



ILUVIEN[®]
(fluocinolone acetonide
intravitreal implant) 0.19mg

What to
EXPECT
with multiyear **ILUVIEN**

A single implant that delivers steroid for
diabetic macular edema (DME) for 36 months.

Indication

ILUVIEN[®] (fluocinolone acetonide intravitreal implant) 0.19 mg is an implant injected into the eye (vitreous) and used for the treatment of diabetic macular edema in patients who have been treated with corticosteroids before and did not have a significant increase in eye pressure.

Important Safety Information

- Do not use ILUVIEN if you have or think you might have an infection in or around the eye.
- ILUVIEN should not be used if you have glaucoma.

Please see Important Safety Information on back cover and enclosed full Prescribing Information.

Shifting to ILUVIEN

About this guide

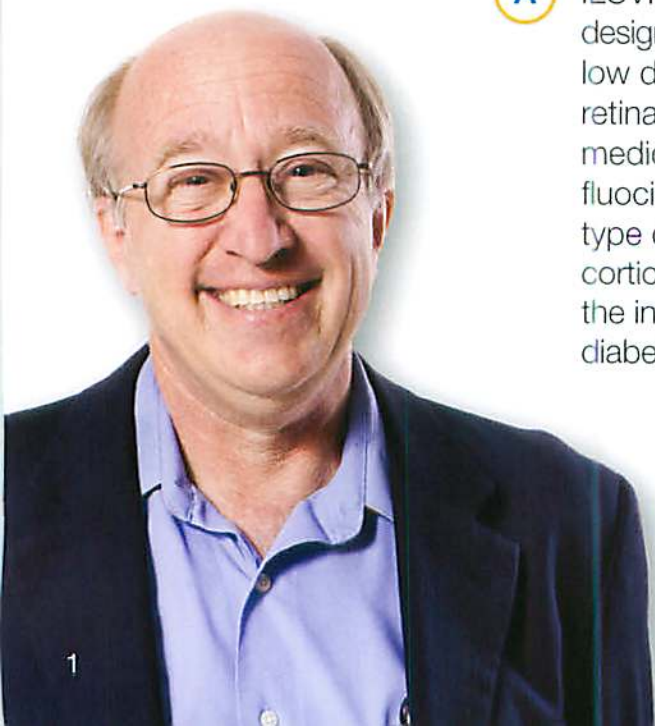
Your doctor may have decided it's time to shift to a multiyear option. Use this guide to learn about ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg and how it works. Write down any questions you have and talk to your doctor about ILUVIEN.

Q

What is ILUVIEN?

A

ILUVIEN is a tiny implant designed to release a continuous, low dose of a steroid to the retina for 36 months. The medicine in ILUVIEN is called fluocinolone acetonide (FAC), a type of steroid called a corticosteroid. FAC helps treat the inflammation associated with diabetic macular edema (DME).



Q How does ILUVIEN work?

A When DME develops, fluid collects in a part of the eye called the macula causing it to swell, which results in blurry vision. ILUVIEN[®] (fluocinolone acetonide intraocular implant) 0.19 mg is a corticosteroid used in the treatment of DME.

There are different types of steroids. Corticosteroids are man-made drugs that closely resemble cortisol, a hormone produced by the adrenal glands. Corticosteroids are different from the male hormone-related steroid compounds that some athletes abuse.

ILUVIEN is different from many other DME treatments because of the way it works. The tiny ILUVIEN implant is inserted into the eye and remains in the eye for continuous drug delivery. It is the only FDA-approved implant that delivers steroid for 36 months.

Important Safety Information (continued)

- You should not use ILUVIEN if you are allergic to any ingredients of ILUVIEN.
- Injections into the vitreous in the eye are associated with a serious eye infection (endophthalmitis), eye inflammation, increased eye pressure, glaucoma, and retinal detachments. Your eye doctor should monitor you regularly after the injection.

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About ILUVIEN

Q Why did my doctor prescribe ILUVIEN?

A ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg is used for the treatment of diabetic macular edema (DME) in people who have been treated with corticosteroids before and did not have a significant increase in eye pressure.

