



Dear Healthcare Professional,

Thank you for your unsolicited request for information. Accompanying this letter is the following information you requested on YUTIQ<sup>®</sup> (fluocinolone acetonide intravitreal implant) 0.18 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 [yutiqmedinfo@anipharma.com](mailto:yutiqmedinfo@anipharma.com).

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

YUTIQ 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.

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

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

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

# Migration of YUTIQ<sup>®</sup> Into the Anterior Chamber of the Eye

## Abstract

- This document provides summary information pertaining to YUTIQ<sup>®</sup> (fluocinolone acetonide [FAC] intravitreal implant) 0.18 mg and its indication for use in the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye
- This document provides an overview of the clinical evidence regarding the risk of YUTIQ intravitreal implant migration into the anterior chamber, along with the novel off-label fluocinolone-loop-anchoring technique (FLAT) reported in the literature to minimize this risk
- Prescribing information, clinical trials, and post-marketing case reports are reviewed for YUTIQ (FAC intravitreal implant) 0.18 mg and ILUVIEN<sup>®</sup> (FAC intravitreal implant) 0.19 mg
- The evidence for migration risk post capsular tears in treatment with ILUVIEN and OZURDEX<sup>®</sup> (dexamethasone intravitreal implant) is also examined

**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 YUTIQ (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@anipharmaceuticals.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@anipharmaceuticals.com>**

## Introduction

### Clinical Background

YUTIQ (FAc intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.<sup>1</sup>

### Composition of YUTIQ

YUTIQ is a non-bioerodible intravitreal implant in a drug delivery system containing 0.18 mg FAc, designed to release FAc at an initial rate of 0.25 mcg/day, and lasting 36 months. Each YUTIQ consists of a light brown 3.5mm x 0.37mm implant containing 0.18 mg of the active ingredient FAc and the following inactive ingredients: polyimide tube, polyvinyl alcohol, silicone adhesive, and water for injection.<sup>1</sup>

### Clinical Pharmacology

YUTIQ 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>

### Response to Information Request

In response to the request regarding implant migration to the anterior chamber, please note that the US Prescribing Information for YUTIQ, Section 5.3 Warnings and Precautions, provides the following information: *Section 5.3 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>

## Clinical Summary

Patients with an absent or torn posterior capsule are at risk of an intravitreal implant migrating into the anterior chamber.<sup>1,2</sup> However, no instances of migration have been reported in clinical trials of YUTIQ (FAC intravitreal implant) 0.18 mg. Cases of migration into the anterior chamber have been reported for ILUVIEN (FAC intravitreal implant) 0.19 mg in eyes with preexisting capsular tears.<sup>3</sup>

## Published Reports of FAC Implant Migration Into the Anterior Chamber

A PubMed search was conducted using the terms “fluocinolone acetonide,” “intravitreal implant,” “fluocinolone acetonide intravitreal implant,” “YUTIQ,” and “ILUVIEN,” combined with “migration,” “migrate,” “migrating,” “implant migration,” “anterior chamber,” and the respective Medical Subject Heading (MeSH) terms to identify instances of implant migration up to December 1, 2024. The selection was limited to key studies in patients with non-infectious uveitis affecting the posterior segment of the eye treated with YUTIQ or in patients with diabetic macular edema (DME) treated with ILUVIEN. Studies including case series (N>2 eyes) and prospective studies of trials involving >2 eyes were considered to be of interest. According to the aforementioned search criteria, no relevant articles related to YUTIQ were identified for inclusion in this summary. However, the search did identify a prospective off-label interventional clinical trial (MEFISTO) related to a novel off-label surgical technique for the repositioning of ILUVIEN into the vitreous following anterior migration to be of interest (summarized below). Reports of implant migration due to posterior capsular tears were also identified and reviewed further below.

The composition and pharmacology of ILUVIEN is similar to YUTIQ, with the exception of the difference in dosage of FAC. ILUVIEN is indicated for the treatment of 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>2</sup>

The ILUVIEN US Prescribing Information Warnings and Precautions section states, “*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>2</sup> Additionally, ILUVIEN’s Summary of Product Characteristics, Section 4.8 on Undesirable Effects, notes that, “*there is a potential for implants to migrate into the anterior chamber, especially in patients with posterior capsular abnormalities such as tears. This should be taken into consideration when examining patients complaining of visual disturbance after treatment.*”<sup>3</sup>

## ILUVIEN FAME Studies

FAME A and FAME B were two phase 3, multicenter, randomized, double-masked, sham injection-controlled studies conducted over 36 months. The objective of the FAME studies was to assess the

long-term efficacy and safety of ILUVIEN in patients with DME despite prior macular laser treatment.<sup>4</sup> The US Prescribing Information for ILUVIEN (FAc intravitreal implant) 0.19 mg states that approximately 75% of the ILUVIEN-treated subjects received only one ILUVIEN implant over the 36-month follow-up period of the FAME trials.<sup>2</sup> There were no reports of implant migration into the anterior chamber in FAME.<sup>4</sup>

