

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member's contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider a fluocinolone acetonide intravitreal implant 0.59 mg (Retisert[®])^{\ddagger} for the treatment of chronic non-infectious intermediate uveitis, posterior uveitis, or panuveitis to be **eligible for coverage.****

Based on review of available data, the Company may consider a fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien[®])[‡] for the treatment of diabetic macular edema in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure to be **eligible for coverage.****

Based on review of available data, the Company may consider a fluocinolone acetonide intravitreal implant 0.18 mg $(\text{Yutiq}^{\text{TM}})^{\ddagger}$ for the treatment of chronic non-infectious intermediate uveitis, posterior uveitis, or panuveitis to be **eligible for coverage.****

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member's contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider a dexamethasone intravitreal implant 0.7 mg (Ozurdex^{$^{\text{M}}$})[‡] to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for a dexamethasone intravitreal implant 0.7 mg (Ozurdex) will be considered when ONE of the following criteria are met:

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross Blue Shield Association. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

- Patient has non-infectious ocular inflammation, or uveitis, affecting the intermediate or posterior segment of the eye, OR
- Patient has macular edema following branch or central retinal vein occlusion, OR
- Patient has diabetic macular edema

Based on review of available data, the Company may consider a triamcinolone suprachoroidal injection 4 mg (XipereTM)[‡] to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for a triamcinolone suprachoroidal injection 4 mg (Xipere) will be considered when ALL of the following criteria are met:

- Patient has non-infectious anterior-, intermediate-, posterior-, or pan-uveitis; AND
- Patient has macular edema associated with non-infectious uveitis; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) triamcinolone intravitreal injections 4 mg (Triesence[®])[‡] unless there is clinical evidence or patient history that suggests the use of this alternative product will be ineffective or cause an adverse reaction to the member; AND

(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)

• Dosing does not exceed 4 mg every 12 weeks per impacted eye.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of triamcinolone suprachoroidal injection 4 mg (Xipere) when the patient has NOT tried and failed (e.g., intolerance or inadequate response) triamcinolone intravitreal injections 4 mg (Triesence) to be **not medically necessary****.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers a fluocinolone acetonide intravitreal implant 0.59 mg (Retisert) or 0.19 mg (Iluvien) or 0.18 mg (Yutiq) OR dexamethasone intravitreal implant 0.7 mg (Ozurdex) OR triamcinolone suprachoroidal injection 4 mg (Xipere) when treating the following conditions, to be **investigational***

- Age-Related Macular Degeneration
- Birdshot retinochoroidopathy
- Cystoid macular edema related to retinitis pigmentosa
- Idiopathic macular telangiectasia type 1
- Postoperative macular edema
- Circumscribed choroidal hemangiomas

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

- Proliferative vitreoretinopathy
- Radiation retinopathy

Based on review of available data, the Company considers all other uses of corticosteroid intravitreal implants to be **investigational.***

Based on review of available data, the Company considers all other uses of triamcinolone suprachoroidal injection 4 mg (Xipere) to be **investigational.***

Background/Overview

It should be noted that the dosages reflected in this policy for these products are total doses per administration. The HCPCS codes representing the drugs are typically not indicative of the total dose, but are actually a factor of the dose.

INTRAVITREAL IMPLANTS

Intravitreal implants deliver a continuous concentration of drug to the eye over a prolonged period. Intravitreal corticosteroid implants are being studied for a variety of eye conditions that lead to macular edema, including uveitis, diabetic retinopathy, and retinal venous occlusions. The goal of therapy is to reduce inflammation in the eye while minimizing the adverse effects 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 effects such as hypertension and osteoporosis, while repeated (every 4-6 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, 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 potentially 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.

Policy #	00549	
Original E	Effective Date:	04/19/2017
Current E	ffective Date:	06/01/2025

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 $0.4 \mu g/d$ 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 an inserter with a 25-gauge needle. 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.
- Yutiq (non-biodegradable fluocinolone acetonide intravitreal implant, EyePoint Pharmaceuticals) contains 0.18 mg fluocinolone acetonide, designed to release 0.25 μ g/d consistently over 36 months.

SUPRACHOROIDAL INJECTIONS

Xipere is the only medication currently approved by FDA for suprachoroidal use. A patented suprachoroidal space (SCS) microinjector syringe and 900 micrometer needle is supplied to access the suprachoroidal space. Injection into the SCS delivers drug to the choroid and retina. An alternative to this product is Triesence, which is a 4 mg triamcinolone intravitreal injection approved for sympathetic ophthalmia, temporal arteritis, uveitis, and ocular inflammatory conditions unresponsive to topical corticosteroids. Triesence is also approved for visualization during vitrectomy. These two products have not been studied head-to-head, therefore no superiority claims can be made. Triesence provides an economically sensible option to provide the same corticosteroid product and dosage for the requested condition.

The suprachoroidal corticosteroid injection being evaluated is Xipere (Clearside Biomedical). It is a 4 mg triamcinolone containing injection. Its effects last 12 weeks.

EYE CONDITIONS

Uveitis

Uveitis encompasses various conditions, of infectious and non-infectious etiologies, that are characterized by inflammation of any part of the uveal tract of the eye (iris, ciliary body, choroid).

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Infectious etiologies include syphilis, toxoplasmosis, cytomegalovirus retinitis, and candidiasis. Non-infectious 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. Uveitis can be associated with a variety of complications, including band keratopathy, posterior synechiae, cataracts, intraocular hypertension, and macular edema.

The classification scheme recommended by the Uveitis Study Group and the Standardization of Uveitis Nomenclature (SUN) 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, 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 and glaucoma and to structural damage to the eye, resulting in severe and permanent vision loss.

The primary goal of therapy for uveitis is to preserve vision. Non-infectious 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 (CRVO) and branch retinal vein occlusion (BRVO) differ in pathophysiology, clinical course, and therapy. CRVOs are categorized as ischemic or nonischemic. Ischemic CRVOs are referred to as severe, complete, or total vein obstruction, and account for 20% to 25% of all CRVOs. Macular edema and permanent macular dysfunction occur in virtually all patients with ischemic CRVO, and in many patients with nonischemic CRVO. Intravitreal injections of triamcinolone are used to treat macular edema associated with CRVO, 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.

