Treating Chronic Inflammation Associated With Uveitis Affecting the Posterior Segment in a Retina Setting with YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg

Contributors

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Introduction

In June 2022, a virtual roundtable was convened to discuss how YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg has been integrated into retina practices and can provide an additional treatment option for the long-term control of noninfectious uveitis affecting the posterior segment. The information contained herein is based on that discussion.

Dr. Kitchens: I would call myself an average retina guy because we have a uveitis specialist in the practice who I can easily refer to. So, I think it's unique that I've found many patients who are appropriate for YUTIQ. When it first launched, I thought it was a niche product and didn't expect to use it very often, but I couldn't have been more wrong, and there are many applications and patients who are appropriate for YUTIQ. I have so many patients that have recurrent cystoid macular edema (CME) that I never even thought of as having a form of uveitis. These guys don't need a lot; they just need chronic therapy, which YUTIQ can provide.

Dr. Baumal: I'm certainly using a lot more YUTIQ and I've even been finding patients in whom it probably would've been appropriate for me to use it earlier. There are things that you see in clinic, like chronic postsurgical CME or birdshot, that you may not think about using YUTIQ on, but it is very well suited for them. You definitely want to at least have YUTIQ on your radar for the appropriate patients.

Dr. Kiernan: I use a lot of YUTIQ, and I've found those cases of chronic postsurgical inflammation that typically resulted in vision loss because of CME often respond well to YUTIQ. I've also started to dabble in treating more traditional uveitides with YUTIQ as well.

Dr. Kitchens: When I think about YUTIQ, 2 things come to mind. One, it's not just for uveitis specialists. It's fluocinolone acetonide, but it's an implant administered via an intravitreal, in-office injection. And two, we have lots of suitable patients in our clinics. I usually think about moving to YUTIQ when I need to reinitiate a short-duration local steroid treatment because it's worn off and the patient has recurred.

Dr. Eichenbaum: We definitely know it can work for those patients with chronic postsurgical inflammation. I've successfully treated many of these types of patients with YUTIQ, and it's a good option to move to if the patient needs something for a longer period of time.

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

Contraindications

Ocular or Periocular Infections: 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.

Please see Important Safety Information for YUTIQ continued on pages 2, 4, 6, and 8.

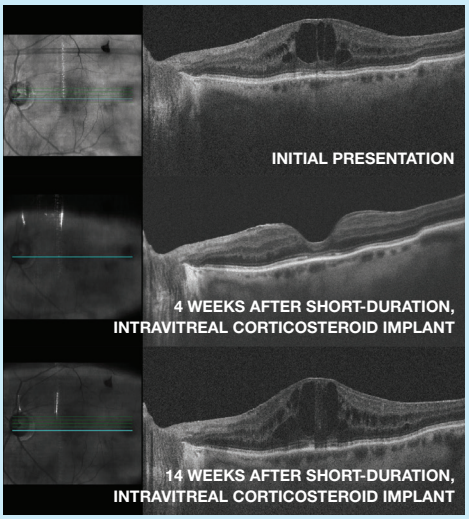
Please see full Prescribing Information for YUTIQ attached.

Case: Chronic Recurrent CME After Complex Retinal Detachment Surgery

Dr. Baumal: This is an 84-year-old female who previously had a vitrectomy for rhegmatogenous detachment in her left eye about 10 years ago. But even before she had her retinal detachment (RD), she was noted to have some inflammation in the eye, which was thought to be related to her chronic detachment. She had a fluorescein angiogram and there was no vein occlusion. In her affected left eye, her vision was 20/60, with pressure at 16 mmHg. I sent her to a uveitis specialist to evaluate the cause of inflammation, but she came back negative for inflammatory markers. So, her diagnosis was post-vitrectomy or retinal detachment CME, with a history of chronic, intermittent macular edema and inflammation.

Subsequent to the vitrectomy and peripheral laser to repair her retina, she had recurrent episodes of CME that were treated with short-duration, intravitreal corticosteroid implants. She did have a mild steroid response, but she did fine with preservative-free, intraocular pressure (IOP)–lowering drops. I don't have the exact number of short-duration, intravitreal corticosteroid implants she got, and while she did well on them, improvement didn't last longer than 3 months. She was also given an intraocular biologic injection but had no response to it.

Figure 1. Optical coherence tomography (OCT) from initial presentation and after a short-duration, intravitreal corticosteroid implant



With the short-duration, intravitreal corticosteroid implants, her vision would improve by about a line, and she felt that her vision was clearer. About 9 weeks after the short-duration, intravitreal corticosteroid implant, she would start to get these perifoveal cystic spaces, and after about 14 weeks, the edema would come back (**Figure 1**). I think this shows that this patient was steroid-responsive, but the short-duration, intravitreal corticosteroid implant wasn't lasting long enough.

So, that's why I chose YUTIQ, for the durability of its effect. You can see improvement, and 7 weeks after the YUTIQ, you can see it's a little bit better, but she still has some cysts. CME was resolved by 11 weeks and remains resolved 6 months after YUTIQ (**Figure 2**). Her IOP remains stable with preservative-free, IOP-lowering drops, and her vision is 20/50. As far as this patient is concerned, I'm going to continue to monitor her for IOP elevation and recurrence and treat accordingly if either occurs.

