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Intravitreal, Punctum, and Intracameral Implants

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

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Coverage

Intravitreal and Punctum Corticosteroid Implants

An intravitreal and punctum corticosteroid implant used according to the United States Food and Drug Administration approved indications **may be considered medically necessary** when used:

- As an alternative in individuals who are intolerant or refractory to other therapies; OR
- In individuals who are likely to experience severe adverse events from systemic corticosteroids

Fluocinolone Acetonide Intravitreal Implant (e.g., Retisert®, Iluvien®, Yutiq®)

A. Retisert®
A fluocinolone acetonide intravitreal implant 0.59 mg (e.g., Retisert®) **may be considered medically necessary** in individuals 12 years of age or older for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

A fluocinolone acetonide intravitreal implant 0.59 mg (e.g., Retisert®) **is considered not medically necessary** for individuals with active viral, bacterial, mycobacterial or fungal infections of ocular structures.

B. Iluvien®
A fluocinolone acetonide intravitreal implant 0.19 mg (e.g., Iluvien®) **may be considered medically necessary** for the following indications:
- The treatment of diabetic macular edema (DME) in adult individuals who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure (IOP) (or had the rise in IOP adequately treated prior to placement of the implant); OR
- The treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

A fluocinolone acetonide intravitreal implant 0.19 mg (e.g., Iluvien®) **is considered not medically necessary** for individuals with the following contraindications:
- Active ocular or periocular infections; OR
- Glaucoma with a cup to disc ratio of greater than 0.8.

C. Yutiq®
A fluocinolone acetonide intravitreal implant 0.18 mg (e.g., Yutiq®) **may be considered medically necessary** in adult individuals for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

A fluocinolone acetonide intravitreal implant 0.18 mg (e.g., Yutiq®) **is considered not medically necessary** for individuals 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.

D. Other Uses of Fluocinolone Acetonide Intravitreal Implant (e.g., Retisert®, Iluvien®, Yutiq®)
All other uses of a fluocinolone acetonide intravitreal implant (e.g., Retisert®, Iluvien®, Yutiq®) **are considered experimental, investigational and/or unproven** including but not limited to the following conditions:
- Birdshot retinochoroidopathy;
- Cystoid macular edema related to retinitis pigmentosa;
- Idiopathic macular telangiectasia type 1;
- Postoperative macular edema;

- Circumscribed choroidal hemangiomas;
- Proliferative vitreoretinopathy;
- Radiation retinopathy;
- Prophylaxis of cystoid macular edema in patients with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery.

Dexamethasone Punctum and Intravitreal Implants (e.g., Ozurdex™, Dextenza®)

A. Ozurdex™

A dexamethasone intravitreal implant 0.7 mg (e.g., Ozurdex™) **may be considered medically necessary** in adult individuals for the treatment of:

- Noninfectious ocular inflammation, or uveitis, affecting the intermediate or posterior segment of the eye; OR
- Macular edema following branch or central retinal vein occlusion; OR
- Diabetic macular edema (DME).

A dexamethasone intravitreal implant 0.7 mg (e.g., Ozurdex™) **is considered not medically necessary** for individuals with the following contraindications:

- Ocular or periocular infections (viral, bacterial, or fungal); OR
- Advanced glaucoma with a cup to disc ratio of greater than 0.8; OR
- Torn or ruptured posterior lens capsule.

Dexamethasone intravitreal implant 0.7 mg (e.g., Ozurdex™) **is considered experimental, investigational and/or unproven** including but not limited to the following conditions:

- Birdshot retinochoroidopathy;
- Cystoid macular edema related to retinitis pigmentosa;
- Idiopathic macular telangiectasia type 1;
- Postoperative macular edema;
- Circumscribed choroidal hemangiomas;
- Proliferative vitreoretinopathy;
- Radiation retinopathy;
- Prophylaxis of cystoid macular edema in patients with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery.

A dexamethasone intravitreal implant 0.7 mg (e.g., Ozurdex™) combined with cataract surgery **is considered experimental, investigational, and/or unproven** for the treatment of cataract and macular edema.

B. Dextenza®

A punctum dexamethasone ophthalmic insert for intracanalicular use 0.4 mg (e.g., Dextenza®) **may be considered medically necessary** for the treatment of:

- Ocular inflammation and pain following ophthalmic surgery in adult and pediatric individuals; OR

- Ocular itching associated with allergic conjunctivitis in adult and pediatric individuals aged 2 years and older.

A punctum dexamethasone ophthalmic insert for intracanalicular use 0.4 mg (e.g., Dextenza®) **is considered not medically necessary** for individuals with the following contraindication:

- Active corneal, conjunctival or canalicular infections.

A punctum dexamethasone ophthalmic insert for intracanalicular use 0.4 mg (e.g., Dextenza®) **is considered not medically necessary** for the treatment of ocular itching associated with allergic conjunctivitis in pediatric individuals who require sedation for the insertion procedure.

All other uses of a punctum dexamethasone ophthalmic insert 0.4 mg (e.g., Dextenza®) **are considered experimental, investigational and/or unproven**.

Intracameral Bimatoprost Implant

A bimatoprost implant for intracameral administration (e.g., Durysta®) **may be considered medically necessary** in adult individuals with open angle glaucoma (OAG) or ocular hypertension (OHT) when:

- The individual has had a trial and failure or intolerance to at least two intraocular pressure-lowering eye-drop agents with different mechanisms of action, and one of which must include a prostaglandin analog (e.g., bimatoprost, latanoprost, travoprost, or tafluprost); AND
- The affected eye has not received prior treatment with an intracameral bimatoprost implant.

All other uses of a bimatoprost implant for intracameral administration (e.g., Durysta®) **are considered experimental, investigational and/or unproven**.

Intracameral Travoprost Implant

A travoprost implant for intracameral administration (e.g., iDose® TR) **may be considered medically necessary** in adult individual with open angle glaucoma (OAG) or ocular hypertension (OHT) when:

- The individual has had a trial and failure or intolerance to at least two intraocular pressure-lowering eye-drop agents with different mechanisms of action, and one of which must include a prostaglandin analog (e.g., bimatoprost, latanoprost, travoprost, or tafluprost); AND
- The affected eye has not received prior treatment with an intracameral travoprost implant.

All other uses of a travoprost implant for intracameral administration (e.g., iDose® TR) **are considered experimental, investigational and/or unproven**.

Policy Guidelines

An intravitreal implant used according to U.S. Food and Drug Administration-approved indications may be an acceptable alternative in individuals who are intolerant or refractory to other therapies, or in individuals who are judged likely to experience severe adverse events from systemic corticosteroids. Given the modest improvement in vision and potential adverse events, individuals should be informed about the potential adverse events of a corticosteroid intravitreal implant (including cataracts), increased intraocular pressure, or hypotony, endophthalmitis, and risk for additional surgical procedures. Because of the differing benefits and risks of treatment with intravitreal implants compared with systemic corticosteroid therapy or intraocular injections, individuals should make an informed choice among treatments.

Description

An intravitreal implant is a drug delivery system, injected or surgically implanted in the vitreous of the eye, for sustained release of a pharmacologic agent to the posterior and intermediate segments of the eye. Fluocinolone acetonide implants are non-erodible and deliver drug up to 30 to 36 months while dexamethasone implants are bio-erodible and last up to 6 months.

A punctum implant is a drug delivery device that is inserted through the lower lacrimal punctum into the canaliculus, for sustained release of a pharmacologic agent to the ocular surface. Dexamethasone ophthalmic insert 0.4 mg (e.g., Dextenza®) is the first corticosteroid intracanalicular insert.

An intracameral implant is a drug delivery device that allows for sustained delivery of a substance directly into the anterior chamber of the eye. (1)

Eye Conditions

Uveitis

Uveitis encompasses various conditions, of infectious and noninfectious etiologies, that are characterized by inflammation of any part of the uveal tract of the eye (iris, ciliary body, choroid). Infectious etiologies include syphilis, toxoplasmosis, cytomegalovirus retinitis, and candidiasis. Noninfectious etiologies include sarcoidosis, Behçet syndrome, and “white dot” syndromes such as multifocal choroiditis or “birdshot” chorioretinopathy. Uveitis may be idiopathic, have a sudden or insidious onset, a duration that is limited (<3 months) or persistent, and a course that may be acute, recurrent, or chronic.

The classification scheme recommended by the Uveitis Study Group and the Standardization of Uveitis Nomenclature Working Group is based on anatomic location. Patients with anterior uveitis typically develop symptoms such as light sensitivity, pain, tearing, and redness of the sclera. In posterior uveitis, which comprises approximately 5% to 38% of all uveitis cases in the United States (U.S.), the primary site of inflammation is the choroid or retina (or both). Patients with intermediate or posterior uveitis typically experience minimal pain, decreased visual acuity, and the presence of floaters (bits of vitreous debris or cells that cast shadows on the

retina). Chronic inflammation associated with posterior segment uveitis can lead to cataracts, glaucoma, and structural damage to the eye, resulting in severe and permanent vision loss.

Treatment
The primary goal of therapy for uveitis is to preserve vision. Noninfectious uveitis typically responds well to corticosteroid treatment. Immunosuppressive therapy (e.g., antimetabolites, alkylating agents, T-cell inhibitors, tumor necrosis factor inhibitors) may also be used to control severe uveitis. Immunosuppressive therapy is typically reserved for patients who require chronic high dose systemic steroids to control their disease. While effective, immunosuppressants may have serious and potentially life-threatening adverse effects, including renal and hepatic failure and bone marrow suppression.

Macular Edema After Retinal Vein Occlusion
Retinal vein occlusions are classified by whether the central retinal vein or one of its branches is obstructed. Central retinal vein occlusion and branch retinal vein occlusion differ in pathophysiology, clinical course, and therapy. Central retinal vein occlusions are categorized as ischemic or nonischemic. Ischemic central retinal vein occlusions are referred to as severe, complete, or total vein obstruction, and account for 20% to 25% of all central retinal vein occlusions. Macular edema and permanent macular dysfunction occur in virtually all patients with ischemic central retinal vein occlusion, and in many patients with nonischemic central retinal vein occlusion. Branch retinal vein occlusion is a common retinal vascular disorder in adults between 60 and 70 years of age and occurs approximately 3 times more often than central retinal vein occlusion.

Treatment
Intravitreal injections of triamcinolone are used to treat macular edema associated with central retinal vein occlusion, with a modest beneficial effect on visual acuity. The treatment effect lasts about 6 months and repeat injections may be necessary. Cataracts are a common side effect, and steroid related pressure elevation occurs in about one third of patients, with 1% requiring filtration surgery.

Macular photocoagulation with grid laser improves vision in branch retinal vein occlusion but is not recommended for central retinal vein occlusion. Although intravitreal injections of triamcinolone have also been used for branch retinal vein occlusion, serious adverse events have stimulated the evaluation of new treatments, including intravitreal steroid implants or the intravitreal injection of antivascular endothelial growth factor.