BRVO is a common retinal vascular disorder in adults between 60 and 70 years of age and occurs approximately 3 times more often than CRVO. Macular photocoagulation with grid laser improves vision in BRVO but is not recommended for CRVO. Although intravitreal injections of

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

triamcinolone have also been used for BRVO, the serious adverse effects have stimulated the evaluation of new treatments, including intravitreal steroid implants or the intravitreal injection of anti-vascular 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 (non-proliferative retinopathy), microaneurysms occur. As the disease progresses, blood vessels that provide nourishment to 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 non-proliferative 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.

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 an 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 (AMD) is a degenerative disease of retina that results in loss of central vision with increasing age. Two distinctively 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 (CNV), which greatly increases the risk of developing severe irreversible loss of vision. CNV is categorized as classic or occult. Effective specific therapies for exudative or wet AMD are intravitreous injection of a vascular endothelial growth factor inhibitor, possibly thermal laser photocoagulation (in selected patients), and photodynamic therapy.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In June 2009, Ozurdex (dexamethasone 0.7 mg intravitreal implant; Allergan) was approved by 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 non-infectious uveitis affecting the posterior segment of the eye. In June 2014, the indication was again expanded to include treatment of diabetic macular edema.

In September 2014, Iluvien (fluocinolone acetonide 0.19 mg intravitreal implant; Alimera Sciences) was approved by FDA for the treatment of diabetic macular edema in patients previously treated with a course of corticosteroids and without a clinically significant rise in intraocular pressure.

In November 2014, Retisert (fluocinolone acetonide 0.59 mg intravitreal implant; Bausch & Lomb) was approved by FDA for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

In October 2018, Yutiq (fluocinolone acetonide 0.18 mg intravitreal implant; EyePoint Pharmaceuticals) was approved by FDA for the treatment of chronic non-infectious uveitis affecting the posterior segment (intermediate, posterior, and panuveitis) of the eye.

In October 2021, Xipere (triamcinolone acetonide 0.4 mg suprachoroidal injection; Clearside Biomedical) was approved by FDA for the treatment of macular edema associated with uveitis.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

INTRAVITREAL IMPLANTS <u>NON-INFECTIOUS UVEITIS</u> <u>Intravitreal Fluocinolone Acetonide Implant (0.59 mg)-Retisert</u>

Pivotal Trials

Two double-blind, randomized trials were conducted in patients with chronic (\geq 1-year history) noninfectious uveitis affecting the posterior segment of 1 or both eyes. The primary efficacy end point in both trials was the rate of recurrence of uveitis. These trials randomized patients to a fluocinolone acetonide 0.59-mg or to 2.1-mg implant. In 2004, the FDA approved only the 0.59-mg dose and its approval was based on comparison of rates of recurrence of uveitis affecting the posterior segment

Policy #	00549	
Original I	Effective Date:	04/19/2017
Current E	ffective Date:	06/01/2025

of the study eye in the 34-week period post-implantation compared to the rates of recurrence in the 34-week period pre-implantation. Data from 224 patients were included. Subsequently, FDA reported recurrence rates 1, 2, and 3 years post-implantation. Results are summarized in Table 1.

Table 1. Summary of Results From FDA Pivotal Trial in Non-infectious Posterior Uveitis					
	Uveitis Recurrence Rates, n (%) ^{a,b}				
Time Point	Study 1 (n=108)	Study 2 (n=116)			
34 weeks pre-implant	58 (53.7%)	46 (39.7%)			
34 weeks post-implant	2 (1.8%)	15 (12.9%)			
1 year post-implant	4 (3.7%)	15 (12.9%)			
2 year post-implant	11 (10.2%)	16 (13.8%)			
3 year post-implant	22 (20.4%)	20 (17.2%)			
3 year post-implant ^c	33 (30.6%)	28 (24.1%)			

FDA: Food and Drug Administration.

^a Recurrence of uveitis for all post-implantation time points was compared to the 34-week preimplantation time point.

^b P<0.01.

^c Results presented include imputed recurrences. Recurrences were imputed when a subject was not seen within 10 wk of his or her final scheduled visit.

Results of 1 of the 2 pivotal trials were reported by Jaffe et al (2006). These trials are not discussed in detailed because the comparator was a nonapproved dose of fluocinolone acetonide. Briefly, the 2 trials randomized 278 patients and 239 patients to a fluocinolone acetonide 0.59-mg or 2.1-mg implant, respectively. Pooled data from both doses in the first trial showed a reduction in recurrence rates in implanted eyes compared with an increase in recurrence in nonimplanted eyes. An increase (≈ 6 mm Hg) in intraocular pressure (IOP) and cataracts were observed in implanted eyes compared to nonimplanted eyes. The second trial was not published, and results reported in FDA documents are similar to the first trial.

Additional Randomized Controlled Trials (RCTs)

Pavesio et al (2010) reported results of an industry-sponsored, open-label trial in which 140 patients with chronic non-infectious posterior uveitis were randomized to the fluocinolone acetonide 0.59mg implant (n=66) or systemic corticosteroid therapy (and immunosuppression when indicated; n=74). To be included in the trial, subjects had to have at least a 1-year history of recurrent uveitis. The primary efficacy outcome was time to first recurrence of uveitis. Patients in whom tapering of adjunctive anti-inflammatory therapy was insufficient despite receiving the implant were referred to as imputed or inferred failures. Results were therefore presented as both true recurrences and true plus inferred recurrences. When inferred recurrences were censored (11 subjects removed from the at-risk population), Kaplan-Meier analysis showed a significant decrease in the time to uveitis recurrence (6.3 months for 12 failures vs 7.0 months for 44 failures). When all subjects were included in the analysis, time to uveitis recurrence did not differ statistically (p=0.07). The relative risk (RR)

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

of recurrence of uveitis was reduced by 71% with implants compared to standard therapy (RR=0.29; 95% confidence interval [CI], 0.14 to 0.59; 132 eyes). Secondary efficacy outcomes included visual acuity improvement. Visual acuity in the implant group decreased after the surgery and again in the 15- to 18-month interval as a result of cataracts, then returned to baseline levels at 24 months, following extraction of the cataracts. Visual acuity in the systemic corticosteroid group remained consistent over the 2-year study.