Dr. Kiernan: Yeah, there is a sort of delayed response, so what this reinforces in my mind is to use it sooner, before the prior treatment wears off. Maybe get the ball rolling on the prior authorization process as soon as you start thinking about treatment options. Then you can inject the YUTIQ as soon as you get it, without having to wait for it to be approved and having the patient come in because the previous treatment has worn off in the meantime.

Dr. Baumal: So how many other treatments would you do before you think about going to YUTIQ? Are you saying that maybe I should have given her a YUTIQ 7 or 8 weeks after her last short-duration, intravitreal corticosteroid implant, even if I know she was going to come back at 3 months?

Dr. Kiernan: Absolutely. In fact, I start thinking about YUTIQ immediately. I may even just go straight to YUTIQ because I know it'll work and last longer. But I really wouldn't push anyone to use it first-line without some experience and the ability to predict what's going to happen in your own hands.

IMPORTANT SAFETY INFORMATION (CONT'D)

Contraindications (cont'd)

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

Warnings and Precautions

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments.

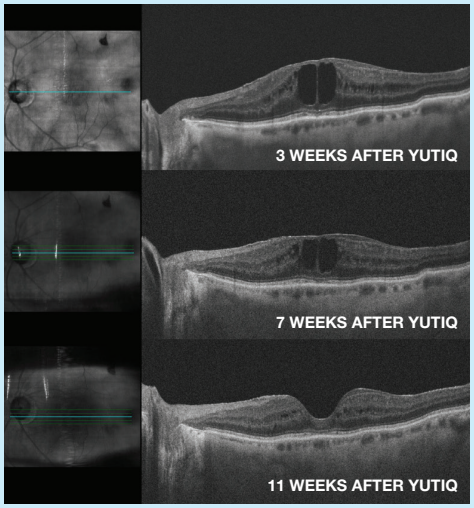
Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Please see Important Safety Information for YUTIQ continued on pages 1, 4, 6, and 8.
Please see full Prescribing Information for YUTIQ attached.

Dr. Baumal: Does everyone find this kind of delayed response? When do you find the effect starts?

Dr. Eichenbaum: Yeah, as you'll see in my case, sometimes you have to give it some time or something extra. It's not a "one-and-done" treatment; for a lot of patients, it's more like a "one-and-sometimes-a-little-extra" drug. And I am moving it earlier, like Dan said. It's 1 of those things that takes some time to ramp up in these chronic patients, like those with CME for 10 years. I would say to people thinking about using YUTIQ that they should quiet the patient with something else and then use YUTIQ as long-term maintenance.

Figure 2. OCT from after YUTIQ treatment



Dr. Kitchens: Unlike Dan, I probably wouldn't give just 1 short-duration, intravitreal corticosteroid implant and start the approval process because I would still hope that 1 treatment would take care of it. But if they come back at 12 or 14 weeks and they've recurred, I'd give them a second short-duration, intravitreal corticosteroid implant, start the prior authorization process, and then give them a YUTIQ 6 to 8 weeks after. Patient perception may be that they were given a YUTIQ and didn't get any better, but they, and sometimes the doctor, don't necessarily realize that the effect is coming later on. So, by the time they are seeing improvements 12 weeks later, they maybe don't associate it with YUTIQ and will want to go back to another treatment option because that got them better sooner. So, starting to think about YUTIQ when they're on that second treatment is important.

Dr. Baumal: When would you consider reinjecting? Would you wait for the edema to come back? Would you wait for perifoveal cysts to appear?

Dr. Kiernan: I follow my patients quarterly when they're on YUTIQ. I would probably wait until I saw a little bit of edema and then follow them a little more closely, say monthly, and if the edema was definitely recurring, then plan to reinject with YUTIQ.

Dr. Kitchens: It kind of depends on when they recur. If it's within a few months, I'd probably try to boost them with a local steroid injection or implant and sometimes that just sets them right for the next 6 months or so. You might have to pulse the additional treatments every now and then to help keep the eye quiet.

Dr. Eichenbaum: Yeah, if they recur early, I probably wouldn't try another YUTIQ. I'd try a local steroid. I don't think adding another YUTIQ after a couple of months is going to get you what you want because you need a bolus dose, not just maintenance. But I would expect a good result after the local steroid, with YUTIQ carrying you on once you quiet things down.

Case: Chronic Postoperative Posterior Inflammation

Dr. Eichenbaum: So, this is not a super exciting postop case, but this is the kind of thing we see all the time and it's where I'm employing YUTIQ more and more. As we discussed before and as you can see in this case, the patient requires a booster with a local steroid injection or implant.

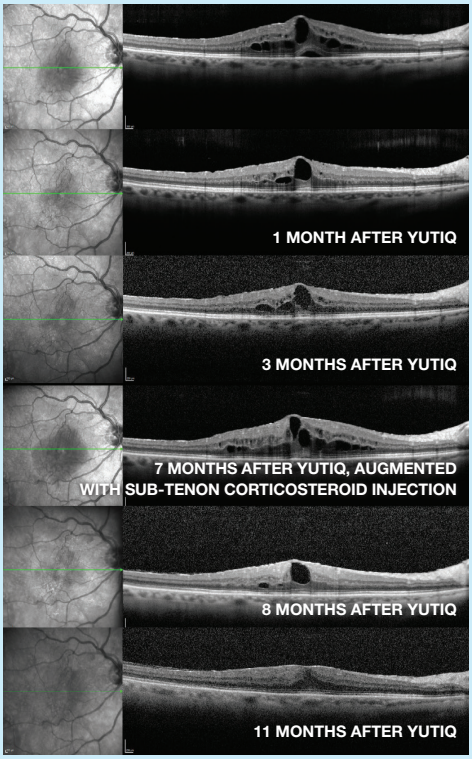
This is a routine surgical case of a 76-year-old female who had uncomplicated cataract surgery with a YAG and got a vitrectomy for floaters, all in her right eye. And as so often happens, she got inflamed after this series of uncomplicated surgeries. So, she got multiple sub-tenon corticosteroid injections and topical steroids. She was a steroid-responder but was controlled with IOP-lowering drops. In her right eye at her initial presentation, her vision was pretty poor, 20/125, with a little bit of inflammation, and this was a second opinion consult, so she had already been treated for a while before seeing me.