Diabetic Macular Edema
Diabetic retinopathy is a common microvascular complication of diabetes and a leading cause of blindness in adults. The 2 most serious complications for vision are diabetic macular edema (DME) and proliferative diabetic retinopathy. At its earliest stage (nonproliferative retinopathy), microaneurysms occur. As the disease progresses, blood vessels that nourish the retina are blocked, triggering the growth of new and fragile blood vessels (proliferative retinopathy). Severe vision loss with proliferative retinopathy arises from leakage of blood into the vitreous.

DME is characterized by swelling of the macula due to gradual leakage of fluids from blood vessels and breakdown of the blood-retinal barrier. Moderate vision loss can arise from the fluid accumulating in the center of the macula (macular edema) during the proliferative or nonproliferative stages of the disease. Although proliferative disease is the main blinding complication of diabetic retinopathy, macular edema is more frequent and is the leading cause of moderate vision loss in people with diabetes.

Treatment
Tight glycemic and blood pressure control is the first line of treatment to control diabetic retinopathy, followed by laser photocoagulation for patients whose retinopathy is approaching the high-risk stage. Although laser photocoagulation is effective at slowing the progression of retinopathy and reducing visual loss, it does not restore lost vision. Alternatives to intravitreal implants include intravitreal injection of triamcinolone acetonide, which is used as off-label adjunctive therapy for DME. Angiostatic agents such as injectable vascular endothelial growth factor inhibitors, which block stages in the pathway leading to new blood vessel formation (angiogenesis), have demonstrated efficacy in DME.

Age-Related Macular Degeneration
Age related macular degeneration is a degenerative disease of the retina that results in loss of central vision with increasing age. Two different forms of degeneration, known as dry and wet, may be observed. The dry form (also known atrophic or areolar) is more common and is often a precursor to the wet form (also known as exudative neovascular or disciform). The wet form is more devastating and characterized by serous or hemorrhagic detachment of the retinal pigment epithelium and development of choroidal neovascularization, which greatly increases the risk of developing severe irreversible loss of vision. Choroidal neovascularization is categorized as classic or occult.

Treatment
Effective specific therapies for exudative or wet age-related macular degeneration are an intravitreous injection of a vascular endothelial growth factor inhibitor, possibly thermal laser photocoagulation (in selected patients), and photodynamic therapy.

Glaucoma
Glaucoma is a disease that damages the eye's optic nerve due to a build-up of fluid in the anterior portion of the eye which increases the pressure in the eye. The most common type of glaucoma is primary open-angle glaucoma. This type of glaucoma is painless and causes no vision changes in the early stages. As the disease progresses, blind spots develop in the peripheral vision. (2)

Treatment
While damage from glaucoma is permanent and cannot be reversed, medicine and surgery can help to stop further damage. Glaucoma is most commonly treated with eye drops that work to lower eye pressure. As an alternative to daily eye drops which can be challenging for many patients and lead to poor compliance, recently there has been an increased interest in

biodegradable, intracameral implants that allow for 24/7 medication delivery over several months. (2)

Intravitreal and Punctum Corticosteroid Implants
Intravitreal and punctum implants deliver a continuous concentration of a pharmacologic agent to the eye over a prolonged period. The goal of therapy is to reduce inflammation in the eye while minimizing the adverse events of the therapeutic regimen.

Selection of the route of corticosteroid administration (topical, systemic, periocular, or intraocular injection) is based on the cause, location, and severity of the disease. Each therapeutic approach has drawbacks. For example, topical corticosteroids require frequent (e.g., hourly) administration and may not adequately penetrate the posterior segment of the eye due to their poor ability to penetrate ocular tissues. Systemically administered drugs penetrate poorly into the eye because of the blood-retinal barrier, and high-dose or long-term treatments may be necessary. Long-term systemic therapies can be associated with substantial adverse events such as hypertension and osteoporosis, while repeated (every 4 to 6 weeks) intraocular corticosteroid injections may result in pain, intraocular infection, globe perforation, fibrosis of the extraocular muscles, reactions to the delivery vehicle, increased intraocular pressure (IOP), and cataract development.

Corticosteroid implants are biodegradable or nonbiodegradable. Nonbiodegradable systems are thought to be preferable for treating chronic, long-term disease, while biodegradable products may be preferred for conditions that require short-term therapy. Although the continuous local release of steroid with an implant may reduce or eliminate the need for intravitreal injections and/or long-term systemic therapy, insertion or surgical implantation of the device carries risks, and the device could increase ocular toxicity due to increased corticosteroid concentrations in the eye over a longer duration. With any route of administration, cataracts are a frequent complication of long-term corticosteroid therapy.

Intraocular corticosteroid implants being evaluated include:

- Retisert® (nonbiodegradable fluocinolone acetonide intravitreal implant; Bausch & Lomb) is a sterile implant that consists of a tablet containing fluocinolone acetonide 0.59 mg, a synthetic corticosteroid that is less soluble in aqueous solution than dexamethasone. The tablet is encased in a silicone elastomer cup with a release orifice and membrane; the entire elastomer cup assembly is attached to a suture tab. Following implantation (via pars plana incision and suturing) in the vitreous, the implant releases the active drug at a rate of 0.3 to 0.4 µg/d over 2.5 years.
- Iluvien® (nonbiodegradable injectable intravitreal implant with fluocinolone acetonide; Alimera Sciences) is a rod-shaped device made of polyimide and polyvinyl alcohol. It is small enough to be placed using a 25-gauge applicator. It is expected to provide sustained delivery of fluocinolone acetonide for up to 3 years.
- Ozurdex™ (previously known as Posurdex; biodegradable dexamethasone intravitreal implant; Allergan, Irvine, CA) is composed of a biodegradable copolymer of lactic acid and glycolic acid with micronized dexamethasone. This implant is placed into the vitreous cavity

through the pars plana using a customized, single-use, 22-gauge applicator. The implant provides intravitreal dexamethasone for up to 6 months. The mean number of Ozurdex injections reported in the literature is 4.2 injections per year, and more than 6 consecutive injections have been reported. (3, 4)

- Dextenza® (biodegradable dexamethasone intracanalicular insert; Ocular Therapeutix™) is a rod-shaped hydrogel device that is designed to deliver a sustained and tapered release of 0.4 mg of dexamethasone over 4 weeks. Following ophthalmic surgery, it is inserted through the inferior punctum into the canaliculus of the operative eye. To allow for visualization and retention monitoring, the hydrogel device is conjugated with fluorescein. No removal is required as the device is designed to resorb and exit the nasolacrimal system independently.
- Yutiq® (nonbiodegradable fluocinolone acetonide intravitreal implant; EyePoint Pharmaceuticals U.S., Inc.) is a sterile 3.3 mm long implant consisting of fluocinolone acetonide 0.18 mg that is preloaded into a single dose applicator and injected directly into the vitreous. It is designed to provide a sustained release of fluocinolone acetonide at an initial rate of 0.25 mcg/day within over a 36-month period.

Intracameral Bimatoprost Implant

Durysta® is an ophthalmic drug delivery system for a single intracameral administration of a biodegradable implant. The implant is a solid polymer matrix containing 10 mcg of bimatoprost and is approximately 1 mm in length. It is preloaded into a single-use applicator that is used to inject the implant directly into the anterior chamber of the eye. Following administration, the implant is intended to settle within the inferior angle to deliver a sustained release of bimatoprost for several months. Bimatoprost is believed to lower IOP by increasing the outflow of aqueous humor through both the trabecular meshwork and the uveoscleral routes. Placement of the implant within the anterior chamber angle allows for close proximity to the tissues involved in both of these outflow pathways. (5)

Intracameral Travoprost Implant

iDose® TR is a travoprost delivery system consisting of an intracameral implant containing 75 mcg of travoprost that is pre-loaded in a single-dose inserter that is administered through a small, clear corneal incision and is anchored into the sclera at the iridocorneal angle. (11) Although the exact mechanism of action is unknown, travoprost is believed to reduce IOP by increasing uveoscleral outflow.

Regulatory Status

In 2009, Ozurdex® (dexamethasone 0.7 mg intravitreal implant; Allergan) was approved by the U.S. FDA for the treatment of macular edema following branch retinal vein occlusion or central retinal vein occlusion. Subsequently, in September 2010, the indication was expanded to include treatment of noninfectious uveitis affecting the segment of the eye. In 2014, the indication was again expanded to include treatment of DME. Per the FDA label, Ozurdex® is contraindicated in patients with ocular or periocular infections (viral, bacterial, or fungal), advanced glaucoma with a cup to disc ratio of greater than 0.8 and in patients with a torn or ruptured posterior lens capsule. (6)

In September 2014, Iluvien® (fluocinolone acetonide 0.19 mg intravitreal implant; Alimera Sciences) was approved by the FDA for the treatment of DME in patients previously treated with a course of corticosteroids and without a clinically significant rise in IOP. Per the FDA label, Iluvien is contraindicated in patients with active ocular and periocular infections or in patients diagnosed with glaucoma with a cup to disc ratio of greater than 0.8. In March 2025, the FDA expanded the label for Iluvien® to include approval for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye. (7)

In November 2004, Retisert® (fluocinolone acetonide 0.59 mg intravitreal implant; Bausch & Lomb) was approved by the FDA for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye. Per the FDA label, Retisert® is contraindicated in patients with active viral, bacterial, mycobacterial and fungal infections of ocular structures. Additionally, the safety and effectiveness of Retisert has not been established for use in pediatric patients below 12 years of age. (8)

In October 2018, Yutiq® (fluocinolone acetonide 0.18 mg intravitreal implant; EyePoint Pharmaceuticals, Inc.) was approved by the FDA for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye. Per the FDA label, 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. In addition, the safety and effectiveness of Yutiq has not been established in pediatric patients. (9)

In November 2018, Dextenza® (dexamethasone 0.4 mg intracanalicular implant; Ocular Therapeutix) was approved by the FDA for the treatment of ocular inflammation and pain following ophthalmic surgery. In October 2021, the indication was expanded to include treatment of ocular itching associated with allergic conjunctivitis. Per the FDA label, Dextenza is contraindicated in patients with active corneal, conjunctival or canalicular infections. (10)

In March 2020, Durysta® (bimatoprost implant, for intracameral administration; Allergan) was approved by the FDA for the reduction of IOP in patients with open angle glaucoma or ocular hypertension. Per the FDA label, Durysta is contraindicated in patients with ocular or periocular infections, corneal endothelial cell dystrophy, prior corneal transplantation, absent or ruptured posterior lens capsule, and hypersensitivity. Additionally, Durysta should not be re-administered to an eye that received a prior Durysta implant. (1)

In December 2023, iDose® TR (travoprost intracameral implant; Glaukos) was approved by the FDA for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension. Per the FDA label, iDose® TR is contraindicated in patients with ocular or periocular infections, corneal endothelial cell dystrophy, prior corneal transplantation, and hypersensitivity. iDose® TR should not be readministered to an eye that received a prior iDose® TR. (11)

Rationale

INTRAVITREAL AND PUNCTUM CORTICOSTEROID IMPLANTS

Intravitreal Fluocinolone Acetonide Implant (8)

Retisert

In two randomized, double-masked, multicenter controlled clinical trials, 224 patients with chronic (a one year or greater history) non-infectious uveitis affecting the posterior segment of one or both eyes were randomized to receive a 0.59 mg Retisert. The primary efficacy endpoint in both trials was the rate of recurrence of uveitis affecting the posterior segment of the study eye in the 34-week pre-implantation period compared to the rate of recurrence in the 34-week post-implantation period. Uveitis recurrence rates at 1-, 2-, and 3-year post-implantation were also compared to the 34-week preimplantation period.