The MUST Trial, sponsored by the National Eye Institute, is a partially blind RCT (N=255) designed to compare visual acuity at 2 years with fluocinolone acetonide implants to systemic corticosteroid therapy (and immunosuppression when indicated) in patients with intermediate, posterior, or panuveitis.8 Assessment of the primary outcome measure of best-corrected visual acuity (BCVA) using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart was blinded. After 24 and 54 months of follow-up, the vision improvement from baseline in the implant groups compared to systematic therapy group was not statistically significant (+6.0 and +3.2 letters, p=0.16; +2.4 and 3.1 letters; p=0.073, respectively). Notably, approximately 21% of patients in the systemic group had received an implant by 54 months. At 24 and 54 months, the proportion of patients with a minimally important improvement did not differ significantly for any of the quality of life metrics (results not shown). Patients receiving systemic therapy (in which corticosteroid-sparing immunosuppressive therapy was used to minimize ongoing use of prednisone to <10 mg/d for the large majority of patients) was associated with relatively little additional systemic morbidity compared with implant therapy. Systemic adverse events were infrequent in both groups. At 2 years, the proportion of patients with systolic blood pressure greater than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg at any visit was lower in the implant group than in the systemic group (13% vs 27%; hazard ratio [HR], 0.44; p=0.030), but the rate of antihypertensive treatment initiation did not differ substantially between the 2 groups (5% vs 11%; hazard ratio [HR], 0.40; p=0.13), respectively. The incidences of other adverse systemic outcomes, including hyperlipidemia, diabetes, osteoporosis, fractures, and blood count/chemistry abnormalities, were not statistically distinguishable between groups (data not shown). Weight was stable over time in both groups.

Systematic Reviews

Brady et al (2016) reported results of a Cochrane review of RCTs comparing fluocinolone acetonide or dexamethasone intravitreal implants with standard therapy with at least 6 months of follow-up posttreatment. The primary outcome was recurrence of uveitis. Included trials enrolled patients of all ages who had chronic non-infectious posterior uveitis, intermediate uveitis, or panuveitis with vision that was "better than hand motion." Two trials, Pavesio et al (2010) and Kempen et al (2011), were included and judged to be of moderate quality (both are discussed above). Because the 2 studies were designed to answer different questions (1 measured recurrence, 1 visual acuity), reviewers did not combine efficacy data. However, they did perform a meta-analysis of common side effects, which showed increased risks of needing cataract surgery (RR=2.98; 95% CI, 2.33 to 3.79; 371 eyes)

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

and surgery to lower IOP (RR=7.48; 95% CI, 3.94 to 14.19; 599 eyes) in the implant group compared with the standard therapy group through 2 years of follow-up. Reviewers were unable to conclude that the implants were superior to traditional systemic therapy for the treatment of non-infectious uveitis.

Subsection Summary: Intravitreal Fluocinolone Acetonide Implant (0.59 mg) for Non-infectious Uveitis

Four RCTs have established the efficacy of fluocinolone acetonide implants (0.59 mg) for patients with non-infectious intermediate or posterior uveitis. Two of the 4 RCTs compared 2 doses of implants and 2 trials compared implants with systemic steroids (and immunosuppression when indicated). All trials supported the efficacy of fluocinolone acetonide intravitreal implants in preventing recurrence and improving vision over a 4-year follow-up. The head-to-head trial comparing implants with systemic corticosteroids did not show substantial superiority in the overall effectiveness of either approach. The major limitation of these implants is nearly all phakic patients will develop cataracts and will require cataract surgery. Further, most will also develop glaucoma, with 75% patients requiring IOP-lowering medications and 35% requiring filtering surgeries.

Intravitreal Dexamethasone Implant (0.7 mg)-Ozurdex

The evidence for dexamethasone intravitreal implants consists of 1 pivotal, double-blind RCT (HURON). In this 8-week, manufacturer-sponsored, multicenter trial (46 study sites in 18 countries), 229 patients with non-infectious intermediate or posterior uveitis were randomized to 0.7-mg implants (n=77), 0.35-mg implants (n=76), or sham procedure (n=76). The primary outcome measure was the proportion of eyes with a vitreous haze score of 0 (0 = no inflammation) at week 8. At baseline, the mean vitreous haze score was approximately +2 (moderate blurring of the optic nerve head). At 8 weeks posttreatment, the proportion of eyes with a vitreous haze score of 0 was 47% with the 0.7-mg implant and 12% with the sham procedure. At 8 weeks, visual acuity, as assessed by gain of 15 or more letters in BCVA from baseline, was achieved by 40% of patients who received implants compared to 10% who received sham control. The incidences of elevated IOP (≥25 mm Hg) and cataracts in phakic eyes were higher in 0.7-mg implant-treated eyes versus sham control eyes (7.1% vs 4.2% and 15% vs 7%, respectively). Unlike the fluocinolone acetonide 0.59mg implant, the long-term efficacy and safety data for the dexamethasone 0.7-mg implant is not available. Lightman et al (2013) reported 26-week data for vision-related functioning using National Eye Institute-Visual Function Questionnaire (NEI-VFQ) from HURON trial. Using the distributionand anchor-based methods, the authors reported that a clinically meaningful change for the NEI VFQ-25 composite score was 3.86 and 10 points, respectively. Others have reported that range changes of 2.3 to 3.8 units in the composite score are meaningful. In the HURON trial, the proportion of patients with a 5 or more point improvement in composite score at week 26 was 58% (42/73) in the 0.7-mg implant group versus 32% (24/74) in the sham-controlled arm (p<0.05).

Subsection Summary: Intravitreal Dexamethasone Implant (0.7 mg) for Non-infectious Uveitis

One RCT comparing 2 doses of implants with sham-control has supported the efficacy of dexamethasone implants (0.7 mg) for patients with non-infectious intermediate or posterior uveitis.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Results of this trial have demonstrated the efficacy of the dexamethasone 0.7-mg implant in reducing inflammation and resulted in clinically meaningful improvements in vision at week 8 compared to sham controls. Further, at week 26, patients treated with implants reported meaningful improvements in vision-related functioning. The major limitation of this trial was its lack of long-term follow-up. Further, as a class effect, use of dexamethasone implants resulted in higher incidences of cataracts and elevated IOP.