Your doctor may recommend ILUVIEN to treat the inflammation related to your DME. Based on the results of 2 clinical studies, ILUVIEN was proven to be safe and effective in the treatment of this condition as demonstrated for 24 months.

You should not be treated with ILUVIEN if you have glaucoma, an infection in or around the eye, or if you are allergic to any of the ingredients of ILUVIEN.

Important Safety Information (continued)

- Use of corticosteroids including ILUVIEN may produce cataracts (ILUVIEN 82%; sham 50%), increased eye pressure (ILUVIEN 34%; sham 10%), glaucoma, and may increase secondary eye infections due to bacteria, fungi, or viruses. Let your doctor know if you have a history of herpes viral infections of the eye.

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Q What should I expect during the ILUVIEN injection procedure?

A A single ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg is administered by a retina specialist during an in-office procedure. No surgery or hospital stay is typically required. And there are no stitches.

Prior to the procedure, your eye is numbed. The ILUVIEN implant is then delivered via a tiny needle. As the implant is being injected, you may feel some pressure on your eye.

Your doctor will check your eye after the injection for possible side effects, including development of cataracts, eye infection (endophthalmitis), eye inflammation, increased eye pressure, glaucoma, and retinal detachments.

A single ILUVIEN implant is administered by a retina specialist during an in-office procedure.



Risks associated with ILUVIEN

Q What else should I know about ILUVIEN?

A ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg is a prescription medicine that is inserted in the eye and has its risks.

The most common risk related to ILUVIEN treatment is the formation of cataracts. If a cataract occurs, your vision will decrease and you will need cataract surgery to restore your vision.

Another risk of ILUVIEN is increased pressure within the eye, which may progress to glaucoma. This increase in pressure can be treated with eye pressure-lowering medicines (usually eye drops). However, some people may require eye surgery to treat their increased eye pressure.

Intravitreal injections, including those with ILUVIEN, have been associated with serious eye infection (endophthalmitis), eye inflammation, increased eye pressure, and retinal detachments. Patients should be monitored following the intravitreal injection.

Important Safety Information (continued)

- If the posterior capsule of the lens of your eye is missing or torn the ILUVIEN implant may move to the front chamber of the eye.
- The most common side effects reported in patients with diabetic macular edema who were treated with ILUVIEN include cataracts (ILUVIEN 82%; sham 50%) and increased eye pressure (ILUVIEN 34%; sham 10%).

Q What type of follow-up can I expect?

A ILUVIEN[®] (fluocinolone acetonide intravitreal implant) 0.19 mg lasts for 36 months. However, your doctor will still want to see you periodically to monitor your condition and to monitor for development of cataracts, eye infection (endophthalmitis), eye inflammation, increased eye pressure, glaucoma, and retinal detachments.

It is important to make sure to keep your routine exams with your doctor. Committing to your eye health with ILUVIEN means keeping your appointments with your doctor.

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Q What more can I do to manage my DME?

A It's important to know that DME can develop without symptoms. Fortunately, early diagnosis can lead to early treatment of DME.

You can also take steps to maintain a healthy lifestyle, like regulating your blood sugar levels with proper diet and exercise. Talk to your doctor about what you can do in addition to treatment with ILUVIEN.

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INDICATION

ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg is an implant injected into the eye (vitreous) and used for the treatment of diabetic macular edema in patients who have been treated with corticosteroids before and did not have a significant increase in eye pressure.

