



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

Scleral Fixation of ILUVIEN[®] Intravitreal Implant

Abstract

- This document provides summary information pertaining to ILUVIEN[®] (fluocinolone acetonide [FAC] intravitreal 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 describes a surgical technique for preventing migration of the ILUVIEN implant into the anterior chamber of the eye and a prospective study evaluating this surgical technique

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 fluocinolone acetonide (FAC), designed to release FAC at an initial rate of 0.25 mcg/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, fluocinolone acetonide 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 fluocinolone acetonide 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

There is no specific information contained within the ILUVIEN Prescribing Information regarding scleral fixation of the implant. In the Warnings and Precautions section, the label states that *“the implant may migrate into the anterior chamber if the posterior lens capsule is not intact.”*¹

Published Reports of Scleral Fixation of the ILUVIEN Implant

A review of the literature (between January 1, 2020-December 1, 2024) using the terms “fluocinolone acetonide,” “intravitreal implant,” “fluocinolone acetonide intravitreal implant,” and “ILUVIEN” combined with “scleral fixation” was conducted, excluding all case reports with N≤2 eyes. From this search, a technical report describing a novel surgical technique for preventing implant migration and a prospective off-label interventional clinical trial (MEFISTO) by the same investigators evaluating this novel technique were identified to be of interest. Both reports are summarized below.

Scleral Fixation of the ILUVIEN Implant: Proof-of-Principal for a New Surgical Technique

Treatment of recalcitrant macular edema with an intravitreal steroid implant can be difficult in eyes that have undergone complicated cataract surgery or experienced posterior capsule rupture. In such eyes, there is a dual risk of cystoid macular edema (CME) and migration of corticosteroid implants injected to treat them.²

Herold and colleagues reported a new surgical technique for implantation and fixation of the ILUVIEN implant to reduce the risk of implant migration.² The procedure is known as the fluocinolone-loop-anchoring technique (FLAT). It is performed in high-risk eyes at the time of implantation rather than as a corrective measure in eyes where the implant has already migrated.²

For the FLAT procedure, a flat-headed lens nucleus rotator was used to insert the ILUVIEN implant into the eye through the sclerotomy, creating two loop-like handles to move the implant into the vitreous cavity.² The implant was further moved to a minimum distance of 3 mm in distance from the ciliary body, and the thread was then fixed to the sclera.²

The Fluocinolone-Loop-Anchoring Technique (FLAT): Long-term Follow-up (MEFISTO)

Herold and colleagues conducted a single-center, prospective, off-label clinical trial of the FLAT technique (described above) in 10 eyes that had undergone complicated cataract surgeries, posterior capsule rupture, or experienced other trauma that left them at an increased risk of persistent cystoid macular edema (PCME).³ A monthly follow-up was done for the first year, then quarterly until Month 24. Best corrected visual acuity (BCVA) and central retinal thickness (CRT) from baseline to Month 24 were assessed along with additional safety signals.³

BCVA significantly improved over the 24 months in all but one patient, with the mean BCVA improving to 20/80 at Month 1 and 20/60 at Month 18, after which it decreased slightly to 20/80 at Month 24.³ The CRT varied among the patients but generally decreased within the first 3 months and remained stable until Month 24.³ Mean CRT decreased by 22% from 601.6-449.1 at Month 1.³ One patient required removal of the implant after experiencing persistent IOP increases.³ The mean IOP in the study did not significantly change from baseline at 12.6 ± 4.2 mmHg to Month 24 at 13.4 ± 3.0 mmHg.³

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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. Herold TR, Liegl R, Koenig S, et al. Scleral fixation of the fluocinolone acetonide implant in eyes with severe iris-lens diaphragm disruption and recalcitrant CME: the Fluocinolone-Loop-Anchoring Technique (FLAT). *Ophthalmol Ther*. 2020;9(1):175-179.
3. Herold TR, Vounotrypidis E, Liegl R, et al. Long-term efficacy of fluocinolone in eyes with iris-lens diaphragm disruption and PCME with medication fixed in the sclera (MEFISTO). *Retina*. 2022;42(7):1392-1398.