When she came in, it was 4 months after a sub-tenon steroid injection, and she was pretty hot and swollen. She got a YUTIQ in her right eye because she didn't want another short-duration local steroid. One month after her YUTIQ, she looked better but not awesome. Her vision improved to 20/50 and the CME decreased, so I could tell that the YUTIQ was working. I continued her on the IOP-lowering drops because I knew she was steroid-responsive and didn't want

her to get a spike. Three months after YUTIQ, her vision is still 20/50- but she had a little bit of persistent, mild CME and was not quite where I wanted her to be.

Seven months after YUTIQ, she noticed that her vision was getting a bit blurrier, and I found that her vision had decreased to 20/80 and she had worsening CME. So, I decided to augment her with a sub-tenon corticosteroid injection. A month after the sub-tenon corticosteroid injection, about 8 months after YUTIQ, her anatomy improved, and her vision went back to 20/50-2. Eleven months after YUTIQ, her vision continued to improve to 20/40- and there was an absence of cysts and the suggestion of foveal contour restoration with only the single augmentation following YUTIQ treatment **(Figure 3**). I continue to see this patient and monitor her for IOP spikes and recurrence, and, of course, if they occur, I'll treat them accordingly.

Figure 3. OCT from before and after YUTIQ treatment



Dr. Kitchens: Dave, in hindsight, would you have done anything differently to get the patient to look like this for 11 months?

Dr. Eichenbaum: I think I probably would have augmented sooner, or maybe I would've done a short-duration, intravitreal corticosteroid implant and then a YUTIQ, just to get her quiet before YUTIQ. We eventually got where I wanted to, but it did take a little longer than I like. I think there's something to the idea of giving a bolus and then maintaining them on YUTIQ.

Dr. Kiernan: I don't always use an intravitreal corticosteroid before a YUTIQ, but I've usually done it in the past. I think if you get a response from an intravitreal corticosteroid, you're more likely to get a response from YUTIQ. And, if you get an IOP spike from other steroids and it's manageable with IOP-lowering drops, then it'll still be manageable with those same drops when you put a YUTIQ in. If there's a crazy pressure spike or the patient has glaucoma, then you have to balance the risk of pressure with that of the macular edema. But I will say that I'm comfortable treating a uveitis patient with glaucoma with YUTIQ, and they're probably seeing a glaucoma person who's aggressively managing them. So, I'm pretty confident that whichever glaucoma colleague they're seeing will be controlling their pressures if I use a steroid. But I am a little bit spoiled because I'm in a multispecialty group and work closely with a glaucoma specialist who can evaluate my glaucoma patients before I start treating them with steroids.

Dr. Eichenbaum: I don't have a glaucoma colleague; I'm in a retina group and my patients all come from general ophthalmologists, so I don't use glaucoma doctors a lot for steroid-responsive glaucoma. I usually just take care of it with IOP-lowering drops, but if they get really bad, like if they need more than 2 drops, I send them back to their general ophthalmologist with a recommendation for an IOP-lowering procedure.

IMPORTANT SAFETY INFORMATION (CONT'D)

Warnings and Precautions (cont'd)

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

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.

Please see Important Safety Information for YUTIQ continued on front cover; pages 1, 2, 6, and 8.

Please see full Prescribing Information for YUTIQ attached.

Dr. Kitchens: Primary guys don't usually want the patient back with pressures that we create, so I start my patients with spikes on an IOP-lowering drop and get them in for an appointment with a glaucoma specialist in 2 to 3 weeks.

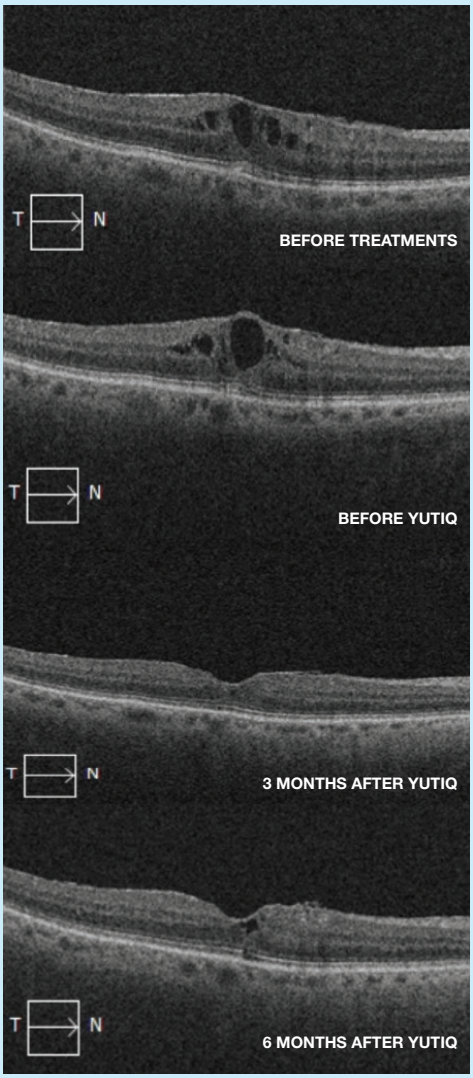
Dr. Baumal: I find it rare to have to put the patient on more than 1 drop. I'll send any patient with suspicious optic nerves to a glaucoma specialist before I start any treatments to get a good preliminary examination and see if they're at an increased risk of anything. You definitely have to weigh the risk-benefit of steroids vs disease progression in some cases.