Intravitreal Fluocinolone Implant (0.18) mg- Yutiq

For individuals with chronic (\geq 1-year history) noninfectious uveitis affecting the posterior segment of one or both eyes who receive fluocinolone acetonide (0.18 mg), the pivotal evidence includes 2 double-blind, randomized trials of 282 patients (range, 129 to 153): A Phase III, Multi-National, Multi-Center, Randomized, Masked, Controlled, Safety and Efficacy Study of a Fluocinolone Acetonide Intravitreal Insert in Subjects With Chronic Non-Infectious Uveitis Affecting the Posterior Segment of the Eye (study #PSV-FAI-001) and A Multi-center, Controlled, Safety and Efficacy Study of a Fluocinolone Acetonide Intravitreal (FAI) Insert in Subjects With Chronic Noninfectious Uveitis Affecting the Posterior Segment of the Eye (study #PSV-FAI-005). Results of 1 of the pivotal trials (study #PSV-FAI-001) were reported by Jaffe et al (2019). The second trial was reported only in FDA documents. The primary efficacy endpoint in both trials was the proportion of recurrence of uveitis within 6 months. Secondary outcomes at 12 months have also been reported.

For the primary outcome of recurrence at 6 months, both trials consistently found significantly lower rates in the fluocinolone groups but the effect size was much smaller in the unpublished trial. Similarly, at 12 months, both trials found significantly lower recurrence rates in the fluocinolone groups, but the odds ratio had more than doubled in the published trial and decreased in the unpublished trial. Results were inconsistent between trials for the remainder of the key outcomes, appearing more favorable in the published trial. Most notable were the differences between trials in mean change in best-corrected visual acuity at 12 months (higher in the published trial, lower in the unpublished trials) and risk of increased intraocular pressure within 12 months (increased risk in the unpublished trial, but not in the published trial).

The most important limitation of these studies is the higher rate of "imputed" recurrences in the sham groups compared to the fluocinolone group (16% vs. 57% at 6 months in study PSV-FAI-001 and 12% vs. 39% in study PSV-FAI-005). Overall, the majority of the recurrences were not directly observed, but were "imputed" based on either the study eye being treated with a prohibited local or systemic medication (oral, systemic, injectable, or topical corticosteroids or systemic immunosuppressants) or the participant had a missing ophthalmic assessment at the 6- or 12-month visit. This means that the between-groups difference in the recurrence rates was mostly driven by imputed outcomes. Although the use of prohibited medications may be a reasonable surrogate for the occurrence of uveitis-related symptoms, it is unclear whether such symptoms would meet the rigorous threshold for a clinical diagnosis of recurrence (eg, a 2-step or more increase in the number of cells in the anterior chamber per high-powered field [1.6 using a 1-mm]; a 2-step or more increase in vitreous haze; or a deterioration in visual acuity of 15 letters or more of best-corrected visual

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

acuity). Therefore, it cannot be ruled out that the imputation led to an overestimation of the number of recurrences. With more imputed recurrences in the sham group than the treatment group, then it also cannot be ruled out that this led to an overestimation of the treatment effect. For example, in the published RCT by Jaffe et al (2019), when the results of observed recurrences were separately reported, the absolute between-group differences were numerically lower than in the imputed subgroups both at 6 months (sham rate – fluocinolone rate difference of 27.5% in observed group [n=13] vs. 35.5% [n=49]) and at 12 months (25.2% for observed group [n=15] vs. 34.5% [n=59]). In the unpublished trial PSV-FAI-005, the discrepancy was even larger. For example, at 6 months the absolute between-group difference in the observed recurrence subgroup was 5% (15% in sham and 10% in the fluorinolone group) versus 27% in the imputed group (39% in sham and 12 in the fluocinolone group). Further, it cannot be ruled out that visibility of the injected fluocinolone acetonide insert - or lack thereof - may have influenced the perceived need for use of prohibited medications. In the publication by Jaffe et al (2019), they noted that "The injected insert typically remains in a peripheral location within the vitreous base and is not detected easily on routine ophthalmologic examination. Regardless, we cannot exclude the possibility that the insert could have been visible in some study participants." Therefore, because of the inconsistency in key findings between the pivotal studies and the questions raised by the use of the imputed recurrence rates, the evidence is not sufficient to draw strong conclusions on the effect on health outcomes.

In 2020, the 3-year results from the pivotal study PSV-FAI-001 study were published. Over 36 months of treatment, cumulative uveitis recurrences were significantly reduced with fluocinolone acetonide (0.18 mg) compared with sham (65.5% vs. 97.6%, respectively). The time to the first recurrence in the fluocinolone acetonide (0.18 mg) group was significantly longer compared to sham-treatment (median 657 days; 95% CI, 395 to 105 vs. median 70.5 days; 95% CI, 57 to 91). The number of recurrences per eye occurring over 36 months was significantly lower in the treatment group compared to sham and a higher proportion of eyes in the fluocinolone acetonide (0.18 mg)group had no uveitis recurrence compared to sham (34.5% vs. 2.4%). Additionally, a greater proportion of eyes in the treatment group compared to sham had uveitis recur only once in 3 years (33.3% vs. 11.9%, respectively). Of note, the 36-month results included imputed recurrences, as in the initial results. However, observed protocol-defined uveitis recurrences occurred in a greater percentage of the sham-treated eyes, whereas the percentage of eyes with an imputed recurrence was more similar in the 2 groups (59.8% and 69.0%, respectively). At 36 months, more eyes in the treatment group had a 15-letter or greater increase in best-corrected visual acuity from baseline compared to the sham-treated group (33.3% vs. 14.7%). There was also a significantly greater mean change in best-corrected visual acuity over 36 months in the treatment group compared to sham. Intraocular pressure was well-controlled in both groups and similar for both groups at month 36. The proportion of eyes in the fluocinolone acetonide (0.18 mg) group that underwent intraocular pressure-lowering surgery was approximately half that in the sham-treated group. Cataract surgery was required more frequently over 36 months in the treatment group compared with the sham-treated group.