Detailed results are shown in Table 1.

Table 1. Uveitis Recurrence Rates

Time Point	Study 1 N=108	Study 2 N=116
	Uveitis Recurrence Rates[a,b] N (%)	
34 Weeks Pre-implantation	58 (53.7)	46 (39.7)
34 Weeks Post-implantation	2 (1.8)	15 (12.9)
1 Year Post-implantation	4 (3.7)	15 (12.9)
2 Years Post-implantation	11 (10.2)	16 (13.8)
3 Years Post-implantation	22 (20.4)	20 (17.2)
3 years[c] Post-implantation	33 (30.6)	28 (24.1)

[a] Recurrence of uveitis for all post-implantation time points was compared to the 34 weeks pre-implantation time point.

[b] p-value <0.01 from McNemar's χ^2 test.

[c] Results presented include imputed recurrences. Recurrences were imputed when a subject was not seen within 10 weeks of their final scheduled visit.

In assessing the effect of Retisert on the corneal endothelial cell density in eyes that have been implanted for a minimum of 1 year, the results indicate that eyes containing the Retisert implant for an average of 3.54 years had a lower mean corneal endothelial cell density (mean paired difference of -435 cells/mm^2) compared with non-implanted eyes (p<0.01).

Iluvien® (7)

Diabetic Macular Edema

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 (DME) 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 2. Baseline BCVA (Letters)

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

BCVA: best corrected visual acuity; SD: standard deviation.

Table 3. Visual Acuity Outcomes at Month 24 (All randomized subjects with LOCF)

Study	**Outcomes**	**Iluvien**	**Sham**	**Estimated Difference (95% CI)**
1 Iluvien: N=190 Sham: N=95	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 Iluvien: N=186 Sham: N=90	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)

BCVA: best corrected visual acuity; CI: confidence interval; LOCF: last observation carried forward.

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.

The BCVA outcomes for the Pseudophakic and Phakic subgroups from Studies 1 and 2 at Month 24 are presented in Table 4.

Table 4. Visual Acuity Outcomes at Month 24 (Subgroup for pooled data with LOCF)

Study	**Outcomes**	**Iluvien**	**Sham**	**Estimated Difference (95% CI)**
Pseudophakic Iluvien: N=140 Sham: N=64	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 Iluvien: N=236 Sham: N=121	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)

BCVA: best corrected visual acuity; CI: confidence interval; LOCF: last observation carried forward; SD: standard deviation.

Chronic Non-Infectious Uveitis Affecting the Posterior Segment

The efficacy of fluocinolone acetonide intravitreal implant was assessed in two randomized (2:1, fluocinolone acetonide intravitreal implant:sham-injection), multi-center, 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 5. Efficacy Results of Recurrence of Uveitis in Randomized Study Eyes

	Study 1		**Study 2**	
	FAc Implant	**Sham**	**FAc Implant**	**Sham**
	N=87	**N=42**	**N=101**	**N=52**
Eyes with recurrence within 6 months, n (%)	16 (87%)	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%)	

CI: confidence interval; FAc: fluocinolone acetonide.

Yutig® (9)

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 6. Efficacy Results of Recurrence of Uveitis in Randomized Study Eyes

	Study 1		Study 2	
	Yutiq	Sham	Yutiq	Sham
	N=87	N=42	N=101	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%)	

CI: confidence interval.

Dexamethasone Punctum and Intravitreal Implants (e.g., Ozurdex®, Dextenza®)

Ozurdex® (6)

Retinal Vein Occlusion

The efficacy of Ozurdex® for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) was assessed in two, multicenter, double-masked, randomized, parallel studies.

Following a single injection, Ozurdex® demonstrated the following clinical results for the percent of patients with ≥ 15 letters of improvement from baseline in best-corrected visual acuity (BCVA).

Table 7. Number (Percent) of Patients with ≥ 15 Letters Improvement from Baseline in BCVA

Study Day	Study 1			Study 2		
	Ozurdex N=201	Sham N=202	p-value[a]	Ozurdex N=226	Sham N=224	p-value[a]
Day 30	40 (20%)	15 (7%)	< 0.01	51 (23%)	17 (8%)	< 0.01
Day 60	58 (29%)	21 (10%)	< 0.01	67 (30%)	27 (12%)	< 0.01
Day 90	45 (22%)	25 (12%)	< 0.01	48 (21%)	31 (14%)	0.039
Day 180	39 (19%)	37 (18%)	0.780	53 (24%)	38 (17%)	0.087

[a] p-values were based on the Pearson's chi-square test.

BCVA: best corrected visual acuity.

In each individual study and in a pooled analysis, time to achieve ≥ 15 letters (3-line) improvement in BCVA cumulative response rate curves was significantly faster with Ozurdex® compared to sham ($p < 0.01$), with Ozurdex® treated patients achieving a 3-line improvement in BCVA earlier than sham-treated patients.

The onset of a ≥ 15 letter (3-line) improvement in BCVA with Ozurdex® occurs within the first two months after implantation in approximately 20-30% of subjects. The duration of effect persists approximately one to three months after onset of this effect.

Posterior Segment Uveitis
The efficacy of Ozurdex® was assessed in a single, multicenter, masked, randomized study of 153 patients with non-infectious uveitis affecting the posterior segment of the eye.

After a single injection, the percent of patients reaching a vitreous haze score of 0 (where a score of 0 represents no inflammation) was statistically significantly greater for patients receiving Ozurdex® versus sham at week 8 (primary time point) (47% versus 12%). The percent of patients achieving a 3-line improvement from baseline BCVA was 43% for patients receiving Ozurdex® versus 7% for sham at week 8.

Diabetic Macular Edema
The efficacy of Ozurdex® for the treatment of diabetic macular edema was assessed in two, multicenter, masked, randomized, sham-controlled studies. Subjects were to be evaluated for retreatment eligibility every three months starting from Month 6 but could only receive successive treatments at least 6 months apart. Retreatment was based on physician's discretion after examination including Optical Coherence Tomography. Patients in the Ozurdex® arm received an average of 4 treatments during the 36 months.

The primary endpoint was the proportion of patients with 15 or more letters improvement in BCVA from baseline at Month 39 or final visit for subjects who exited the study at or prior to Month 36. The Month 39 extension was included to accommodate the evaluation of safety and efficacy outcomes for subjects who received re-treatment at Month 36. Only fourteen percent of the study patients completed the Month 39 visit (16.8% from Ozurdex® and 12.2% from Sham).

Table 8. Visual Acuity Outcomes at Month 39 (All randomized subjects with LOCF[a])

Study	**Outcomes**	**Ozurdex®**	**Sham**	**Estimated Difference (95% CI)**
Study 1: Ozurdex N=163 Sham N=165	Mean (SD) Baseline BCVA (Letters)	56 (10)	57 (9)	
	Median (range) Baseline BCVA (Letters)	59 (34-95)	58 (34-74)	
	Gain of ≥15 letters in BCVA (n (%))	34 (21%)	19 (12%)	9.3% (1.4%, 17.3%)
	Loss of ≥15 letters in BCVA (n (%))	15 (9%)	17 (10%)	-1.1% (-7.5% 5.3%)
	Mean change in BCVA (SD)	4.1 (13.9)	0.9 (11.9)	3.2 (0.4, 5.9)
Study 2: Ozurdex N=165	Mean (SD) Baseline BCVA (Letters)	55 (10)	56 (9)	

Sharm N =163	Median (range) Baseline BCVA (Letters)	58 (34-72)	58 (36-82)	
	Gain of ≥15 letters in BCVA (n (%))	30 (18%)	16 (10%)	8.4% (0.9%, 15.8%)
	Loss of ≥15 letters in BCVA (n (%))	30 (18%)	18 (11%)	7.1% (-0.5%, 14.7%)
	Mean change in BCVA (SD)	0.4 (17.5)	0.8 (13.6)	-0.7 (-4.1, 2.6)

[a] 14% (16.8%) from Ozurdex and 12/2% from Sham) of patients had BCVA outcome at Month 39, for the remaining patients, the data at Month 36 or earlier was carried forward.
BCVA: best corrected visual acuity; CI: confidence interval; LOCF: last observation carried forward; SD: standard deviation

The occurrence of cataracts impacted visual acuity during the study. The visual acuity improvement from baseline increases during a treatment cycle, peaks at approximately 3 Months posttreatment and diminishes thereafter. Patients who were pseudophakic at baseline achieved greater mean BCVA change from baseline at the final study visit.

The best corrected visual acuity outcomes for the Pseudophakic and Phakic subgroups from Studies 1 and 2 at Month 39 are presented in Table 9.

Table 9. Visual Acuity outcomes at Month 39 (Subgroup for pooled data with LOCF[a])

Subgroup (Pooled)	**Outcomes**	**Ozurdex**	**Sham**	**Estimated Difference (95% CI)**
Pseudophakic: Ozurdex N=82 Sham N=99	Gain of ≥15 letters in BCVA (n (%))	16 (20%)	11 (11%)	8.4% (-2.2%, 19.0%)
	Loss of ≥15 letters in BCVA (n (%))	4 (5%)	7 (7%)	-2.2% (-9.1%, 4.7%)
	Mean change in BCVA (SD)	5.8 (11.6)	1.4 (12.3)	4.2 (0.8, 7.6)
Phakic: Ozurdex N=246 Sham N=229	Gain of ≥15 letters in BCVA (n (%))	48 (20%)	24 (11%)	9.0% (2.7%, 15.4%)
	Loss of ≥15 letters in BCVA (n (%))	41 (17%)	28 (12%)	4.4% (-1.9%, 10.7%)
	Mean change in BCVA (SD)	1.0 (16.9)	0.6 (12.9)	0.3 (-2.4, 3.0)

[a] 14% (16.8% from Ozurdex® and 12.2% from Sham) of patients had BCVA outcome at Month 39, for the remaining patients the data at Month 36 or earlier was used in the analysis.
BCVA: best corrected visual acuity; CI: confidence interval; LOCF: last observation carried forward; SD: standard deviation.

Dextenza® (10)

<u>Ocular Inflammation and Pain Following Ophthalmic Surgery</u>

In three randomized, multicenter, double-masked, parallel group, vehicle-controlled efficacy trials, patients received Dextenza or its vehicle immediately upon completion of cataract surgery (NCT02034019, NCT02089113, NCT02736175). In all three trials, Dextenza had a higher proportion of patients than the vehicle group who were pain free on post-operative Day 8. On postoperative Day 14, in two of the three studies, Dextenza had a higher proportion of patients than the vehicle group who had an absence of anterior chamber cells that was statistically significant. Results are shown in Table 10 and Table 11.