Case: Chronic Postoperative Inflammation

Dr. Kitchens: I think we've all seen cases like this. The patient was a 72-year-old female who had an RD in her right eye that was fixed with a primary vitrectomy, but then had a dislocated intraocular lens (IOL) and ended up needing a vitrectomy and IOL exchange for an anterior chamber IOL (ACIOL). Of course, then the patient came back with CME, so we put her on steroid eye drops. After the steroid drops were tapered down, she started to have a recurrence, but she didn't want to do drops anymore. So, we gave her an intravitreal corticosteroid injection and she initially responded well. But after 7 months, she had worsening edema and felt a little more symptomatic. At that point, we gave her another intravitreal corticosteroid injection and told her that if she recurred again, we would think about a longer-duration option. Eight months after the second injection, she had a major recurrence, so we gave her a YUTIQ. She did go a pretty long time between intravitreal corticosteroid injections, which is why I thought this made her a good candidate for YUTIQ.

Three months after YUTIQ treatment, she showed a good response. Still a little nidus of swelling and maybe a little bit of an ERM, but pretty good otherwise. Six months after YUTIQ treatment, she's still doing well. There's a little bit more swelling, but her vision is still fine (**Figure 4**). Her pressure is also good, so we're just going to watch her every 2 to 3 months. I'm really hoping that YUTIQ will get her out to 12 or 18 months, but we would be happy to get anything beyond 6 months. If she does recur, I'll probably boost her with a short-duration, intravitreal corticosteroid and see if that gets us to a full year. I'll also keep monitoring her pressures and if they spike, I'll treat her for that too.

Figure 4. OCT from before and after YUTIQ treatment



Dr. Baumal: This is a great case because with an ACIOL you have to be cautious about using some inserts and implants that can migrate to the front of the eye and injure the cornea. While it's a Warning and Precaution, it's not a Contraindication for YUTIQ use, which is useful in cases like this one.

Dr. Kitchens: Has anyone had a YUTIQ come forward and does it cause a problem?

Dr Kiernan: I've had 1 patient whose YUTIQ came forward, and it hasn't caused any problems; I haven't taken it out. In fact, I didn't even notice it until the patient brought their head forward into the slit lamp and it caught my eye. I asked them to tilt their head forward and back and decided it was okay where it was. I barely noticed it, they barely noticed it, so it was probably fine. We will continue to monitor the location of the implant and take appropriate action if it becomes problematic.

Case: Serpiginous Chorioretinitis With Choroidal Neovascularization

Dr. Kiernan: This is a 71-year-old female with a history of cataract surgery, who was being treated for what was thought to be wet age-related macular degeneration (AMD), but which was later diagnosed as serpiginous chorioretinitis with secondary choroidal neovascularization (CNV). On presentation, her vision was 20/100 on the right and 20/50 on the left; she had a posterior chamber IOL (PCIOL) only on the right and, interestingly, it seemed that it was after the cataract surgery when everything seemed to go downhill in that eye. That was when she was diagnosed with wet AMD and started treatments. So, she's always had it in the back of her mind that this is when her vision got bad, and it's made her hesitant about additional treatments or procedures. Keep that in mind because she had a clear lens in the left eye on initial presentation.

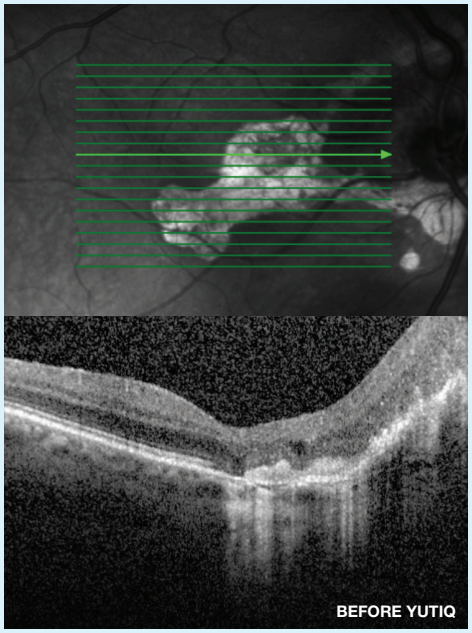
Color fundus showed typical serpiginous extensive peripapillary atrophy and scarring with tendrils reaching into the macula and causing permanent vision loss, especially in the right eye. It was not so advanced in the left eye, but the view was hazy due to inflammation. Angiography showed transmission defects, a slight leakage in the right eye, and more diffuse leakage in the left eye. OCT showed a little bit of fluid in the right eye and cystoid spaces in the left eye meaning both eyes have CNV. In the right eye, there are atrophic areas, and the ellipsoid zone is lost through the fovea, whereas in the left eye, the fovea is mostly uninvolved.