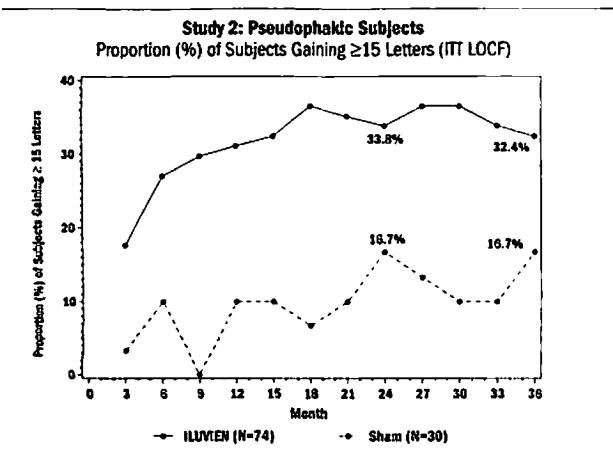
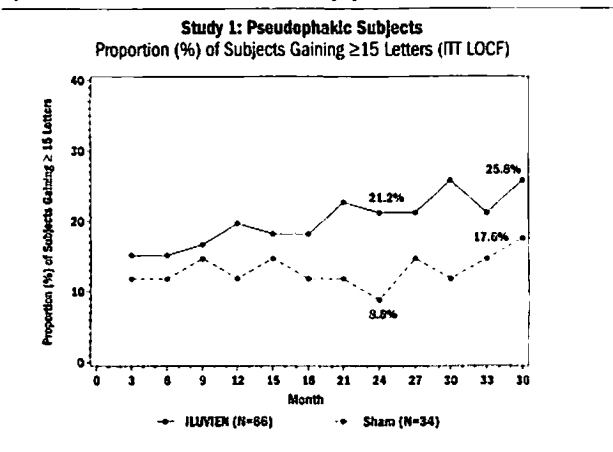
IMPORTANT SAFETY INFORMATION

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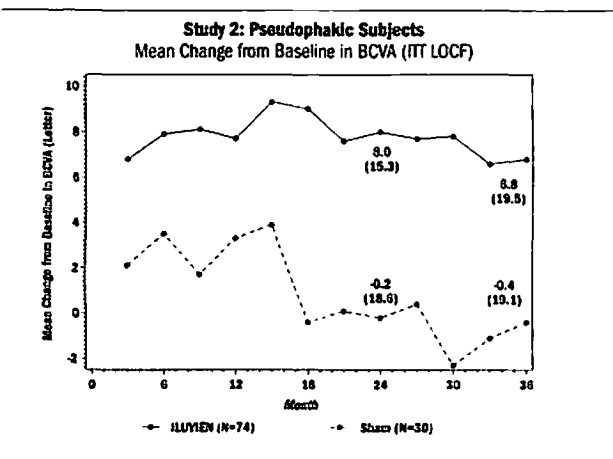
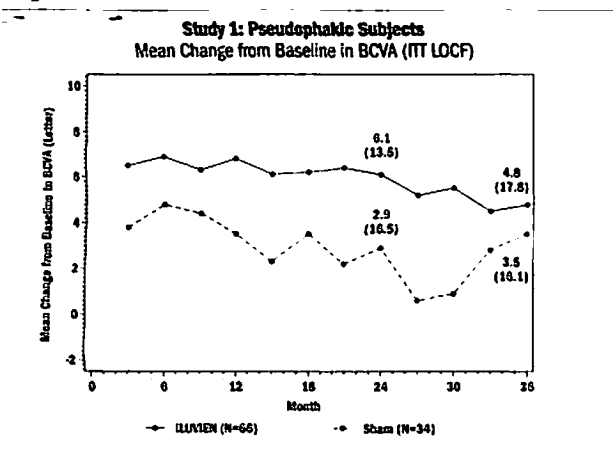
You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see enclosed full Prescribing Information.

Improvement from Baseline BCVA In the Study Eye



Change from Baseline



The BCVA outcomes for the Pseudophakic and Phakic subgroups from Studies 1 and 2 at Month 24 are presented in Table 5.

Table 5: Visual Acuity outcomes at Month 24 (Subgroup for pooled data with LOCF)

Lens Status	Outcomes	ILUVIEN	Sham	Estimated Difference (95% CI)
*Pseudophakic	Gain of ≥15 letters in BCVA (n (%))	39 (28%)	8 (13%)	15.4% (4.4%, 26.3%)
	Loss of ≥15 letters in BCVA (n (%))	7 (5%)	7 (11%)	-5.9% (-14.4%, 2.5%)
	Mean change from baseline in BCVA (SD)	7.1 (14.5)	1.5 (17.4)	5.6 (0.7, 10.6)
*Phakic	Gain of ≥15 letters in BCVA (n (%))	69 (29%)	22 (18%)	11.1% (2.1%, 20.1%)
	Loss of ≥15 letters in BCVA (n (%))	41 (17%)	7 (6%)	11.6% (5.2%, 18%)
	Mean change from baseline in BCVA (SD)	2.8 (20.1)	1.8 (12.6)	1 (-2.5, 4.4)

*Pseudophakic: ILUVIEN, N=140; Sham, N=64

*Phakic: ILUVIEN, N=236; Sham, N=121

16 HOW SUPPLIED/STORAGE AND HANDLING

ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg is supplied in a sterile single use preloaded applicator with a 25-gauge needle, packaged in a tray sealed with a lid inside a carton.