Table 10. Percentage of Patients with Absence of Anterior Chamber Cells

Study 1	**Visit**	**Dextenza (N=164) n (%)**	**Vehicle (N=83) n (%)**	**Difference (95% CI)**
	Day 14	54 (33%)	12 (14%)	18% (8%, 29%)
Study 2	**Visit**	**Dextenza (N=161) n (%)**	**Vehicle (N=80) n (%)**	**Difference (95% CI)**
	Day 14	63 (39%)	25 (31%)	8% (-5%, 21%)
Study 3	**Visit**	**Dextenza (N=216) n (%)**	**Vehicle (N=222) n (%)**	**Difference (95% CI)**
	Day 14	113 (52%)	69 (31%)	21 % (12%, 30%)

CI: confidence interval.

Table 11. Percentage of Patients with Absence of Pain

Study 1	**Visit**	**Dextenza (N=164) n (%)**	**Vehicle (N=83) n (%)**	**Difference (95% CI)**
	Day 8	131 (80%)	36 (43%)	37% (24%, 49%)
Study 2	**Visit**	**Dextenza (N=161) n (%)**	**Vehicle (N=80) n (%)**	**Difference (95% CI)**
	Day 8	124 (77%)	47 (59%)	18% (6%, 31%)
Study 3	**Visit**	**Dextenza (N=216) n (%)**	**Vehicle (N=222) n (%)**	**Difference (95% CI)**
	Day 8	172 (80%)	136 (61%)	18% (10%, 27%)

CI: confidence interval.

Section Summary: Ocular Inflammation and Pain Following Ophthalmic Surgery

For individuals scheduled to undergo clear corneal cataract surgery who receive punctum dexamethasone insert (0.4 mg), the evidence includes 3 RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Compared with the sham insert, all 3 trials generally consistently found significant improvements with the punctum dexamethasone insert (0.4 mg) across both coprimary efficacy endpoints of an absence of pain at 8 days and absence of anterior chamber cells at day 14. Adverse events were generally similar between punctum dexamethasone insert (0.4 mg) and sham.

Itching associated with Allergic Conjunctivitis

In three randomized, multicenter, double-masked, parallel group, vehicle-controlled efficacy trials, patients received Dextenza or its vehicle utilizing a repeat conjunctival allergen challenge

model (NCT02445326, NCT02988882, NCT04050865). In all three trials, Dextenza resulted in lower mean ocular itching scores compared with the vehicle group at all time points throughout the one-month duration of the study. In two of the three studies, a higher proportion of patients had statistically significant reductions in ocular itching on Day 8, at 3 minutes, 5 minutes and 7 minutes post-challenge in the Dextenza group than in the vehicle group. Results are shown in Table 12.

Table 12. Reduction in Ocular Itching

Study 1	**Visit**	**Time Point**	**Dextenza (N=35)**	**Vehicle (N=38)**	**Difference (95% CI)**
			Least Square means		
	Day 8	3 min	1.9	2.7	-0.7 (-1.2, -0.3)
		5 min	2.1	2.8	-0.7 (-1.2, -2.3)
		7 min	1.9	2.7	-0.8 (-1.2, -0.4)
Study 2	**Visit**	**Time Point**	**Dextenza (N=44)**	**Vehicle (N=42)**	**Difference (95% CI)**
			Least Square means		
	Day 8	3 min	2.1	2.3	-0.2 (-0.7, 0.3)
		5 min	2.1	2.3	-0.2 (-0.8, 0.3)
		7 min	2.1	2.4	-0.3 (-0.8, 0.3)
Study 3	**Visit**	**Time Point**	**Dextenza (N=48)**	**Vehicle (N=48)**	**Difference (95% CI)**
			Least Square means		
	Day 8	3 min	1.8	2.7	-0.9 (-1.2, -0.4)
		5 min	1.8	2.7	-1.0 (-1.4, -0.6)
		7 min	1.7	2.7	-1.0 (-1.4, -0.6)

CI: confidence interval.

Section Summary: Ocular Itching Associated with Allergic Conjunctivitis

For individuals with ocular itching associated with allergic conjunctivitis who receive punctum dexamethasone insert (0.4 mg), the evidence includes 3 RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Compared with the sham insert, punctum dexamethasone inserts (0.4) demonstrated a significant decrease in patient-reported ocular itching after 1-week post-implant, and throughout most time points up to 30 days. Adverse events were similar in both groups and were all considered mild to moderate. The safety, efficacy, and the improvement on health outcomes were adequately demonstrated; therefore, Dextenza may be considered medically necessary when the clinical criteria are met. Dextenza is considered experimental, investigational and/or unproven for all other indications.

Intracameral Bimatoprost Implant

Durysta® (1)

The efficacy of Durysta was evaluated in two multicenter, randomized, parallel-group, controlled 20-month (including 8-month extended follow-up) studies compared to twice daily topical timolol 0.5% drops, in patients with open angle glaucoma (OAG) or OHT. Durysta demonstrated an IOP reduction of approximately 5-8 mmHg in patients with a mean baseline IOP of 24.5 mmHg. The most common ocular adverse reaction observed in the two trials was conjunctival hyperemia, which was reported in 27% of patients. Other common ocular adverse reactions reported in 5-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, IOP increased, corneal endothelial cell loss, vision blurred, and iritis. Due to possible corneal endothelial cell loss, administration of Durysta should be limited to a single implant per eye without retreatment.

Summary of Evidence

The U.S. Food and Drug Administration (FDA) approved bimatoprost implant (Durysta®) for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT) based on two randomized, controlled clinical studies. The safety, efficacy, and the improvement on health outcomes were adequately demonstrated, therefore Durysta may be considered medically necessary when established criteria are met. Durysta is considered experimental, investigational, and/or unproven for all other indications. Per the FDA label, Durysta should not be readministered to an eye that has received a prior Durysta.

Intracameral Travoprost Implant

iDose® TR (11)

iDose TR was evaluated in two multicenter, 12-month, randomized, parallel-group, double-masked, controlled clinical trials in patients with open angle glaucoma (OAG) or ocular hypertension (OHT). In both trials (GC-010, NCT03519386, and GC012, NCT03868124), iDose TR was compared to twice-daily topical administration of timolol maleate ophthalmic solution, 0.5%. In the first 3 months following administration, iDose TR demonstrated an intraocular pressure (IOP) change from baseline of -6.6 to -8.4 mmHg in the study eye of patients with a mean baseline IOP of 24 mmHg. iDose TR demonstrated non-inferiority to timolol ophthalmic solution in IOP reduction during the first 3 months. Subsequently, iDose TR did not demonstrate non-inferiority over the next 9 months.

Summary of Evidence

The U.S. Food and Drug Administration (FDA) approved travoprost implant (iDose® TR) for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT) based on two randomized, controlled clinical studies. The safety, efficacy, and the improvement on health outcomes were adequately demonstrated, therefore iDose® TR may be considered medically necessary when established criteria are met. iDose® TR is considered experimental, investigational, and/or unproven for all other indications. Per the FDA label, travoprost intracameral implant (iDose® TR) should not be readministered to an eye that received a prior iDose® TR.

Other Conditions

Birdshot Retinochoroidopathy

Retrospective Cohort Studies

Birdshot retinochoroidopathy, also known as birdshot chorioretinopathy or vitiliginous chorioretinitis, is a chronic, bilateral rare form of posterior uveitis with characteristic hypopigmented lesions. No RCTs were identified for the treatment of this indication for any corticosteroid intravitreal implants. Bajwa et al. (2014) published a retrospective case series involving 11 patients (11 eyes) refractory or intolerant to conventional immunomodulatory therapy who received fluocinolone acetonide implants (0.59 mg). (12) Reported outcomes were disease activity markers. The proportion of patients with intraocular inflammation was 55% at baseline, which decreased to 10%, 11%, and 0% at year 1, 2, and 3, respectively. Active vasculitis was noted in 36.3% of patients at baseline and 0% at 3-year follow-up. More than 20% reduction in central retinal thickness was noted in all patients with cystoid macular edema at 6 months, 1 year, 2 years, and 3 years postimplant. Another retrospective cohort study (2013), which included 11 eyes with birdshot chorioretinitis, reported improved control of inflammation and decreased reliance on adjunctive therapy with fluocinolone acetonide implants (0.59 mg). (13) Authors observed a more robust increase in intraocular pressure compared with the observed elevation in patients with other types of posterior uveitis and panuveitis. In another retrospective study, which included 32 eyes with birdshot chorioretinopathy who received fluocinolone acetonide implant (0.59 mg) with 12-month follow-up, Rush et al. (2011) also reported a decrease in vitreous haze from 26% at baseline to 100% at 12 months. (14) In 2 small retrospective studies with 6 eyes in 3 patients (15) and 6 eyes in 4 patients, (16) respectively, reported the favorable effects of dexamethasone implants on ocular inflammation and macular edema during treatment. All eyes exhibited control of ocular inflammation and macular edema. In the first study, all 3 patients achieved best-corrected visual acuity of at least 20/25 during treatment. In the second, there was a mean improvement of 70 letters on best-corrected visual acuity using the Early Treatment Diabetic Retinopathy Study chart.

<u>Section Summary: Birdshot Retinochoroidopathy</u>

No RCTs were identified on the treatment of birdshot retinochoroidopathy with any corticosteroid intravitreal implants. Available evidence includes multiple observational studies that noted improvements in anatomic and visual acuity outcomes in individuals refractory or intolerant to the current standard of treatment. Long-term follow-up for efficacy and safety is limited. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in refractory or intolerant patients with birdshot retinochoroidopathy.

<u>Cystoid Macular Edema</u>

Randomized Controlled Trials

No large, multi-center, sham-controlled RCTs were identified that evaluate the treatment of this indication using any corticosteroid intravitreal implants.

The only RCT identified for this indication is for individuals who have cystoid macular edema related to retinitis pigmentosa. Park et al. (2019) published a small (N=14), single-center, observation-controlled RCT from South Korea. (17) In this RCT, 14 patients with bilateral cystoid macular edema related to retinitis pigmentosa with macular cystic changes as shown by

spectral domain optical coherence tomography with central macular thickness of .250 mm in both eyes had 1 eye randomized to intravitreal dexamethasone implant 0.7 mg and the other eye was observed. At 2 months, compared to the control eyes, the intravitreal dexamethasone implant eyes resulted in improved central macular thickness (-147.5µm vs. -14µm, p<.001) and median change of best-corrected visual acuity (+6 vs. +1; p<.001). But, at month 6, the central macular thickness of the study eyes returned to baseline level and there were no longer any significant differences between the eyes. At month 12, 40% of study eyes and 12.5% control eyes experienced cataract formation or progression. But none required cataract surgery.

Comparative Observational Studies

Three observational studies have compared intravitreal dexamethasone to other treatments in patients with cystoid macular edema. (18, 19, 20) Tables 13 and 14 summarize their key characteristics and results. These studies are heterogenous in the type of cystoid macular edema treated, the comparator treatment, and outcome assessment approaches. The strength and relevancy of their findings are limited as they have included only small numbers of patients and lack responder analysis of the proportion of patients with a 15-or-more letter improvement from baseline in best-corrected visual acuity.