Policy #	00549	
Original E	Effective Date:	04/19/2017
Current Et	ffective Date:	06/01/2025

Table 2	. Summarv	of Kev	RCT	Results
I able 2	. Summary	ULINCY	NUI	Itcourto

Study	6-mo Recurrence	12-mo Recurrence	Mean change in BCVA at 12 mo	Increased intraocular pressure within 12 mo	Cataract within 12 mo
Jaffe et al (2019)	129	129	124	129	129
Fluocinolone acetonide (0.18 mg)	24 (27.6%)	33 (37.9%)	+5.8	23 (26.4%)	24 (27.6%)
Sham	$38 (90.5\%)^1$	41 (97.6%)	+3.3	11 (26.2%)	2 (4.8%)
OR (95% CI)	24.94 (8.04 to 77.39)	67.09 (8.81 to 511.06)	NR	NR	NR
PSV-FAI-005	153	153	142	153	153
Fluocinolone acetonide (0.18 mg)	22 (22%) ¹	33 (33%) ²	+3.0	29 (28.7%)	12 (11.9%)
Sham	$28 (54\%)^1$	31 (60%)	+7.4	1 (1.9%)	7 (13.5%)
OR (95% CI)	4.2 (2.0 to 8.6)	3.04 (1.52 to 6.08)	NR	NR	NR
	36-mo Recurrence	Mean number of recurrences per eye at 36- mo (SD)	Mean change in BCVA at 36 mo (SD)	Increased intraocular pressure within 36 mo	Cataract surgery over 36 mos
Jaffe et al (2020) 3-year results	129	129	129	129	129
Fluocinolone acetonide (0.18 mg)	57 (65.5%) ¹	1.7 (2.4)	+9.1 (13)	14.5 (16.6%)	73.8%
Sham	$41 (97.6\%)^1$	5.3 (3.8)	+2.5 (14.2)	14.8 (35.2%)	23.8%
OR (95% CI)	21.58 (2.83 to 164.7)	NR	NR	NR	NR
p-value	<.001	<.001	.020	NR	NR

BCVA: best-corrected visual acuity; CI: confidence interval; NR: Not Reported; OR: odds ratio; PSV-FAI-005: A Multi-center, Controlled, Safety and Efficacy Study of a Fluocinolone Acetonide Intravitreal (FAI) Insert in Subjects With Chronic Non-infectious Uveitis Affecting the Posterior Segment of the Eye; SD: standard deviation; RCT: randomized controlled trial.

¹ Primarily imputed, not observed recurrence

² From FDA statistical review

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Subsection Summary: Intravitreal Fluocinolone Implant (0.18 mg) for Non-Infectious Uveitis For individuals with chronic noninfectious posterior uveitis affecting the posterior segment of the eye and who receive intravitreal fluocinolone acetonide implant (0.18 mg), the evidence includes 2 pivotal RCTs. Relevant outcomes are symptom improvement, change in disease status, functional status, and quality of life. Harmful outcomes of interest are treatment-related morbidity. Both RCTs consistently found statistically significantly lower uveitis recurrence rates for intravitreal fluocinolone acetonide implant (0.18 mg) at both 6 and 12 months. The 3-year follow-up for Jaffe et al also found statistically significant lower uveitis recurrence rates at 36 months. However, serious limitations of these findings include inconsistency in the magnitude of the benefit at 12 months (odds ratio [OR]=67.09; 95% CI, 8.81 to 511.06 in published RCT and OR 3.04; 95% CI, 1.52 to 6.08 in the unpublished RCT) and, with more imputed recurrences in the sham groups than the treatment groups, we also cannot rule out an overestimation of the treatment effect. For the remainder of key outcomes, results were inconsistent between RCTs, appearing more favorable in the published trial. Most notable were the differences between RCTs in mean change in best-corrected visual acuity at 12 months (higher for fluocinolone acetonide in the published trial, lower in the unpublished trials) and risk of increased intraocular pressure within 12 months (increased risk in the unpublished trial, but not in the published trial).

MACULAR EDEMA AFTER RETINAL VEIN OCCLUSION

In 2015, the American Academy of Ophthalmology (AAO) published a technology assessment on therapies for macular edema associated with CRVO. AAO identified 4 clinical trials that provided level I evidence supporting the use of anti-vascular endothelial growth factor (anti-VEGF) pharmacotherapies and 2 clinical trials providing level I evidence for intravitreal corticosteroid injection with the dexamethasone intravitreal implants or triamcinolone. Evidence on the safety and efficacy of other reported interventions was of lesser strength. The assessment noted that evidence on long-term efficacy of corticosteroid treatments is limited and that intravitreal corticosteroids led to a higher frequency of adverse events, including cataracts and IOP elevation compared with anti-VEGF treatments. There was limited information on combination therapy with anti-VEGF and corticosteroid injections compared with monotherapy.

A Bayesian network meta-analysis of the efficacy and safety of treatments for macular edema secondary to BRVO was published in 2015. A total of 8 RCTs (total N=1743 patients) were included; patients were treated with ranibizumab given as needed, aflibercept monthly, dexamethasone implant, laser photocoagulation, ranibizumab plus laser, or sham intervention. The probability of being the most efficacious treatment, based on letters gained, or for a gain 15 letters or more, was highest for monotherapy of anti-VEGF treatments (30%-54% probability), followed by ranibizumab plus laser, and lowest (0%-2% probability) for the dexamethasone implant, laser, or sham treatment. Treatment with ranibizumab resulted in an average increase of 8 letters compared with the dexamethasone implant. Patients treated with the dexamethasone implant had statistically significant higher rates of ocular hypertension than patients given anti-VEGF monotherapy (odds ratio, 13.1).

Policy #	00549	
Original E	Effective Date:	04/19/2017
Current Ef	ffective Date:	06/01/2025

Intravitreal Dexamethasone Implant (0.7 mg)-Ozurdex

Data presented to FDA for the dexamethasone intravitreal implant (Ozurdex) were from two, 6month, double-masked RCTs called GENEVA (167 clinical sites in 24 countries). A 6-month openlabel extension of these 2 pivotal trials was reported in 2011. A total of 1267 patients who had clinically detectable macular edema associated with either CRVO or BRVO were randomized to a single treatment with a dexamethasone 0.7-mg implant (n=427), dexamethasone 0.35-mg implant (n=414), or sham control (n=426). The primary outcome measure was time to achieve a 15-or-more letter improvement in BCVA. A secondary outcome was the proportion of eyes achieving a 15-ormore letter improvement from baseline at 180 days. In individual studies as well as pooled analysis, time to achieve a 15-or-more letter (3-line) improvement in BCVA was significantly faster with implants than with sham (p<0.01) (data not shown). As evident from Table 2, the proportion of patients with a 15-or-more letter improvement from baseline in BCVA was higher in the implant with the FDA-approved dose (0.7 mg) compared to sham for the first 3 months. There was no significant difference in the proportion of patients who improved by 15 letters or more at 6-month follow-up. Note that the implant lasts for 6 months.