NDC 68611-190-02

Storage: Store at 15°-30° C (59°-86° F).

17 PATIENT COUNSELING INFORMATION

Steroid-related Effects

Advise patients that a cataract may occur after treatment with ILUVIEN. If this occurs, advise patients that their vision will decrease, and they will need an operation to remove the cataract and restore their vision.

Advise patients that they may develop increased intraocular pressure with ILUVIEN treatment, and the increased IOP may need to be managed with eye drops, or surgery.

Intravitreal Injection-related Effects

Advise patients that in the days following intravitreal injection of ILUVIEN, patients are at risk for potential complications including in particular, but not limited to, the development of endophthalmitis or elevated intraocular pressure.

When to Seek Physician Advice

Advise patients that if the eye becomes red, sensitive to light, painful, or develops a change in vision, they should seek immediate care from an ophthalmologist.

Driving and Using Machines

Inform patients that they may experience temporary visual blurring after receiving an intravitreal injection. Advise patients not to drive or use machines until this has been resolved.

Manufactured for:

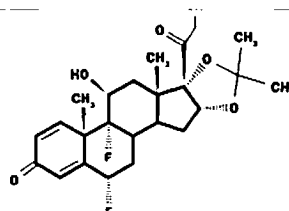
Alimera Sciences, Inc.
6120 Windward Parkway
Alpharetta, GA 30005

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ALIMERA
SCIENCES

US-ILV-MMM-0115

Event	ILUVIEN (N=375) n (%)	Sham (N=185) n (%)
IOP elevation ≥ 10 mmHg from Baseline	127 (34%)	18 (10%)
IOP elevation ≥ 30 mmHg	75 (20%)	8 (4%)
Any IOP-lowering medication	144 (38%)	26 (14%)
Any surgical intervention for elevated intraocular pressure	18 (5%)	1 (1%)



MW 452.50; molecular formula C₂₄H₃₃F₂O₆

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ILUVIEN® safely and effectively. See full prescribing information for ILUVIEN.

ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg For Intravitreal Injection
 Initial U.S. Approval: 1963

INDICATIONS AND USAGE

ILUVIEN contains a corticosteroid and is indicated for the treatment of diabetic

Fluocinolone acetonide is a white or almost white, microcrystalline powder, practically insoluble in water, soluble in methanol, ethanol, chloroform and acetone, and sparingly soluble in ether.

Each ILUVIEN consists of a light brown 3.5mm x 0.37mm implant containing 0.19 mg of the active ingredient fluocinolone acetonide and the following inactive ingredients: polyimide tube, polyvinyl alcohol, silicone adhesive and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Corticosteroids inhibit inflammatory responses to a variety of inciting agents. 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.

12.3 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.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to determine the carcinogenic potential or the effect on fertility of ILUVIEN.

Fluocinolone acetonide was not genotoxic *in vitro* in the Ames test (*S. typhimurium* and *E. coli*) and the mouse lymphoma TK assay, or *in vivo* in the mouse bone marrow micronucleus assay.

14 CLINICAL STUDIES

The efficacy of ILUVIEN was assessed in two three-year, randomized (2:1, active: sham), multicenter, double-masked, parallel-groups studies that enrolled patients with diabetic macular edema that had previously been treated with laser photocoagulation.

The primary efficacy endpoint in both trials was the proportion of subjects in whom vision had improved by 15 letters or more from baseline after 24 months of follow-up.