Table 13. Summary of Key Comparative Observational Study Characteristics

Study	Study Type	Country	Dates	Participants	Treatment 1	Treatment 2	Follow-Up
Ozkok et al. (2016) (18)	Pro-spective	U.S.	2009-2013	Refractory cystoid macular edema due to retinal vein occlusion, initially treated with bevacizumab	Intravitreal dexamethasone, n=35	Intravitreal triamcinolone, n=39	12 w
Laine et al. (2017) (19)	Retro-spective	Finland	2011-2015	Treatment-naive cystoid macular edema due to retinal vein occlusion	Intravitreal dexamethasone, n=14	Intravitreal bevacizumab, n=121	12 w
Veritti et al. (2019) (20)	Pro-spective	Italy	2015-2016	Cystoid macular edema secondary to retinitis pigmentosa	Intravitreal dexamethasone, n=30	Oral acetazolamide 500 mg/day, n=30	12 mo

Mo: month; w: weeks; U.S.: United States.

Table 14. Summary of Key Comparative Observational Study Results: Dexamethasone versus Comparator

Study	BCVA	Central Retinal Thickness	IOP (mmHg)

Ozkok et al. (2016) (18)	Final: 0.36 vs. 0.36; p=.920	Final: 310.3 vs. 311.6; p=.962	IOP increase >6 mmHg or needed IOP decreasing drops: 20% vs. 25.6%; p=.462
Laine et al. (2017) (19)	3-month mean gain estimated from graph: 0.33 vs. 0.37; p-value NR, but described as not significantly different	3-month reduction estimated from graph: -150 vs. -200; p-value NR, but described as not significantly different	IOP ≥ 25 mmHg and elevation ≥ 5 mmHg from baseline: 2 (14%) vs. 0; p=.010
Veritti et al. (2019) (20)	+4.2 letters vs. +1.6 letters; p<.05	-327 µm vs. -180 µm; p< .001	Elevated IOP requiring topical treatment: 4 (13%) vs. 0; p=.11

BCVA: best-corrected visual acuity; IOP: intraocular pressure; NR: not reported; vs.: versus.

Noncomparative Observational Studies

Multiple case series have assessed improvements in visual acuity and anatomic changes following intravitreal dexamethasone implant (0.7 mg) in patients with cystoid macular edema of various etiologies. (21-25) However, these studies have generally included only small numbers of patients (N range of 26 to 112) and lacked responder analysis of clinically meaningful changes in outcomes. One exception is the case series by Fortoul et al. (2015), which evaluated the efficacy of the first intravitreal injection of dexamethasone implant in 26 eyes with cystoid macular edema secondary to retinal vein occlusion over 6 months in a single center in France. (24) Fortoul et al. (2015) reported that although 88% of patients achieved at least a 3-line improvement in best-corrected visual acuity 2 months, this was not sustained and only 27.8% of eyes still achieved clinically significant response at 6 months.

Section Summary: Cystoid Macular Edema

Evidence for this indication includes 1 observation controlled RCT (N=14), 3 comparative observational studies, and numerous case series. The RCT found improved mean visual acuity and eye anatomy outcomes with intravitreal dexamethasone compared to the control eyes, but these differences were not sustained at 6 months. The comparative observational studies included 269 patients (range, 60 to 135) and also lacked responder analysis of the proportion of patients with a 15-or-more letter improvement. One case series evaluated the proportion of patients with a 3-line improvement in best-corrected visual acuity. Although 88% of patients achieved this outcome at 2 months, the proportion with improvement was not sustained at 6 months (27.8%). Additional blinded, multicenter RCTs are needed that compare intravitreal dexamethasone to another established treatment. The trials should be adequately powered for measuring the proportion of patients in whom vision had improved by 15 letters or more.

Idiopathic Macular Telangiectasia Type 1

Case Reports

No RCTs were identified on the treatment of macular telangiectasia with any corticosteroid intravitreal implants. Three case reports with a total of 9 patients with type 1 idiopathic macular telangiectasia treated with dexamethasone implants have described mixed results on improvements in visual acuity and reduction in inflammation. (16, 26, 27)

Section Summary: Idiopathic Macular Telangiectasia Type 1

No RCTs were identified on the treatment of idiopathic macular telangiectasia type 1 with any corticosteroid intravitreal implants. Available evidence includes multiple case reports, which have noted mix results for visual acuity and inflammation-related outcomes. Long-term follow-up on efficacy and safety is limited. Better quality studies with long-term follow-up are needed to permit conclusions on the efficacy of corticosteroid implants inpatients with this indication.

Postoperative Chronic Macular Edema

Randomized Controlled Trials

Mylonas et al. (2017) published an RCT that compared dexamethasone intravitreal implant to triamcinolone intravitreal injection in 29 patients with refractory postoperative cystoid macular edema. (28) Key characteristics and results of Mylonas et al. (2017) are reported in Tables 15 and 16 below. Participants were mostly female (72%), and the mean age was 73 years in the dexamethasone group and 71 years in the triamcinolone group. No primary outcome was specified. There were no significant differences between the groups in improvement in mean best corrected visual acuity, but central millimeter retinal thickness reduction was significantly greater for triamcinolone at 1 week and 6 months. Minimal information on adverse events was reported.

Table 15. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Mylonas et al. (2017) (28)	Austria, Greece	2	Not reported	Refractory (minimum 3 months) macular edema, developing after cataract extraction or vitreoretinal surgery	Dexamethasone intravitreal implant, 0.7 mg	Triamcinolone intravitreal injection, 4 mg; retreatment after 3 months was dependent on functional and anatomic outcome

mg: milligram; RCT: randomized controlled trial.

Table 16. Summary of Key RCT Results

Study	BCVA	Central Millimeter Thickness	IOP
Mylonas et al. (2017) (28)	Mean (SD) at baseline, 1 mo, 3 mo, and 6 mo	Mean (SD) at baseline, 1 w, 1 mo, 3 mo, and 6 mo	Data not provided; "All cases of IOP elevation were managed readily by observation or topical pressure lowering medications and no glaucoma surgery was necessary"
Dexamethasone	60 (10), 72 (10), 72 (11), and 66 (13)	548 (110), 406 (72), 357 (69), 391 (102), and 504 (159)	
Triamcinolone	63 (13), 73 (11), 73 (11), and 71 (13)	516 (121), 350 (54) 355 (59), 389 (89), and 365 (74)	
p-value	>.05	≤.05 at 1 w and 6 mo	

BCVA: best corrected visual acuity; IOP: intraocular pressure; mo: month(s); RCT: randomized controlled trial; SD: standard deviation; w: week(s).

Tables 17 and 18 summarize the relevance and design and conduct limitations of Mylonas et al. (2017). (28)

Table 17. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Mylonas et al. (2017) (28)	1. Refractory was undefined; thus, the adequacy of the intensity and duration of the first- line therapy regimen is unclear			6. The proportion of patients in whom vision had improved by 15 letters or more was not reported	

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 18. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Complete-ness[d]	Power[e]	Statistical[f]
Mylonas et al. (2017) (28)	3. Allocation concealment unclear	1. All the examiners were unmasked to the injected medication used			2. Power not calculated for primary outcome	

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Comparative Observational Studies

Two observational studies have compared intravitreal dexamethasone to other treatments in patients with postoperative macular edema. (29, 30) Tables 19 and 20 summarize their key characteristics and results. However, these studies have included only small numbers of patients and lack responder analysis of the proportion of patients with a 15-or-more letter improvement from baseline in best-corrected visual acuity.

Table 19. Summary of Key Comparative Observational Study Characteristics

Study	Study Type	Country	Dates	Participants	Treat-ment 1	Treat-ment 2	Follow-Up
Dang et al. (2014) (29)	Prospective	China	2011 - 2013	Patients with diabetes and persistent PCME after 1-month of topical diclofenac and fixed-dose combination product of	Intravitreal dexamethasone, n=18	Intravitreal triamcinolone, n=25	6 mo

				tobramycin/ dexamethasone			
Guclu et al. (2019) (30)	Retrospective	Turkey	2013 - 2015	Previously untreated Irvine-Gass syndrome after phacoemulsification with posterior chamber intraocular lens implantation	Intravitreal dexamethasone, n=32	Topical nepafenac, n=30	6 mo

Mo: month(s); PCME: pseudophakic cystoid macular edema.

Table 20. Summary of Key Observational Comparative Study Results

Study	Improvement in BCVA	IOP (mmHg)	Other adverse events
Dang et al. (2014) (29)	Percentage of patients who gained improvements ≥ 10 ten letters: n=43	Mean change, n=43	% with conjunctival hemorrhage, n=43
Intravitreal dexamethasone	33%	+1.6	4/18 (22.2%)
Intravitreal triamcinolone	36%	+3.4	2/25 (8%)
p-value	.856	.006	.184
Guclu et al. (2019) (30)	Mean BCVA at baseline and 6 months (change), n=62	Mean at baseline and 6 months (change), n=62	Surgery-related complications (posterior capsule rupture, iridodialysis, vitreous incarceration, zonular dialysis)
Intravitreal dexamethasone	25 vs 49.3 (+24.3)	13.1 vs 14.9 (+1.8)	10/32 (31%)
Topical nepafenac	20.9 vs 32.9 (+12)	13.6 vs 13.6 (+0)	9/30 (30%)
p-value	.000	.184	NR

BCVA: best-corrected visual acuity; IOP: intraocular pressure; NR: not reported.

Case Series

Multiple case series have assessed improvements in visual acuity and anatomic changes. (31-38) However, these studies have included only small numbers of patients and reported mean pre-post changes in visual acuity and eye anatomy that lack responder analysis using clinically meaningful changes in outcomes. Effectiveness and safety of dexamethasone implants for postsurgical macular edema including Irvine-Glass syndrome (EPISODIC), a 2017 observational retrospective study conducted in France, included 100 patients with postsurgical macular edema who received dexamethasone implants between 2011 and 2014 and who had a

minimum of 1-year follow-up. (39) Mean improvement in best-corrected visual acuity was 9.6 Early Treatment Diabetic Retinopathy Study letters at month 6 and 10.3 at month 12. The proportions of eyes with gains in best-corrected visual acuity of 15 or more letters were 32.5% and 37.5% at months 6 and 12, respectively. The average reduction in central subfield macular thickness was 135.2 and 160.9 µm at months 6 and 12.

Section Summary: Postoperative Chronic Macular Edema

Evidence for this indication includes 1 RCT (N=29) that compared dexamethasone intravitreal implant, 0.7 mg to triamcinolone intravitreal injection 4 mg, 2 comparative observational studies, and numerous case series. The RCT found no statistically significant difference between treatments in mean visual acuity improvement at 3 or 6 months. The proportion of patients in whom vision had improved by 15 letters or more was not reported. The comparative observational studies included only small numbers of patients and also lack responder analysis of the proportion of patients with a 15-or-more letter improvement. In the largest case series (N=100), 2 of every 5 patients experienced clinically meaningful improvements in visual acuity after 1 year of follow-up. Additional RCTs are needed that have clearly defined and representative populations (i.e., for chronic and refractory patients, documentation of intensity and duration of the first-line therapy regimens) and are adequately powered for measuring the proportion of patients in whom vision had improved by 15 letters or more.