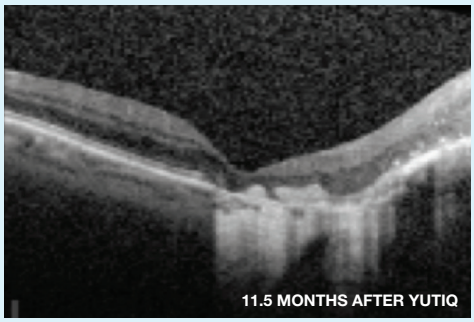
Prior to coming to me, she had received 6 intravitreal biologic injections in her right eye, which I continued, and I started injections in her left eye on a more or less monthly basis with alternating eyes on different days. Because I was concerned about the serpiginous progressing, I also gave her a short-duration, intravitreal corticosteroid implant in her left eye. I figured that I don't have a lot of systemic biologic experience, but I have a lot of steroid experience and steroids can work for this sort of thing. I also started thinking about YUTIQ at this time. After a few months of intravitreal biologics injections, I ended up putting YUTIQ into her right eye first and then into her left eye 2 months later. This was 3 months after the short-duration, intravitreal corticosteroid implant in her left eye and she was starting to have symptoms of a recurrence.

Subsequent follow-ups after YUTIQ showed that the vision in her right eye had been lost due to scarring that occurred prior to YUTIQ treatment, whereas vision in her left eye was relatively preserved but started to decrease due to the development of a cataract. She continued to get monthly intravitreal biologic injections in both eyes.

Almost a year after getting a YUTIQ in the right eye, things looked a little stable with no real change in the lesion size (**Figure 5**). Vision was 20/200 with a PCIOL. There were similar results in the left eye,

Figure 5. OCT from before and after YUTIQ treatment OD





IMPORTANT SAFETY INFORMATION (CONT'D)

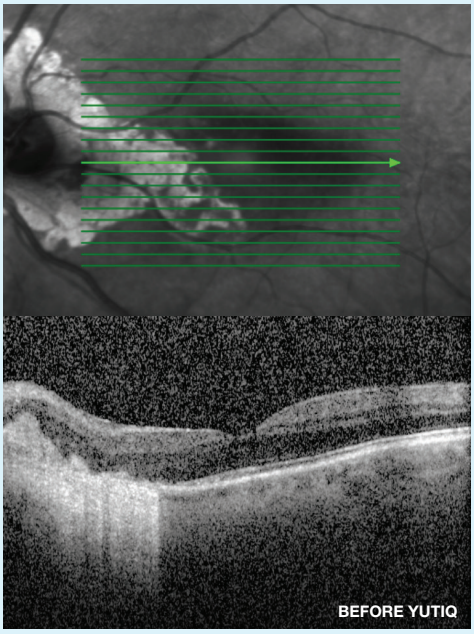
Adverse Reactions

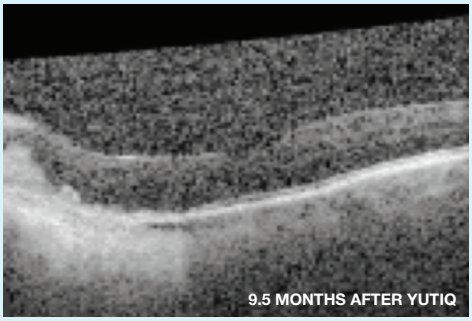
In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

Please see Important Safety Information for YUTIQ continued on front cover; pages 1, 2, 4, and 8.

Please see full Prescribing Information for YUTIQ attached.

Figure 6. OCT from before and after YUTIQ treatment OS





which was 9.5 months after YUTIQ treatment, but there was no autofluorescence view because of the cataract, which was 3+, had caused her vision to drop to 20/100. But what OCTs show us is that before YUTIQ, the choroidal lesion in the ellipsoid zone was advancing toward the fovea and would have destroyed her vision in her remaining eye (**Figure 6**). But after YUTIQ, it has not advanced at all, and her visual function has been preserved.

This shows that you can use YUTIQ, a local, long-term steroid, for what is considered a fairly bad uveitic disease like serpiginous choroiditis. I don't have a lot of experience with serpiginous and everyone thinks I'm kind of crazy to not refer it out or use systemics, but I'm fairly happy with the result. Unfortunately, the patient is unhappy with her vision, but I've been encouraging her to get cataract surgery and she's finally considering it. I still see her every 2 weeks for intravitreal biologic injections, but I have referred her to a uveitis specialist for further evaluation. But, looking at her results, I'm pretty happy with where we're at, especially if she gets the cataract surgery. This was a very rare case without typical standard-of-care treatments.

Dr. Kitchens: We also have these multifocal cases where we have CNV, multifocal choroiditis, and tons of scarring, and they very predictably would need short-duration, intravitreal corticosteroid implants every 3 months and intravitreal biologic injections every month. They'll very predictably come in for their treatments because they can tell when they are recurring. So, how do you predict what the YUTIQ is going to do for patients who were on this very predictable schedule? After all, you're adding something new to an established routine.

Dr. Kiernan: I really have no idea. This is my first patient like this, and she only has 1 good eye, so she insists on coming in every 2 to 3 weeks for intravitreal biologic injections. She's getting a second opinion as well, so I'm open to whatever is suggested from that consult and her rheumatologist. I'm pretty comfortable seeing her as often as she wants because frequent follow-up is absolutely critical in a case like this, not just for recurrences but also for IOP spikes. I have a short-duration, intravitreal corticosteroid implant ready to use the moment I see something is going on with that ellipsoid zone, if it starts to slip a little.