	N (%) of Patients With ≥15 Letters Improvement From Baseline in BCVA							
Time		Study 1			Study 2			
Point		-			-			
	Implant (0.7	Sham	р	Implant (0.7	Sham	р		
	mg)			mg)				
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		

Table 3. Summary of Results From FDA Pivotal Trial in Retinal Vein Occlusion

BCVA: best-corrected visual acuity; FDA: Food and Drug Administration.

Intravitreal Fluocinolone Acetonide Implant (0.59 mg)-Retisert

No RCTs were identified with fluocinolone acetonide implants for the treatment of macular edema following retinal vein occlusion.

Additional RCTs

Several additional RCTs have evaluated the comparative effects of dexamethasone intravitreal implants to other therapies and found mixed results. Kuppermann (2007) reported results for an RCT in which 315 patients with persistent macular edema of different etiology (diabetic retinopathy [n=172], BRVO [n=60], CRVO [n=42], uveitis [n=14], or post–cataract surgery macular edema [n=27]) were assigned to the dexamethasone 0.35-mg implant, the dexamethasone 0.7-mg implant, or observation. At 6 months, the proportion of patients meeting the primary outcome of an improvement in visual acuity of 10 letters was 24%, 35% and 13% in 0.35-mg implants, 0.7-mg implants, and observation-only groups, respectively. In a small trial in 50 patients, Pichi et al (2014)

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

found that the combination of dexamethasone 0.7-mg intravitreal implants plus macular grid laser increased both visual acuity and the interval between repeated implants. Gado and Macky (2014; n=60) reported no significant differences in visual acuity outcomes between dexamethasone implants and bevacizumab. Maturi et al (2014) reported results for 30 patients randomized to dexamethasone implants plus bevacizumab or to bevacizumab monotherapy and found no additional benefit for visual acuity with the combination treatment at 6 months. Compared to anti-VEGF for the treatment of macular edema after branch retinal vein occlusion, a meta-analysis by Ji et al (2019) of 6 studies (1 RCT, 4 retrospective studies, 1 prospective study; N = 452 eyes) found similar bestcorrected visual acuity change at 3 or 6 months with dexamethasone intravitreal implants (0.7 mg), but a higher risk of intraocular pressure elevation for dexamethasone treatment. Another metaanalysis by Tang et al (2024) also compared anti-VEGF agents to dexamethasone 0.7 mg intravitreal implants for the treatment of macular edema after branch retinal vein occlusion and included 8 RCTs (N = 336 eyes). In this analysis, dexamethasone resulted in superior best corrected visual acuity (mean difference, -3.68; 95% CI, -6.11 to -1.25; p=.003) and significantly reduced central macular thickness (mean difference, 31.32; 95% CI, -57.92 to -4.72; p = 0.02). However, dexamethasone also increased the risk of elevated intraocular pressure (relative risk, 6.98; 95% CI, 2.16 to 22.50; p = 0.001). The risk of cataract progression did not significantly differ between treatments (relative risk, 1.83; 95% CI, 0.63 to 5.27; p = 0.31). In another 60 patients with macular edema following branch retinal vein occlusion from a single-center in New Delhi, a randomized, open-label trial by Kumar et al (2019) found that best-corrected visual acuity gains at 6 months for 0.7 mg dexamethasone intravitreal implants, with or without laser photocoagulation (+ 9.50 and + 10.50, respectively), were similar to intravitreal ranibizumab (1 injection of 0.5 mg) with laser photocoagulation (+ 10.00), but lower than for 3 injections of 0.5 mg ranibizumab without laser photocoagulation (+18.00).

For the comparison to triamcinolone, the evidence includes the open-label multicenter PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) trial by Thorne et al (2019), in which 192 patients with macular edema, defined as a central subfield thickness 2 standard deviations greater than the population normative mean, were randomized to receive periocular triamcinolone acetonide 40 mg, intravitreal triamcinolone acetonide 4 mg, or the 0.7 mg intravitreal dexamethasone implant. Retreatment was permitted for the triamcinolone treatments at 8 weeks and at 12 weeks for dexamethasone. The proportion of eyes with macular edema resolution varied between treatments at 8 weeks (61% for dexamethasone, 47% for intravitreal triamcinolone, 20% for periocular triamcinolone) but not at 24 weeks (41%, 36%, and 35%, respectively). Change in best-corrected visual acuity was similar for intravitreal dexamethasone, intravitreal triamcinolone, and periocular triamcinolone at 8 weeks (+9.53 vs. +9.70 vs. +4.37 letters) and 24 weeks (+9.21 vs. +9.60 vs. +4.07). The main limitation was that, at 24 weeks, follow-up was relatively short-term. Longer-term data will be needed to confirm these findings.

An open-label, prospective, real-world study evaluated the effectiveness of dexamethasone intravitreal implant (0.7 mg) in a subgroup of patients with treatment-naive diabetic macular edema (Fraser-Bell et al 2021). Of the 200 eyes enrolled in the original AUSSIEDEX study, 57 were

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

treatment-naive. Changes in mean best-corrected visual acuity and central subfield retinal thickness from baseline to 52 weeks in this subgroup were + 3.4 letters (p = 0.042) and -89.6 micrometers (p < 0.001), respectively, with a mean of 2.5 injections of dexamethasone intravitreal implant 0.7 mg. The most common adverse event was increased intraocular pressure, with 20% of eyes requiring intraocular-pressure lowering medications.