Circumscribed Choroidal Hemangioma

Case Reports

No RCTs were identified on the treatment of circumscribed choroidal hemangiomas with any corticosteroid intravitreal implants. A single case report (2012) has described the use of photodynamic therapy combined with dexamethasone implants. Authors concluded that implants potentiated the effect of photodynamic therapy with less risk of local side effects than triamcinolone acetonide. (40)

Section Summary: Circumscribed Choroidal Hemangiomas

No RCTs were identified on the treatment of circumscribed choroidal hemangiomas with any corticosteroid intravitreal implants. Available evidence includes a single case report that does not permit a conclusion on the efficacy and safety of adding dexamethasone implants to photodynamic therapy for the treatment of circumscribed choroidal hemangiomas. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in patients with this indication.

Proliferative Vitreoretinopathy

Case Series/Reports

No RCTs were identified on the treatment of proliferative vitreoretinopathy with any corticosteroid intravitreal implants. A case series (2017) of 5 patients with proliferative vitreoretinopathy has described the combined use of surgery, endolaser, and dexamethasone implants. (41) A case report (2013) found a benefit of dexamethasone implants in preventing proliferative vitreoretinopathy in a patient with a rhegmatogenous retinal detachment, who experienced improvements in visual acuity and retinal attachment 9 months postsurgery. (42)

Section Summary: Proliferative Vitreoretinopathy

No RCTs were identified on the treatment of proliferative vitreoretinopathy with any corticosteroid intravitreal implants. Available evidence includes a case series and a case report. These studies reported multiple interventions, including dexamethasone implants in conjunction with surgery and laser, for preventing proliferative retinopathy after retinal detachment surgery. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in patients with proliferative retinopathy.

Radiation Retinopathy

Retrospective Cohort Studies

No RCTs were identified on the treatment of radiation retinopathy with any corticosteroid intravitreal implants. In a retrospective study (2015), 12 eyes diagnosed with radiation maculopathy secondary to plaque brachytherapy were treated with dexamethasone implants. (43) Anatomic improvements in foveal thickness were reported, with nonsignificant improvements in visual acuity. In a 2014 retrospective case series, 2 patients who developed radiation maculopathy after radiotherapy for uveal melanoma were treated with dexamethasone implants. (44) They had limited responses to bevacizumab and intravitreal triamcinolone. Dexamethasone implants provided a prolonged period of anatomic stabilization. In a retrospective chart review of 5 patients with choroidal melanoma treated with dexamethasone implants for radiation macular edema, Baillif et al. (2013) reported mixed improvements in visual acuity. (45) The mean improvement in Early Treatment Diabetic Retinopathy Study letters was 5. Visual acuity improved for 3 patients (+4, +9, and +15 letters) and remained unchanged for 2.

Section Summary: Radiation Retinopathy

No RCTs were identified on the treatment of radiation retinopathy with any corticosteroid intravitreal implants. Available evidence includes multiple observational studies that noted improvements in anatomic stability and visual acuity. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in patients with radiation retinopathy.

Prophylaxis of Cystoid Macular Edema in Individuals with Noninfectious Intermediate Uveitis or Posterior Uveitis and Cataract Undergoing Cataract Surgery

Randomized Controlled Trials

For individuals with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery who receive prophylactic intravitreal dexamethasone implant (0.7 mg), the best evidence includes 1 single-center, open-label RCT of 43 patients in India (Table 21). (46) Compared with prophylaxis with systemic corticosteroids, intravitreal dexamethasone 0.7 mg led to similar rates of cystoid macular edema and change in best-corrected visual acuity and avoided the need for early steroid taper due to adverse effects on blood glucose, but potentially increased risk of developing intraocular pressure (Table 22). These findings should be interpreted with caution, however, to due important study limitations including its small sample size, unclear allocation concealment methods, and lack of blinding (Tables 23 and 24).

Table 21. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
Sudhalkar et al. (2019) (46)	India	1	2015-2016	≥ 18 years of age, previous unilateral recurrent noninfectious intermediate uveitis or posterior uveitis with CMO and cataract of sufficient degree to warrant surgery; well controlled uveitis for at least 3 months prior to scheduled date of cataract surgery	Intravitreal dexa-methasone 0.7 mg, n=20	Oral cortico-steroids, n=23

CMO: cystoid macular edema; mg: milligram; n: number; RCT: randomized controlled trial.

Table 22. Summary of Key RCT Results

Study	Development of CMO at 6 months	BCVA at 6 months	Developed ocular hypertension, n (%)	Required rapid taper of systemic steroids due to adverse blood glucose effects, n (%)
Sudhalkar et al. (2019) (46)	43	43	43	43
Intravitreal dexamethasone 0.7 mg	1 (5%)	0.04 logMAR	4 (20%)	0
Oral corticosteroids	2 (8%)	0.06 logMAR	0	3 (13%)
p-value	NR, but described as NSD	0.42	NR	NR

logMAR: Logarithm of the Minimum Angle of Resolution; mg: milligram; NR: not reported; NSD: not significantly different; CMO: cystoid macular edema; BCVA: best corrected visual acuity; RCT: randomized controlled trial.

Table 23. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Sudhalkar et al. (2018) (46)	4. Study population potentially had better prognosis than intended use				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps limitation assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not present.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 24. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Sudhalkar et al. (2018) (46)	3. Allocation concealment unclear	1. Not blinded				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps limitations assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Unclear blinding of outcome assessment.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat anal.

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Prophylaxis of Cystoid Macular Edema in Individuals With Noninfectious Intermediate Uveitis or Posterior Uveitis and Cataract Undergoing Cataract Surgery
For individuals with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery who receive intravitreal dexamethasone implant (0.7 mg), the best evidence includes 1 single-center, open-label RCT of 43 patients in India. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Compared with oral corticosteroids, intravitreal dexamethasone 0.7 mg had similar benefits and avoided the need for early steroid taper due to adverse effects on blood glucose, but potentially increased risk of developing intraocular pressure. Due to important study limitations including its small sample size, unclear allocation concealment methods and lack of blinding, conclusions cannot be drawn based on these findings.

Practice Guidelines and Position Statements
American Academy of Ophthalmology
In 2019, the American Academy of Ophthalmology (AAO) published its preferred Practice Pattern® for retinal vein occlusions. (47) The Academy stated: “Macular edema may complicate both central retinal vein occlusions and branch retinal vein occlusions. The first line of treatment for associated macular edema is anti-vascular endothelial growth factors. Intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy. Also, laser photocoagulation surgery in branch retinal vein occlusion has a potential role in treatment."

In 2019, AAO published its preferred Practice Pattern® for diabetic retinopathy. (48) Related to therapy with intravitreal corticosteroids, the Academy stated: "Because of their side-effect profile, including cataract progression and elevated IOP [intraocular pressure], they [intravitreal corticosteroids] are generally used as second-line agents for DME [diabetic macular edema], especially for phakic patients."

In 2019, AAO published its preferred Practice Pattern® for age-related macular degeneration. (49) Regarding intravitreal corticosteroid use, the Academy stated that the "data do not currently support the use of combination therapy with steroids, especially given the long-term side effects of glaucoma and cataract that are associated with corticosteroid use."

In 2023, AAO published its preferred Practice Pattern® for conjunctivitis. (50) The use of punctum corticosteroid implants was not mentioned as a treatment option for allergic conjunctivitis.

In 2024, AAO published an Ophthalmic Technology Assessment® evaluating the evidence for periocular and intraocular corticosteroid therapies for noninfectious uveitic macular edema. (51) The assessment reviewed 18 studies that provided level I or II evidence on the use of periocular, suprachoroidal, and intravitreal triamcinolone acetonide injections, as well as intravitreal dexamethasone and fluocinolone acetonide implants or inserts. The authors reported that study findings consistently demonstrated that all investigated corticosteroid therapies improved visual acuity, macular structure, or both. However, the studies also highlighted the potential for these therapies to elevate intraocular pressure and accelerate cataract formation.

National Institute for Health and Care Excellence (NICE)

In 2024, NICE released guidance on the use of fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien) for treating chronic diabetic macular edema that is insufficiently responsive to available therapies in an eye with a natural lens (phakic eye). (52) The NICE guidance states, "Fluocinolone acetonide intravitreal implant is recommended, within its marketing authorisation, as an option for treating visual impairment caused by chronic diabetic macular oedema that has not responded well enough to available treatments in adults." Furthermore, NICE states: "For people with the condition in an eye with a natural (phakic) lens, if the person and their clinicians consider fluocinolone acetonide intravitreal implant to be 1 of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, use the least expensive."

In 2019, NICE released guidance on the use of fluocinolone acetonide intravitreal implant for treating recurrent non-infectious uveitis. (53) The guidance stated, "Fluocinolone acetonide intravitreal implant is recommended, within its marketing authorisation, as an option for preventing relapse in recurrent non-infectious uveitis affecting the posterior segment of the eye."

In 2017, NICE released guidance on the use of dexamethasone intravitreal implant (with adalimumab) for the treatment of noninfectious uveitis. (54) NICE recommended the implant only in cases of “active disease” with “worsening vision” and the “risk of blindness.”

In 2011, NICE provided guidance on the use of the dexamethasone intravitreal implant for macular edema secondary to retinal vein occlusion. (55) The dexamethasone implant was recommended as an option for the treatment of macular edema following retinal vein occlusion. NICE also recommended it as an option for treating macular edema following branch retinal vein occlusion when treatment with laser photocoagulation has not been beneficial or suitable.

In 2022, NICE provided guidance on the dexamethasone intravitreal implant (Ozurdex) for treating diabetic macular edema. (56) Intravitreal dexamethasone implant was recommended as a possible treatment for patients with diabetic macular edema "only if their condition has not responded well enough to, or if they cannot have non-corticosteroid therapy." This recommendation is irrespective of whether patients have aphakic or pseudophakic lens.

In 2013, the NICE updated its guidance on the intravitreal fluocinolone acetonide implant (Iluvien), recommending it as an option for treating patients with chronic diabetic macular edema that is insufficiently responsive to available therapies only if "the implant is to be used in an eye with an intraocular [pseudophakic] lens and their diabetic macular oedema has not got better with other treatments." (52)

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 25.