Table 3: Baseline BCVA (Letters)

	Study 1		Study 2	
	ILUVIEN (N=190)	Sham (N=95)	ILUVIEN (N=186)	Sham (N=90)
Mean (SD)	53 (13)	55 (11)	53 (12)	55 (11)
Median (Range)	57 (19-75)	58 (25-69)	56 (20-70)	58 (21-68)

Table 4: Visual Acuity outcomes at Month 24 (All randomized subjects with LOCF)

Study	Outcomes	ILUVIEN	Sham	Estimated Difference (95% CI)
1*	Gain of ≥15 letters in BCVA (n (%))	51 (27%)	14 (15%)	12.1% (2.6%, 21.6%)
	Loss of ≥15 letters in BCVA (n (%))	26 (14%)	5 (5%)	8.4% (1.8%, 15.1%)
	Mean change from baseline in BCVA (SD)	3.7 (18.7)	3.2 (13.1)	1.8 (-2.8, 6.3)
2*	Gain of ≥15 letters in BCVA (n (%))	57 (31%)	16 (18%)	13.0% (2.7%, 23.4%)
	Loss of ≥15 letters in BCVA (n (%))	22 (12%)	9 (10%)	1.8% (-5.9%, 9.6%)
	Mean change from baseline in BCVA (SD)	5.2 (18.0)	0.0 (15.6)	6.1 (1.4, 10.8)

*Study 1: ILUVIEN, N=190; Sham, N=95

*Study 2: ILUVIEN, N=186; Sham, N=90

Visual acuity outcomes by lens status (Phakic or Pseudophakic) at different visits are presented in Figure 2 and Figure 3. The occurrence of cataracts impacted visual acuity during the study. Patients who were pseudophakic at baseline achieved greater mean BCVA change from baseline at the Month 24 study visit.

2.2 Administration

The intravitreal injection procedure should be carried out under aseptic conditions, which include use of sterile gloves, a sterile drape, a sterile caliper, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum microbicide should be given prior to the injection.

The injection procedure for ILUVIEN is as follows:

1. The exterior of the tray should *not* be considered sterile. An assistant (non-sterile) should remove the tray from the carton and examine the tray and lid for damage. If damaged, do not use unit.

Figure 2: Proportion of subjects with >=15 Letters

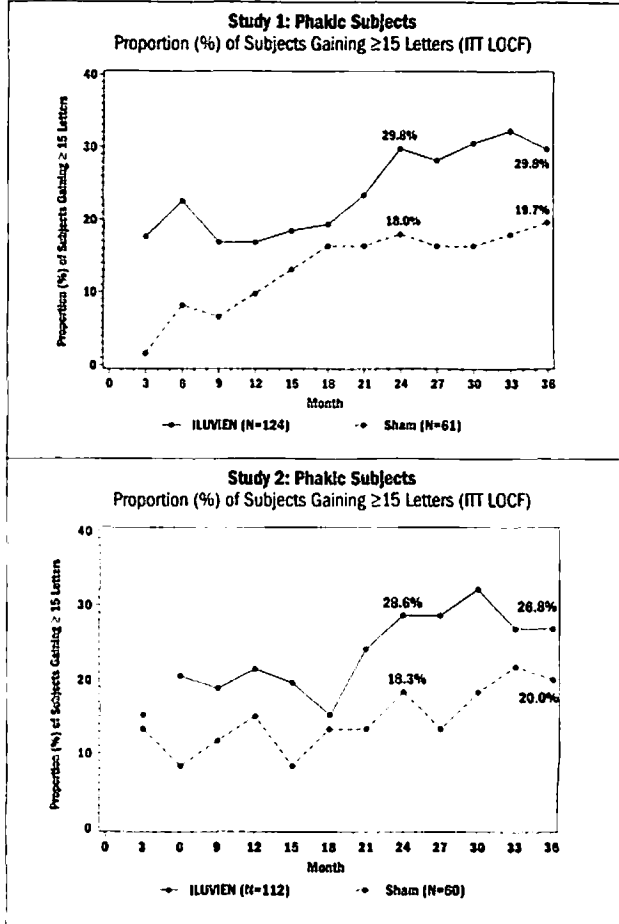


Figure 3: Mean BCVA

