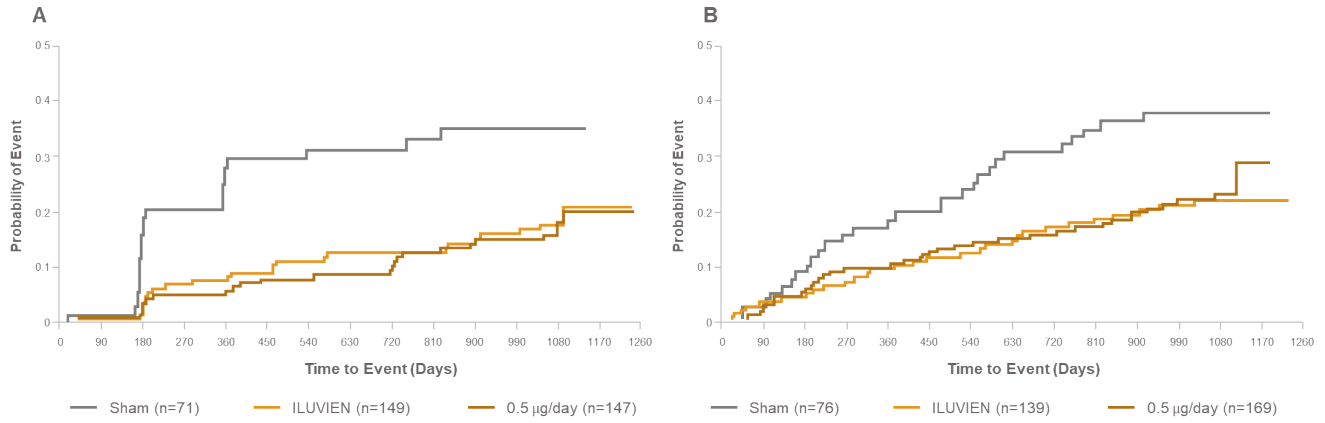
At Month 36, statistically significantly fewer ILUVIEN-treated eyes experienced progression of PDR (17%) versus sham-treated eyes (31%) ( $P < 0.001$ ). Progression of PDR in the FAME study was determined based on fundus photographs that were graded by a masked, certified reading center. The need for panretinal photocoagulation (PRP) and pars plana vitrectomy (PPV) were assessed.<sup>3</sup>

Over 36 months, 28.6% (53/185) of the sham group, 16.2% (61/376) of the low-dose ILUVIEN group, and 17.2% (68/395) of the high-dose ILUVIEN group experienced a predefined PDR event. These included 13.0%, 7.2%, and 6.8% of subjects, respectively, who developed PDR; 14.1%, 7.2%, and 8.9% who underwent PRP; and 1.6%, 1.9%, and 1.5% who underwent PPV. Compared with sham treatment, time to a first PDR event was significantly longer with ILUVIEN treatment ( $P < 0.001$ ), an effect that was independent of ILUVIEN dose (Figure 3).<sup>3</sup>



**Figure 3. Time to Progression to a First PDR Event in All Patients**

The delay in time to a first PDR event with ILUVIEN compared with sham was evident in patients with baseline DR severity of 47–53 and in those with baseline severity of 60–75 (Figure 4).<sup>3</sup>



**Figure 4. Time to Progression of PDR (Integrated FAME Studies in Patients With Baseline DR Grade 47–53 (Panel A) and Grade 60–75 (Panel B))**

## References

1. ILUVIEN (fluocinolone acetonide intravitreal implant) 0.19 mg, for intravitreal injection. Prescribing Information. ANI Pharmaceuticals, Inc. Updated 2023. Accessed January 17, 2025. <https://hcp.iluvien.com/prescribing-information/>
2. Campochiaro PA, Brown DM, Pearson A, et al; FAME Study Group. Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema. *Ophthalmology*. 2012;119(10):2125-2132.
3. Wykoff CC, Chakravarthy U, Campochiaro PA, et al. Long-term effects of intravitreal 0.19 mg fluocinolone acetonide implant on progression and regression of diabetic retinopathy. *Ophthalmology*. 2017;124(4):440-449.