Table 25. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT06539481	Open Label Trial Studying the Safety and Effectiveness of ILUVIEN® (190µg) in Children and Adolescents, Who Have Recurrent Non-infectious Uveitis Affecting the Posterior Segment of the Eye	25	Oct 2028
NCT06536491	EC-104 Intravitreal Implant for the Treatment of Diabetic Macular Edema (BETTIS-1)	75	Dec 2025
NCT05101928	Ozurdex as Monotherapy for Treatment of Non-infectious Intermediate, Posterior, or Panuveitis	84	Sept 2027
NCT04469595[a]	A Randomized, Masked, Controlled Study of Intravitreal ILUVIEN® Implant as Baseline Therapy in Patients With Early Diabetic Macular Edema (DME)	300	Dec 2024
NCT05003258	Functional and Anatomical Outcomes of Dexamethasone Intra-vitreal Implant in Patients With Resistant Macular Edema Secondary to Retinal Vein Occlusion After Intravitreal Anti-VEGF Injection	25	Oct 2024
Unpublished			
NCT01827722	Ozurdex® Versus Ranibizumab Versus Combination for Central Retinal Vein Occlusion	45	Dec 2016 (unknown)
NCT01998412[a]	An Open Label, Registry Study of the Safety of Iluvien® 190 Micrograms Intravitreal Implant in Applicator	559	Jan 2020 (unknown)
NCT02556424	Efficacy and Tolerance Comparison Between Subconjunctival Injection of Triamcinolone	114	Feb 2021

	and Intravitreal Implant of Dexamethasone for the Treatment of Inflammatory Macular Edema		
NCT02471651	Dexamethasone Intravitreal Implant (0.7mg) for the Treatment of Persistent Diabetic Macular Edema Following Intravitreal Anti-Vascular Endothelial Growth Factor Therapy	40	Oct 2018 (has results, but no peer-reviewed publication)
NCT02988882[a]	A Multi-Center, Randomized, Double-Masked, Vehicle Controlled Phase 3 Study Evaluating the Efficacy and Safety of OTX-DP for the Treatment of Chronic Allergic Conjunctivitis Using a Modified Conjunctival Allergen Challenge Model (CAC®)	86	Apr 2016 (has results, but no peer-reviewed publication)

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	67027, 67028, 68841, 0660T, 0661T
HCPCS Codes	J1096, J7311, J7312, J7313, J7314, J7351, J7355

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

1. U.S. Food and Drug Administration. Highlights of prescribing information: Durysta (bimatoprost intracameral implant) for intracameral administration. Nov 2020. Available at: <http://www.accessdata.fda.gov> (accessed October 13, 2025).
2. McKinney JK. Glaucoma. Understanding Glaucoma: Symptoms, causes, diagnosis, treatment. American Academy of Ophthalmology. Oct 29 2024. Available at: <http://www.aao.org> (accessed October 17, 2025).
3. Haller JA, Bandello F, Belfort R Jr., et al. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology. Jun 2010; 117(6):1134-1146.e1133. PMID 20417567

4. Haller JA, Bandello F, Belfort R, Jr., et al. Dexamethasone intravitreal implant in patients with macular edema related to branch or central retinal vein occlusion twelve-month study results. Ophthalmology. Dec 2011; 118(12):2453-2460. PMID 21764136
5. Durysta. A first-in-class, biodegradable, intracameral implant for IOP control. 2021. Available at: <https://www.durystahcp.com> (accessed October 16, 2025).
6. U.S. Food and Drug Administration. Highlights of prescribing information: Ozurdex (dexamethasone intravitreal implant). Oct 2020. Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).
7. U.S. Food and Drug Administration. Highlights of prescribing information: Iluvien (fluocinolone acetonide intravitreal implant) 0.19 mg. Nov 2016. Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).
8. U.S. Food and Drug Administration. Highlights of prescribing information: Retisert (fluocinolone acetonide intravitreal implant) 0.59 mg. Application number 21-737. May 2011. Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).
9. U.S. Food and Drug Administration. Highlights of prescribing information: Yutiq™ (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection. Application number 210331. Oct 2018. Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).
10. U.S. Food and Drug Administration. Highlights of prescribing information: Dextenza® (dexamethasone ophthalmic insert) 0.4mg for intracanalicular use. Oct 2021. Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).
11. U.S. Food and Drug Administration. Highlights of prescribing information: iDose® TR (travoprost intracameral implant). Dec 2023. Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).
12. Bajwa A, Aziz K, Foster CS. Safety and efficacy of fluocinolone acetonide intravitreal implant (0.59 mg) in birdshot retinochoroidopathy. Retina. Nov 2014; 34(11):2259-2268. PMID 24999722
13. Burkholder BM, Wang J, Dunn JP, et al. Postoperative outcomes after fluocinolone acetonide implant surgery in patients with birdshot chorioretinitis and other types of posterior and panuveitis. Retina. Sep 2013; 33(8):1684-1693. PMID 23549097
14. Rush RB, Goldstein DA, Callanan DG, et al. Outcomes of birdshot chorioretinopathy treated with an intravitreal sustained-release fluocinolone acetonide-containing device. Am J Ophthalmol. Apr 2011; 151(4):630-636. PMID 21277557
15. Srour M, Querques G, Leveziel N, et al. Intravitreal dexamethasone implant (Ozurdex) for macular edema secondary to retinitis pigmentosa. Graefes Arch Clin Exp Ophthalmol. Jun 2013; 251(6):1501-1506. PMID 23275039
16. Erdoğan G, Aydoğan T, Ünlü C, et al. Dexamethasone Implant for the Treatment of Type 1 Idiopathic Macular Telangiectasia. J Ocul Pharmacol Ther. May 2016; 32(4):211-215. PMID 26985700
17. Park UC, Park JH, Ma DJ, et al. A randomized pair-eye trial of intravitreal dexamethasone implant for cystoid macular edema in retinitis pigmentosa. Retina. Jul 2020; 40(7):1359-1366. PMID 31166248

18. Ozkok A, Saleh OA, Sigford DK, et al. THE OMAR STUDY: Comparison of Ozurdex and Triamcinolone Acetonide for Refractory Cystoid Macular Edema in Retinal Vein Occlusion. Retina. Jul 2015; 35(7):1393-1400. PMID 25748280
19. Laine I, Lindholm JM, Ylinen P, et al. Intravitreal bevacizumab injections versus dexamethasone implant for treatment-naïve retinal vein occlusion related macular edema. Clin Ophthalmol. 2017; 11:2107-2112. PMID 29225460
20. Veritti D, Sarao V, De Nadai K, et al. Dexamethasone Implant Produces Better Outcomes than Oral Acetazolamide in Patients with Cystoid Macular Edema Secondary to Retinitis Pigmentosa. J Ocul Pharmacol Ther. Apr 2020; 36(3):190-197. PMID 31886707
21. Donati S, Gandolfi C, Caprani SM, et al. Evaluation of the Effectiveness of Treatment with Dexamethasone Intravitreal Implant in Cystoid Macular Edema Secondary to Retinal Vein Occlusion. Biomed Res Int. 2018; 2018:3095961. PMID 30175123
22. Novais EA, Maia M, Filho PA, et al. Twelve-Month Follow-Up of Dexamethasone Implants for Macular Edema from Various Diseases in Vitrectomized and Nonvitrectomized Eyes. J Ophthalmol. 2016; 2016:7984576. PMID 27721989
23. Bansal P, Agarwal A, Gupta V, et al. Spectral domain optical coherence tomography changes following intravitreal dexamethasone implant, Ozurdex® in patients with uveitic cystoid macular edema. Indian J Ophthalmol. May 2015; 63(5):416-422. PMID 26139803
24. Fortoul V, Denis P, Kodjikian L. Anatomical and functional recurrence after dexamethasone intravitreal implants: a 6-month prospective study. Eye (Lond). Jun 2015; 29(6):769-775. PMID 25853447
25. Bezatis A, Spital G, Höhn F, et al. Functional and anatomical results after a single intravitreal Ozurdex injection in retinal vein occlusion: a 6-month follow-up -- the SOLO study. Acta Ophthalmol. Aug 2013; 91(5):e340-e347. PMID 23638803
26. Lei S, Lam WC. Efficacy and safety of dexamethasone intravitreal implant for refractory macular edema in children. Can J Ophthalmol. Jun 2015; 50(3):236-241. PMID 26040225
27. Loutfi M, Papathomas T, Kamal A. Macular oedema related to idiopathic macular telangiectasia type 1treated with dexamethasone intravitreal implant (Ozurdex). Case Rep Ophthalmol Med. 2014; 2014:231913. PMID 25045562
28. Mylonas G, Georgopoulos M, Malamos P, et al. Comparison of Dexamethasone Intravitreal Implant with Conventional Triamcinolone in Patients with Postoperative Cystoid Macular Edema. Curr Eye Res. Apr2017; 42(4):648-652. PMID 27612922
29. Dang Y, Mu Y, Li L, et al. Comparison of dexamethasone intravitreal implant and intravitreal triamcinolone acetonide for the treatment of pseudophakic cystoid macular edema in diabetic patients. Drug Des Devel Ther. 2014; 8:1441-1449. PMID 25258512
30. Guclu H, Pelitli Gurlu V. Comparison of topical nepafenac 0.1% with intravitreal dexamethasone implant for the treatment of Irvine-Gass syndrome. Int J Ophthalmol. 2019; 12(2):258-267. PMID 30809482
31. Klamann A, Böttcher K, Ackermann P, et al. Intravitreal Dexamethasone Implant for the Treatment of Postoperative Macular Edema. Ophthalmologica. 2016; 236(4):181-185. PMID 27915343
32. Sudhalkar A, Chhablani J, Vasavada A, et al. Intravitreal dexamethasone implant for recurrent cystoid macular edema due to Irvine-Gass syndrome: a prospective case series. Eye (Lond). Dec 2016; 30(12):1549-1557. PMID 27858937

33. Keilani C, Halalchi A, Wakpi Djeugue D, et al. Evaluation of best corrected visual acuity and central macular thickness after intravitreal dexamethasone implant injections in patients with Irvine-Gass syndrome: A retrospective study of six cases. Therapie. Oct 2016; 71(5):457-465. PMID 27203164
34. Mayer WJ, Kurz S, Wolf A, et al. Dexamethasone implant as an effective treatment option for macular edema due to Irvine-Gass syndrome. J Cataract Refract Surg. Sep 2015; 41(9):1954-1961. PMID 26603404
35. Landré C, Zourdani A, Gastaud P, et al. [Treatment of postoperative cystoid macular edema (Irvine-Gass syndrome) with dexamethasone 0.7 mg intravitreal implant]. J Fr Ophtalmol. Jan 2016; 39(1):5-11. PMID 26520410
36. Degoumois A, Akesbi J, Laurens C, et al. [Efficacy of intravitreal dexamethasone implants in macular edema excluding venous occlusions: results for a cohort of 80 patients]. J Fr Ophtalmol. Feb 2015; 38(2):126-133. PMID 25592383
37. Dutra Medeiros M, Navarro R, Garcia-Arumí J, et al. Dexamethasone intravitreal implant for treatment of patients with recalcitrant macular edema resulting from Irvine-Gass syndrome. Invest Ophthalmol VisSci. May 07 2013; 54(5):3320-3324. PMID 23599334
38. Freissinger S, Vounotrypidis E, Wolf A, et al. Evaluation of Functional Outcomes and OCT-Biomarkers after Intravitreal Dexamethasone Implant for Postoperative Cystoid Macular Edema in Vitrectomized Eyes. J Ophthalmol. 2020; 2020:3946531. PMID 32411428
39. Bellocq D, Pierre-Kahn V, Matonti F, et al. Effectiveness and safety of dexamethasone implants for postsurgical macular oedema including Irvine-Gass syndrome: the EPISODIC-2 study. Br J Ophthalmol. Mar 2017; 101(3):333-341. PMID 27190126
40. Bazin L, Gambrelle J. [Combined treatment with photodynamic therapy and intravitreal dexamethasone implant (Ozurdex®) for circumscribed choroidal hemangioma]. J Fr Ophtalmol. Dec 2012; 35(10):798-802. PMID 23040445
41. Sherif M, Wolfensberger TJ. Intraocular Dexamethasone Implant as Adjunct to Silicone Oil Tamponade for Proliferative Vitreoretinopathy. Klin Monbl Augenheilkd. Apr 2017; 234(4):501-504. PMID 28147403
42. Reibaldi M, Russo A, Longo A, et al. Rhegmatogenous Retinal Detachment with a High Risk of Proliferative Vitreoretinopathy Treated with Episcleral Surgery and an Intravitreal Dexamethasone 0.7-mg Implant. Case Rep Ophthalmol. Jan 2013; 4(1):79-83. PMID 23687501
43. Caminal JM, Flores-Moreno I, Arias L, et al. Intravitreal dexamethasone implant for radiation maculopathy secondary to plaque brachytherapy in choroidal melanoma. Retina. Sep 2015; 35(9):1890-1897. PMID 26035401
44. Bui KM, Chow CC, Mieler WF. Treatment of recalcitrant radiation maculopathy using intravitreal dexamethasone (Ozurdex) implant. Retin Cases Brief Rep. 2014; 8(3):167-170. PMID 25372430
45. Baillif S, Maschi C, Gastaud P, et al. Intravitreal dexamethasone 0.7-mg implant for radiation macular edema after proton beam therapy for choroidal melanoma. Retina. Oct 2013; 33(9):1784-1790. PMID23652581
46. Sudhalkar A, Vasavada A, Bhojwani D, et al. Intravitreal dexamethasone implant as an alternative to systemic steroids as prophylaxis for uveitic cataract surgery: a randomized trial. Eye (Lond). Mar 2020; 34(3):491-498. PMID 31320735