However, there was one retrospective report of a patient enrolled in the phase 2 FAMOUS (pharmacokinetic) trial that experienced implant migration. This patient received two implants during the study, followed by cataract surgery, which led to a tear in the lens capsule. One of the implants migrated to the anterior chamber. There were no other adverse events reported for this patient in the study eye.<sup>5</sup>

### **The Fluocinolone-Loop-Anchoring Technique (FLAT): Long-Term Follow-up (MEFISTO)**

A novel surgical approach for implanting and securing an FAc (ILUVIEN) intravitreal implant to minimize the risk of migration was outlined in a single-center, prospective off-label interventional clinical trial. In this trial, scleral fixation of the FAc implant was performed on 10 eyes that had undergone complicated cataract surgeries, globe rupture, or other trauma, putting them at increased risk of persistent cystoid macular edema. The authors introduced a technical procedure called the fluocinolone-loop-anchoring technique (FLAT). A flat-headed lens nucleus rotator was used to insert the fluocinolone implant through the sclerotomy, creating two loop-like handles to maneuver the implant into the vitreous cavity. The implant was positioned at least 3 mm away from the ciliary body, and the thread was then fixed to the sclera. The eyes were monitored monthly for the first year and quarterly until Month 24. Best-corrected visual acuity (BCVA) and central retinal thickness (CRT) were assessed from baseline to Month 24, along with additional safety measures. BCVA significantly improved over the 24 months in all but one patient. CRT varied among the patients but generally decreased within the first three months and remained mostly stable until Month 24. One patient required implant removal due to IOP increases. The study's mean IOP showed no significant change from  $12.6 \pm 4.2$  mmHg at baseline to  $13.4 \pm 3.0$  mmHg at Month 24. In conclusion, the authors determined that the loop technique offers a viable option for utilizing the FAc implant while significantly reducing the risk of migration, thereby enhancing the safety and efficacy of intravitreal steroid injections in clinical practice.<sup>4</sup>

### **ILUVIEN Implant Migration Due to Posterior Capsular Tear**

Meireles and colleagues conducted a retrospective analysis across six centers in four European countries, involving 26 eyes from 25 patients with DME who had previously undergone vitrectomy and had been treated with one ILUVIEN implant. The study aimed to assess the safety and efficacy of this treatment by collecting data on changes in Early Treatment Diabetic Retinopathy Study (ETDRS) letter scores, central retinal thickness, and intraocular pressure.<sup>5</sup>

In this study, ILUVIEN implant migration to the anterior chamber was reported in two eyes due to the presence of a previous capsular tear. These incidents required surgical intervention to reposition the implants back into the vitreous cavity, which was achieved without further complications. The authors emphasized the need for caution in managing the risk of implant migration in patients with vitrectomized eyes and disruptions in the posterior capsule.<sup>5</sup>

### **OZURDEX® Implant Migration due to Capsular Tear**

In a retrospective observational case series, Khurana and colleagues reported on 18 instances of OZURDEX migration to the anterior chamber in 15 patients, detailing the associated risk factors, clinical progression, and complications. All patients had prior vitrectomy; 14 (93%) lacked a lens capsule and 14 out of 15 patients (16 cases) experienced corneal edema. Of those with corneal edema, six patients required corneal transplantation. Corneal edema may result from endothelial decompensation caused by chemical toxicity from any component of the OZURDEX implant (such as dexamethasone, lactic acid, or glycolic acid) or from mechanical trauma inflicted by a rigid object. Khurana and colleagues concluded that a combination of lens capsule defect, whether aphakic or pseudophakic, and a history of vitrectomy increases the likelihood of anterior migration of the OZURDEX implant.<sup>6</sup>

Please note that the US Prescribing Information for OZURDEX, Section 4.3 Contraindications states, *“OZURDEX is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber.<sup>7</sup> Laser posterior capsulotomy in pseudophakic patients is not a contraindication for OZURDEX use.”<sup>7</sup>*

To date, there are no known head-to-head studies that examine the risk of post capsular tears among patients treated with either ILUVIEN or OZURDEX (dexamethasone intravitreal implant). Please refer to the [OZURDEX PI](#) for further information. OZURDEX is a registered trademark of AbbVie Inc.<sup>7</sup>

## References

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4. Campochiaro PA, Brown DM, Pearson A, et al. 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.
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6. Meireles A, Goldsmith C, El-Ghrably I, et al. Efficacy of 0.2 µg/day fluocinolone acetonide implant (ILUVIEN) in eyes with diabetic macular edema and prior vitrectomy. *Eye (Lond)*. 2017;31(5):684-690.
7. Khurana RN, Appa SN, McCannel CA, et al. Dexamethasone implant anterior chamber migration: risk factors, complications, and management strategies. *Ophthalmology*. 2014;121(1):67-71.
8. OZURDEX (dexamethasone intravitreal implant) – Prescribing Information. North Chicago, IL: Abbvie Inc. 2024.