An open-label, retrospective, 5-year real world study evaluated the effectiveness of dexamethasone intravitreal implant (0.7 mg) compared to anti-VEGF treatment in patients with diabetic macular edema secondary to retinal vein occlusion (Zhang et al 2022). There were 16 patients included, with 8 patients in each group. At the end of the 5-year evaluation period, changes in the best-corrected visual acuity (0.69 \pm 0.36 LogMAR vs. 0.57 \pm 0.30 LogMar; p = 0.574) and central macular thickness (183.25 \pm 97.31 μ m vs. 195.38 \pm 40.92 μ m; p = 0.442) were not significantly different between the dexamethasone and anti-VEGF groups, respectively. The dexamethasone group had a higher foveal avascular zone circularity index and higher retinal perfusion density than the anti-VEGF group.

Garay-Aramburu et al (2024) conducted a multicenter, retrospective study comparing dexamethasone intravitreal implants (0.7 mg) and anti-VEGF agents for branch (n = 407 eyes) and central (n = 318 eyes) retinal vein occlusion using data from the European Fight Retinal Blindness! Registry. At 12 months, changes in visual acuity were not significantly different between groups (branch retinal vein occlusion: dexamethasone, + 6.7 vs. anti-VEGF, + 10.6 letters; central retinal vein occlusion: dexamethasone, + 6.8 letters). Dexamethasone therapy required fewer injections and visits but had higher rates of intraocular pressure elevation in patients with branch retinal vein occlusion (dexamethasone, 5 of 47 [11%] vs. anti-VEFG, 9 of 360 [2%] patients; p = 0.015).

Subsection Summary: Intravitreal Dexamethasone Implant (0.7 mg) for Macular Edema After Retinal Vein Occlusion

Two identical RCTs have established the efficacy of dexamethasone intravitreal implants (0.7 mg) for patients with macular edema following retinal vein occlusion. The 2 RCTs compared 2 doses of implants with a sham control. Compared to sham, both doses of the dexamethasone implant resulted in clinically meaningful improvements in visual acuity within 1 to 3 months post-implantation. Further, implant-treated patients achieved improvement in vision faster than the sham controls. However, the vision gain was similar at 6 months. Several additional RCTs, systematic reviews, and observational studies have evaluated the comparative effects of dexamethasone intravitreal implants versus other therapies and found mixed results. A few notable findings include that the combination of implants with macular grid laser may increase the interval between repeated implants and dexamethasone intravitreal implants may have similar efficacy to other types of treatments. Further, as a class effect, use of dexamethasone implants resulted in higher incidences of cataracts and elevated IOP.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

DIABETIC MACULAR EDEMA

Intravitreal Fluocinolone Acetonide Implant (0.59 mg)-Retisert

Rittiphairoj et al (2020) published a Cochrane review that evaluated the efficacy of intravitreal steroids for macular edema in diabetes. It is an update of the previously published Cochrane review by Grover et al (2008). Ten trials were included, involving 4505 eyes with diabetic macular edema. Among those, 4 trials examined the effectiveness of intravitreal steroid implantation with fluocinolone acetonide (Retisert) or the dexamethasone drug delivery system compared with sham or an anti-VEGF agent (all discussed below) and 6 examined triamcinolone. Cochrane reviewers concluded that, compared to sham or control, intravitreal steroids may improve visual outcomes in people with diabetic macular edema, but that these benefits should be weighed against the risk of intraocular pressure elevation.

In 2011, Pearson et al reported on the 3-year efficacy and safety results of an industry-sponsored, single-blind (evaluator) RCT in which 196 patients with persistent or recurrent unilateral or bilateral DME (referred to as refractory DME) were randomized to implants (n = 127) or standard of care, defined as additional laser as needed after 6 months or observation (n = 69). All patients had received focal/grid laser photocoagulation prior to randomization. At 6 months, the proportions of patients who received laser retreatment in implant and standard of care groups were 4% and 13%, respectively; the percentages after 3 years of follow-up were 15% and 41%, respectively. The primary efficacy outcome (\geq 15-letter improvement in BCVA at 6 months before any additional laser treatment) was achieved in 16.8% of implanted eyes versus 1.4% of standard of care eyes (p < 0.05). Between 6 and 24 months, visual acuity was statistically significant in favor of the implant group but not beyond 30 months. At 3 years, there was no significant differences between the groups (eg, 31.1% of implanted eyes vs 20.0% of standard of care eyes improved \geq 15 letters at 3 years). As expected, there were higher incidences of elevated IOP (\geq 30 mm Hg; 61.4% vs 5.8%), need for surgery to treat glaucoma (33.8% vs 2.4%), and cataracts extraction in phakic eyes (91% vs 20%), respectively, for eyes treated with implants compared to standard of care. The incidence of vitreous hemorrhage (40.2% vs 18.8%), pruritus (38.6% vs 21.7%), and abnormal sensation in the eye (37.0%) vs 11.6%), respectively, were also higher in the eyes treated with implants versus standard of care.

Subsection Summary: Intravitreal Fluocinolone Acetonide Implant (0.59 mg) for Diabetic Macular Edema

One RCT comparing fluocinolone acetonide implants (0.59 mg) with standard of care (as needed laser or observation) has supported the efficacy of implants for patients with DME. The primary efficacy outcome, at least a 15-letter improvement in BCVA was significantly improved in a greater proportion of patients given implants versus laser at all time points assessed, except at or beyond 30 months. Note that this implant is active for 30 months. As a class effect, in patients with phakic eyes, use of implants resulted in 90% requiring cataract surgery and 60% developing elevated IOP. Due to the substantial increase in adverse events and availability of agents with safer tolerability profiles (eg, VEGF inhibitors), this implant is not indicated for DME.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Intravitreal Fluocinolone Acetonide Implant (0.19 mg)-ILUVIEN

Two double-blind, randomized trials (FAME) have assessed patients with DME previously treated with laser photocoagulation. The primary efficacy end point of both trials was the proportion of subjects in whom vision had improved by 15 letters or more at 2 years from baseline. These trials randomized patients to fluocinolone acetonide 0.19-mg or 0.5-mg implants or to sham. Results of these trials were published by Campochiaro et al (2011). In 2014, FDA approved the 0.19-mg dose only based on similar efficacy at 2 years between the low and high dose in improving vision by 15 letters or more from baseline (data not shown). Relevant results with FDA-approved dosing are summarized in Table 3. Subsequently, 3-year results were reported in 2012. The percentage of patients who gained 15 letters or more using the last observation carried forward was 28.7% in the implant group and 18.9% in the sham group. Results of sensitivity analysis without imputation for missing data ($\approx 70\%$ follow-up) showed similar results; the percentages of patients who gained 15 letters or more in the 2 groups were 33.0% and 21.4%, respectively. Subgroup analysis showed greater improvement in visual acuity in patients who were pseudophakic compared to those who were phakic (difference in mean change in number of letters at 2 years from baseline was 5.6 in pseudophakic patients vs 1 letter in phakic patients). This was due to loss of vision as a result of cataracts in phakic eyes that was observed more frequently in eyes with implants versus sham controls. Subgroup analysis also showed greater efficacy in patients with chronic (\geq 3 years) compared with nonchronic (< 3 years) DME. The difference in the proportion of patients who gained 15 or more letters in the implant group versus the sham control group with chronic DME patients was 21% and -5.5% among nonchronic DME patients.