47. Flaxel CJ, Adelman RA, Bailey ST, et al. Retinal Vein Occlusions Preferred Practice Pattern®. Ophthalmology. Feb 2020; 127(2):P288-P320. PMID 31757503
48. Flaxel CJ, Adelman RA, Bailey ST, et al. Diabetic Retinopathy Preferred Practice Pattern®. Ophthalmology. Jan 2020; 127(1):P66-P145. PMID 31757498
49. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-Related Macular Degeneration Preferred Practice Pattern®. Ophthalmology. Jan 2020; 127(1):P1-P65. PMID 31757502
50. Cheung AY, Choi DS, Ahmad S, et al. Conjunctivitis Preferred Practice Pattern. Ophthalmology. Apr2024; 131(4):P134-P204. PMID 38349304
51. Smith JR, Thorne JE, Flaxel CJ, et al. Treatment of Noninfectious Uveitic Macular Edema with Periocular and Intraocular Corticosteroid Therapies: A Report by the American Academy of Ophthalmology. Ophthalmology. Sep 2024; 131(9):1107-1120. PMID 38647511
52. National Institute for Health and Care Excellence (NICE). Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema [TA953] 2024; Available at: <https://www.nice.org.uk> (accessed October 17, 2025).
53. National Institute for Health and Care Excellence (NICE). Fluocinolone acetonide intravitreal implant for treating recurrent non-infectious uveitis Technology appraisal guidance [TA590] 2019. Available at: <https://www.nice.org.uk> (accessed October 17, 2025).
54. National Institute for Health and Care Excellence (NICE). Adalimumab and dexamethasone for treating non- infectious uveitis [TA460] 2017. Available at: <https://www.nice.org.uk> (accessed October 17, 2025).
55. National Institute for Health and Care Excellence (NICE). Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion [TA229] 2011. Available at: <https://www.nice.org.uk> (accessed October 17, 2025).
56. National Institute for Health and Care Excellence (NICE). Dexamethasone intravitreal implant for treating diabetic macular oedema [TA824]. 2022. Available at: <https://www.nice.org.uk> (accessed October 17, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
01/01/2026	Document updated. The following changes were made to Coverage: Under Iluvien: added “The treatment of chronic non-infectious uveitis affecting the

	posterior segment of the eye" as medically necessary. Under Dextenza: Added "in adults and pediatric individuals" to the medically necessary coverage statements; added "A punctum dexamethasone ophthalmic insert for intracanalicular use 0.4 mg (e.g., Dextenza®) is considered not medically necessary for the treatment of ocular itching associated with allergic conjunctivitis in pediatric individuals who require sedation for the insertion procedure." Added reference 49; others updated, some removed.
07/01/2024	Document updated with literature review. The following change was made to Coverage: Added "A travoprost implant for intracameral administration (e.g., iDose® TR) may be considered medically necessary in adult patients with open angle glaucoma (OAG) or ocular hypertension (OHT) when: Patient has had a trial and failure or intolerance to at least two intraocular pressure-lowering eye-drop agents with different mechanisms of action, and one of which must include a prostaglandin analog (e.g., bimatoprost, latanoprost, travoprost, or tafluprost); AND the affected eye has not received prior treatment with an intracameral travoprost implant. All other uses of a travoprost implant for intracameral administration (e.g., iDose® TR) are considered experimental, investigational and/or unproven.
09/15/2023	Reviewed. No changes.
12/01/2022	Document updated with literature review. The following changes were made in Coverage: 1) Retisert: expanded the existing medically necessary statement to include" uveitis affecting the posterior segment of the eye"; 2) Dextenza: Expanded the medically necessary coverage statement to include use "in the treatment of ocular itching associated with allergic conjunctivitis." Added references 5, 7, 10, 23, 32, 33, 39, 47, 56-60, 62-66, 69-73, 81, 93; others updated, some removed.
09/15/2021	Reviewed. No changes.
10/01/2020	Document updated with literature review. The following Changes were made in Coverage: 1) Retisert: a) Added "in patients 12 years of age or older" to the medically necessary coverage statement and "viral, bacterial, mycobacterial and fungal infections of ocular structures" to the not medically necessary statement; 2) Iluvein: Expanded medically necessary coverage to state "adult patients" and " (or had the rise in IOP adequately treated prior to placement of the implant)"; 3) Yutiq: a) Added medically necessary statement "in adult patients for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye"; b) Added "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 to the not medically necessary statement. 4) Expanded the experimental, investigational and/or unproven statement to a) include **"**Yutiq" as a type of fluocinolone acetonide intravitreal implant; and b) Added "Prophylaxis of cystoid macular edema in patients with noninfectious

	intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery"; 5) Ozurdex: a) Added "in adult patients" to the medically necessary criteria; b) Added "Prophylaxis of cystoid macular edema in patients with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery" to the experimental, investigational and/or unproven statement. 6) Dextenza: a) Added may be considered medically necessary in adult patients for the treatment of ocular inflammation and pain following ophthalmic surgery; b) Added not medically necessary statement for patients with active corneal, conjunctival or canalicular infections. c) Added "All other uses of a dexamethasone ophthalmic insert 0.4 mg (e.g., Dextenza®) are considered experimental, investigational and/or unproven". 7) Added conditional coverage for bimatoprost implant for intracameral administration (e.g., Durysta®). Added references 16, 17, 23-25, 35-39, 47-49, 69-76, and 81-82. Title changed from "Intravitreal Corticosteroid Implants".
06/15/2018	Reviewed. No changes.
01/01/2018	Document updated with literature review. The following was added to Coverage: 1) Added individual doses to the Retisert®, Iluvien® and Ozurdex™ coverage statements 2) Added medically necessary coverage for intravitreal implant when used according to the FDA approved indications as an alternative in patients who are intolerant or refractory to other therapies or in patients who are likely to experience severe adverse events from systemic corticosteroids. 3) Not medically necessary coverage was added for fluocinolone acetonide intravitreal implant 0.59 mg (e.g., Retisert®) for patients with active ocular or periocular infections. 4) Not medically necessary coverage was added for fluocinolone acetonide intravitreal implant 0.19 mg (e.g., Iluvein®) for patients with active ocular or periocular infections or in patients with glaucoma with a cup to disc ratio of greater than 0.8. 5) Not medically necessary coverage was added for dexamethasone intravitreal implant (e.g., Ozurdex™) for patients with ocular or periocular infections (viral, bacterial, or fungal), advanced glaucoma with a cup to disc ratio of greater than 0.8. or torn or ruptured posterior lens capsule. 6) Added experimental, investigational and/or unproven coverage statement for the following conditions: Birdshot retinochoroidopathy; Cystoid macular edema related to retinitis pigmentosa; Idiopathic macular telangiectasia type 1; Postoperative macular edema; Circumscribed choroidal hemangiomas; Proliferative vitreoretinopathy; Radiation retinopathy and for the use of dexamethasone intravitreal implant (e.g., Ozurdex™) combined with cataract surgery for the treatment of cataract and macular edema.
07/15/2016	Reviewed. No changes.
04/01/2015	Document updated with literature review. The following was added to Coverage: 1) clarification that implants must be approved by the FDA, 2) ILUVIEN®, a fluocinolone acetonide intravitreal implant approved by the

	FDA, may be considered medically necessary for the treatment of diabetic macular edema in patients who have been previously treated with a course of corticosteroids without a clinically significant rise in intraocular pressure.
11/15/2014	Document updated with literature review. The following was added to Coverage: Dexamethasone intravitreal implant approved by FDA (i.e., Ozurdex™) may be considered medically necessary for the treatment of diabetic macular edema.
10/15/2014	Document updated with literature review. The following was added to Coverage: Dexamethasone intravitreal implant approved by FDA (i.e., Ozurdex™) may be considered medically necessary for the treatment of diabetic macular edema in patients who are pseudophakic or are phakic and scheduled for cataract surgery.
07/15/2013	Document updated with literature review. Coverage unchanged; however, statement for fluocinolone acetonide implant was clarified that "posterior uveitis" is of the "posterior segment, including intermediate and posterior uveitis, and panuveitis."
12/01/2011	Document updated with literature review. Coverage now states: 1)A fluocinolone acetonide intravitreal implant approved by the U.S. Food and Drug Administration (i.e., Retisert®) may be considered medically necessary for the treatment of chronic noninfectious posterior uveitis; 2) A dexamethasone intravitreal implant approved by the U.S. Food and Drug Administration (i.e., Ozurdex™) may be considered medically necessary for the treatment of: a) non-infectious ocular inflammation, or uveitis, affecting the posterior segment of the eye, OR b) macular edema following branch or central retinal vein occlusion; c) All other uses of a corticosteroid intravitreal implant are considered experimental, investigational and unproven including but not limited to the treatment of diabetic macular edema. In addition, the policy title was changed from Intravitreal Implants.
06/15/2011	New Medical Document. 1) A fluocinolone acetonide intravitreal implant (e.g., Retisert™) may be considered medically necessary for the treatment of chronic noninfectious posterior uveitis, in one or both eyes, in patients who are intolerant of, refractory to, or not a candidate for systemic corticosteroids. All other indications are considered experimental, investigational and unproven. 2) A dexamethasone intravitreal implant (e.g., Ozurdex®) may be considered medically necessary for the treatment of macular edema with any one of the following: a) Post branch retinal vein occlusion (BRVO), or b) Post central retinal branch occlusion (CRVO). All other indications are considered experimental, investigational and unproven