Dr. Baumal: I think this case is great because it highlights that we used to use steroids for CNV before we had intravitreal biologic injections because it did help inflammatory CNV. Some cases could have a systemic basis or be bilateral, but if you can treat it with a local therapy, that's great.

Dr. Kiernan: Much like any case of bilateral inflammation, we did a full workup to try and see if there was a systemic cause, but we didn't really find anything suspicious.

Dr. Eichenbaum: Yeah, it depends on the clinical scenario. In a lot of cases, they're clearly unilateral with some degree of surgery, so there isn't a need to do a full workup. You don't have to do a workup before you use YUTIQ, you just have to see if it's postop, posterior noninfectious uveitis or something more.

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

Contraindications

Ocular or Periocular Infections: 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.

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

Warnings and Precautions

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

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.

Adverse Reactions

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

10/2022
US-YUT-2200180

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection

Initial U.S. Approval: 1963

---------- INDICATIONS AND USAGE ----------

YUTIQ contains a corticosteroid and is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye. (1)

---------- DOSAGE AND ADMINISTRATION ----------

- For ophthalmic intravitreal injection. (2.1)
- The intravitreal injection procedure should be carried out under aseptic conditions. (2.2)
- Following the intravitreal injection, patients should be monitored for elevation in intraocular pressure and for endophthalmitis. (2.2)

---------- DOSAGE FORMS AND STRENGTHS ----------

Non-bioerodible intravitreal implant containing 0.18 mg fluocinolone acetonide in a drug delivery system. (3)

---------- CONTRAINDICATIONS ----------

- Ocular or periocular infections (4.1)
- Hypersensitivity (4.2)

---------- WARNINGS AND PRECAUTIONS ----------

- Intravitreal injections have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments. Patients should be monitored following the injection. (5.1)
- Use of corticosteroids may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. (5.2)
- The implant may migrate into the anterior chamber if the posterior lens capsule is not intact. (5.3)

---------- ADVERSE REACTIONS ----------

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact EyePoint Pharmaceuticals US, Inc. at 1-833-EYEPOINT (1-833-393-7646) or FDA at 1 800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION **Revised: 2/2022**

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

2. DOSAGE AND ADMINISTRATION

2.1. General Dosing Information

For ophthalmic intravitreal injection.

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 YUTIQ is as follows:

1. Just prior to injection, administer topical and/or subconjunctival anesthesia at the injection site (inferotemporal quadrant recommended).
2. Administer 2-3 drops of a broad-spectrum microbicide into the lower fornix. The lids may be scrubbed with cotton-tipped applicators soaked with a broad-spectrum microbicide. Place a sterile lid speculum. Have the patient look up and apply additional microbicide solution to the injection site. Allow 30-60 seconds for the topical antiseptic to dry prior to injection of YUTIQ.
3. Optimal placement of YUTIQ is inferior to the optic disc and posterior to the equator of the eye. Measure 4 millimeters inferotemporal from the limbus with the aid of callipers for point of entry into the sclera.
4. Using sterile procedure, open the sterile foil pouch containing YUTIQ.
5. Remove the YUTIQ applicator from the sterile pouch by grasping the barrel of the applicator; do not grasp the plunger.
6. Remove the black plunger stop from the plunger.
7. Carefully remove the protective cap from the needle and inspect the needle tip to ensure it is not bent.
8. Remove the trombone wire from the distal end of the needle. Prior to injection, keep the applicator tip above the horizontal plane to ensure that the YUTIQ implant does not fall out of the applicator.
9. Gently displace the conjunctiva so that after withdrawing the needle, the conjunctival and scleral needle entry sites will not align. Care should be taken to avoid contact between the needle and the lid margin or lashes.
10. Insert the needle through the conjunctiva and sclera up to the positive stop of the applicator.
11. Depress the plunger at the back of the applicator fully to deliver the YUTIQ implant into the back of the eye.
12. Remove the YUTIQ applicator from the eye and discard in biohazard sharps container.
13. Remove the lid speculum and perform indirect ophthalmoscopy to verify adequate central retinal artery perfusion, absence of any other complications, and to verify the placement of the implant. Scleral depression may enhance visualisation of the implant. Immediate measurement of intraocular pressure (IOP) may be performed at the discretion of the ophthalmologist.

Following the injection, patients should be monitored for change in intraocular pressure and for endophthalmitis. Monitoring may consist of a check for perfusion of the optic nerve head immediately after the injection, tonometry within 30 minutes following the injection, and biomicroscopy between two and seven days following the injection. Patients should be instructed to report without delay any symptoms suggestive of endophthalmitis.

3. DOSAGE FORMS AND STRENGTHS

YUTIQ is a non-bioerodible intravitreal implant in a drug delivery system containing 0.18 mg fluocinolone acetonide, designed to release fluocinolone acetonide at an initial rate of 0.25 mcg/day, and lasting 36 months.

4. CONTRAINDICATIONS

4.1. Ocular or Periocular Infections

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.

4.2. Hypersensitivity

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

5. WARNINGS AND PRECAUTIONS

5.1. Intravitreal Injection-related Effects

Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. 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)]*.

5.2. Steroid-related Effects

Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses.

Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

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.

6. ADVERSE REACTIONS

6.1. Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions associated with ophthalmic steroids including YUTIQ include cataract formation and subsequent cataract surgery, elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

Studies 1 and 2 were multicenter, randomized, sham injection-controlled, masked trials in which patients with non-infectious uveitis affecting the posterior segment of the eye were treated once with either YUTIQ or sham injection, and then received standard care for the duration of the study. Study 3 was a multicenter, randomized, masked trial in which patients with non-infectious uveitis affecting the posterior segment of the eye were all treated once with YUTIQ, administered by one of two different applicators, and then received standard care for the duration of the study.

Table 1 summarizes data available from studies 1, 2 and 3 through 12 months for study eyes treated with YUTIQ (n=226) or sham injection (n=94). The most common ocular (study eye) and non-ocular adverse reactions are shown in Table 1 and Table 2.

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Cataract[1]	63/113 (56%)	13/56 (23%)
Visual Acuity Reduced	33 (15%)	11 (12%)
Macular Edema	25 (11%)	33 (35%)
Uveitis	22 (10%)	33 (35%)
Conjunctival Hemorrhage	17 (8%)	5 (5%)
Eye Pain	17 (8%)	12 (13%)
Hypotony Of Eye	16 (7%)	1 (1%)
Anterior Chamber Inflammation	12 (5%)	6 (6%)
Dry Eye	10 (4%)	3 (3%)
Vitreous Opacities	9 (4%)	8 (9%)
Conjunctivitis	9 (4%)	5 (5%)
Posterior Capsule Opacification	8 (4%)	3 (3%)
Ocular Hyperemia	8 (4%)	7 (7%)
Vitreous Haze	7 (3%)	4 (4%)
Foreign Body Sensation In Eyes	7 (3%)	2 (2%)
Vitritis	6 (3%)	8 (9%)
Vitreous Floaters	6 (3%)	5 (5%)
Eye Pruritus	6 (3%)	5 (5%)
Conjunctival Hyperemia	5 (2%)	2 (2%)
Ocular Discomfort	5 (2%)	1 (1%)
Macular Fibrosis	5 (2%)	2 (2%)
Glaucoma	4 (2%)	1 (1%)
Photopsia	4 (2%)	2 (2%)
Vitreous Hemorrhage	4 (2%)	0
Iridocyclitis	3 (1%)	7 (7%)
Eye Inflammation	3 (1%)	2 (2%)
Choroiditis	3 (1%)	1 (1%)

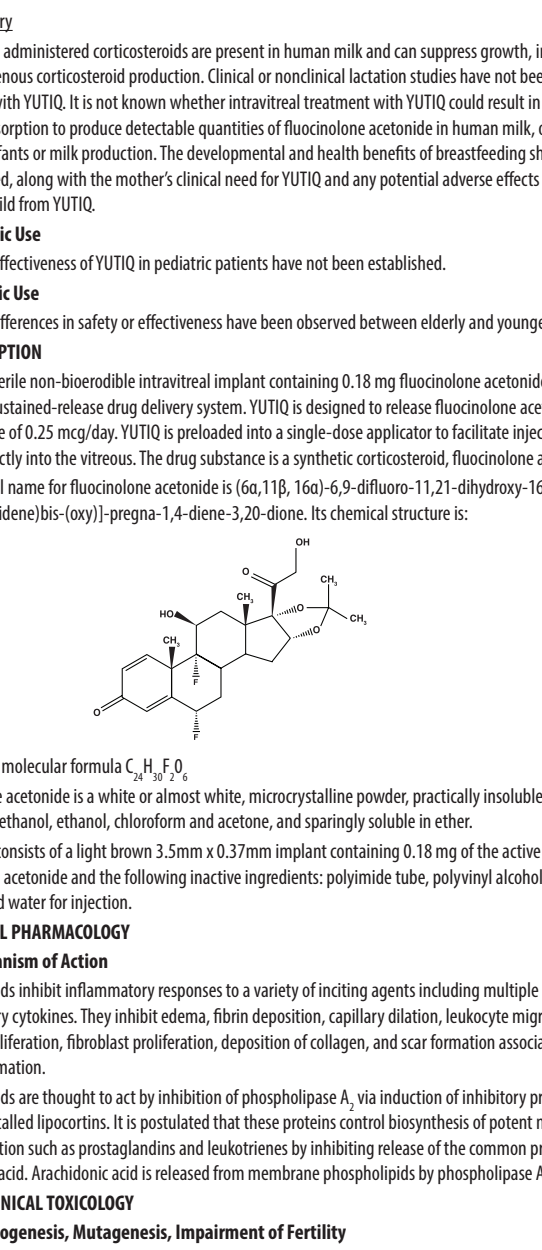
Eye Irritation	3 (1%)	1 (1%)
Visual Field Defect	3 (1%)	0
Lacrimation Increased	3 (1%)	0
Non-ocular		
ADVERSE REACTIONS	**YUTIQ (N=214 Patients) n (%)**	**Sham Injection (N=94 Patients) n (%)**
Nasopharyngitis	10 (5%)	5 (5%)
Hypertension	6 (3%)	1 (1%)
Arthralgia	5 (2%)	1 (1%)

1. Includes cataract, cataract subcapsular and lenticular opacities in study eyes that were phakic at baseline. 113 of the 226 YUTIQ study eyes were phakic at baseline; 56 of 94 sham-controlled study eyes were phakic at baseline.

Table 2: Summary of Elevated IOP Related Adverse Reactions

ADVERSE REACTIONS	YUTIQ (N=226 Eyes) n (%)	Sham (N=94 Eyes) n (%)
IOP elevation ≥ 10 mmHg from Baseline	50 (22%)	11 (12%)
IOP elevation > 30 mmHg	28 (12%)	3 (3%)
Any IOP-lowering medication	98 (43%)	39 (41%)
Any surgical intervention for elevated IOP	5 (2%)	2 (2%)

Figure 1: Mean IOP During the Studies



8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary

Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ.

8.4 Pediatric Use

Safety and effectiveness of YUTIQ in pediatric patients have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

11. DESCRIPTION

YUTIQ is a sterile non-bioerodible intravitreal implant containing 0.18 mg fluocinolone acetonide in a 36-month sustained-release drug delivery system. YUTIQ is designed to release fluocinolone acetonide at an initial rate of 0.25 mcg/day. YUTIQ is preloaded into a single-dose applicator to facilitate injection of the implant directly into the vitreous. The drug substance is a synthetic corticosteroid, fluocinolone acetonide.

The chemical name for fluocinolone acetonide is (6α,11β, 16α)-6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis-(oxy)]-pregna-1,4-diene-3,20-dione. Its chemical structure is:

MW 452.50; molecular formula $C_{24}H_{30}F_2O_6$

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 YUTIQ consists of a light brown 3.5mm x 0.37mm implant containing 0.18 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 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_2 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_2.

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 YUTIQ.

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.

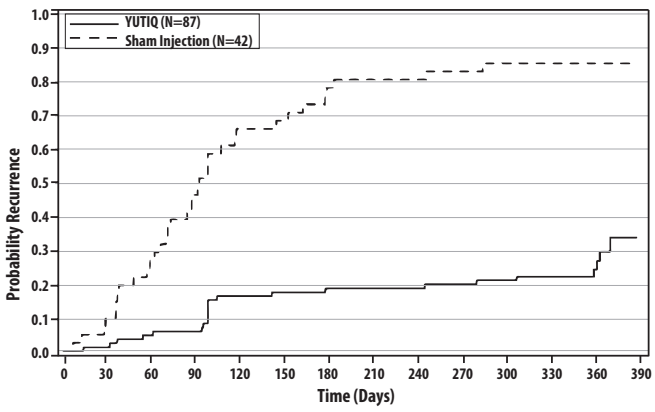
14. CLINICAL STUDIES

The efficacy of YUTIQ was assessed in two randomized (2:1, YUTIQ: sham-injection), multi-centre, double-masked, parallel-groups studies (NCT #01694186 and #02746991) that enrolled patients with non-infectious uveitis affecting the posterior segment of the eye. The primary efficacy endpoint in both trials was the proportion of patients who experienced a recurrence of uveitis in the study eye within 6 months of follow-up; recurrence was also assessed at 12 months. Recurrence of uveitis was defined as either deterioration in visual acuity, vitreous haze attributable to non-infectious uveitis or the need for rescue medications.

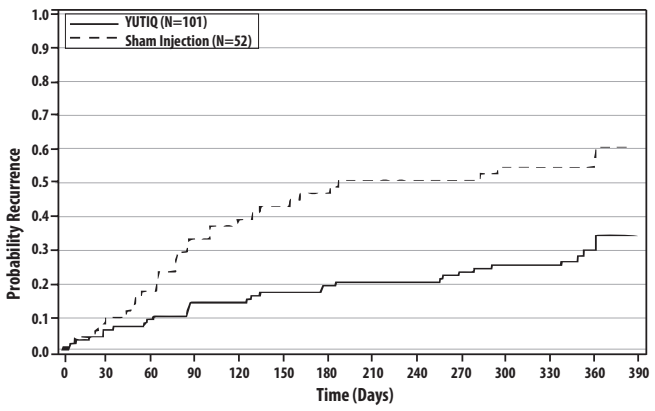
Table 3: Efficacy Results of Recurrence of Uveitis in Randomized Study Eyes

	Study 1		Study 2	
	YUTIQ N = 87	Sham N = 42	YUTIQ N = 101	Sham N = 52
Eyes with recurrence within 6 months, n (%)	**16 (18%)**	**33 (79%)**	**22 (22%)**	**28 (54%)**
Difference (95% CI) in recurrence rates	**60% (41%, 73%)**		**32% (15%, 48%)**	
P-value	< 0.01		< 0.01	
Eyes with recurrence within 12 months, n (%)	**24 (28%)**	**36 (86%)**	**33 (33%)**	**31 (60%)**
Difference (95% CI) in recurrence rates	**58% (40%, 70%)**		**27% (9%, 43%)**	

Figure 2: Time to First Recurrence of Uveitis (ITT: All Randomized Patients)
Time to First Recurrence of Uveitis (ITT; all randomized subjects)
Study 1



Time to First Recurrence of Uveitis (ITT; all randomized subjects)
Study 2



16. HOW SUPPLIED/STORAGE AND HANDLING

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is supplied in a sterile single-dose preloaded applicator with a 25-gauge needle, packaged in a sealed sterile foil pouch inside a sealed Tyvek pouch inside a carton box.

NDC 71879-136-01

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

17. PATIENT COUNSELING INFORMATION

Steroid-related Effects

Advise patients that a cataract may occur after treatment with YUTIQ. 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 YUTIQ 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 YUTIQ, they are at risk for potential complications including, but not limited to, the development of endophthalmitis or changes in 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 by:
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