Outcome	Study I (N=285)				Study 2 (.	N=270)
	Implant	Sham	Difference	Implant	Sham	Difference
	(n=190)	(n=95))	(95% CI)	(n=186)	(n=90)	(95% CI)
↑ 15	51	14	12.1% (2.6% to	57	16 (18%)	13.0% (2.7% to
letters	(27%)	(15%)	21.6%)	(31%)		23.4%)
$\downarrow 15$	26	5 (5%)	8.4% (1.8% to	22	9 (10%)	1.8% (-5.9% to
letters	(14%)		15.1%)	(12%)		9.6%)

Table 4. Summa	ry of Results (2 Years) From F	DA Pivotal Trials in Diabetic Macular Edema
Outcome	Study 1 (N_295)	Study 2 (N_276)

CI: confidence interval; FDA: Food and Drug Administration.

Massin et al (2016) reported the results of a small prospective noncomparative study in 16 patients with DME insufficiently responsive to laser and anti-VEGF who received fluocinolone acetonide 0.19-mg implants. Two groups of patients were evaluated-group 1 (n = 6) included patients ineligible anti-VEGF therapy who received previous treatment with laser photocoagulation while group 2 (n = 10) included patients previously treated with laser photocoagulation and at least 3 monthly anti-VEGF treatments. Central subfield thickness was reduced by -299 µm in group 1 and -251 µm in group 2 at 12 months. Mean change in area under the curve from baseline to last value for all eyes was +4.2 letters in group 1 and +3.9 letters in group 2. The benefit in BCVA letter score was more

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

limited and heterogeneous (the effect was more pronounced in pseudophakic eyes) with some patients achieving high improvements of visual acuity, whereas others did not improve. Small number of patients and lack of a control arm limit the interpretation of these findings.

Morozova et al (2024) reported on a retrospective study that evaluated fluocinolone acetonide 0.19mg intravitreal implants in 115 patients (148 eyes) with diabetic macular edema over an average follow-up of 29.4 months. Results demonstrated that the fluocinolone implant stabilized visual acuity, with a 0.8 letter decrease in the mean best-corrected visual acuity, and an increase in eyes achieving \geq 70 letters (20/40 Snellen equivalent) from 20.6% at baseline to 23.7% at 24 months. Furthermore, the central subfield thickness was reduced from 379.9 µm to 323.7 µm, with 58.7% of eyes achieving central subfield thickness \leq 300 µm at month 24 (p < 0.001). Lastly, the frequency of treatment for diabetic macular edema (intravitreal antivascular endothelial growth factor injections or laser photocoagulation) decreased from 4.9 to 1.5 treatments per year (p < 0.001).

Capone et al (2024) reported on a retrospective study evaluating fluocinolone acetonide 0.19-mg intravitreal implants in 178 patients (241 pseudophakic eyes). In a subset of 111 eyes with 24 months of follow-up, mean best-corrected visual acuity improved by 5.1 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (95% CI, 2.6 to 7.5; p < 0.001), and central macular thickness decreased by 189 µm (95% CI, 151 to 227; p < 0.001). Additional intravitreal treatments were required in 38 (34.2%) eyes. Safety outcomes, based on the full cohort of 241 eyes, revealed that 66 (27.4%) eyes required intraocular pressure-lowering medications (primarily within the first year of follow-up), and 14 (5.8%) eyes underwent trabeculectomy (predominantly during the second year).

Subsection Summary: Intravitreal Fluocinolone Acetonide Implant (0.19 mg) for Diabetic Macular Edema

Two RCTs and several observational studies have established the efficacy of fluocinolone acetonide implants (0.19 mg) for patients with DME. Both RCTs demonstrated the superiority of implants over sham controls. Implant-treated eyes showed clinically meaningful improvement in vision at 2 and 3 years post-implant. Subgroup analysis showed greater improvements in visual acuity in patients who were pseudophakic compared to those who were phakic. Similar results were seen in observational studies with follow up to 2 years. The major limitation of these implants is that nearly 80% all phakic patients will develop cataracts and will require cataract surgery. Further, IOP was elevated in 34% of patients who received this implant compared with 10% of controls, leading to the restricted indication for patients previously treated with corticosteroids who do not have a clinically significant rise in IOP.

Intravitreal Dexamethasone Implant (0.7 mg)-Ozurdex

Two double-blind, randomized trials have assessed patients with DME. These trials randomized patients to a 0.7-mg or to a 0.35-mg implant or to a sham procedure. Retreatment was allowed if it was at least 6 months since the prior treatment and there was evidence of residual edema. The primary efficacy end point in both trials was the proportion of subjects in whom visual acuity had improved by 15 or more letters at 39 months from baseline or at the final visit for patients who exited

Policy #	00549	
Original E	Effective Date:	04/19/2017
Current E	ffective Date:	06/01/2025

the study at or prior to month 36. The month 39 extension was included to accommodate the evaluation of safety and efficacy outcomes for patients who received retreatment at month 36. Results of these trials were published by Boyer et al (2014). In 2014, FDA approved the 0.7 mg dose. Relevant results with FDA-approved dosing are summarized in Table 4. Only 14% of study patients completed the month 39 visit (16.8% from implant, 12.2% from sham). The visual acuity improvement from baseline increased during a treatment cycle, peaked at 3 months posttreatment and diminished thereafter (data not shown). This was due to loss of vision related to development of cataracts. Subgroup analysis showed greater improvements in visual acuity in patients who were pseudophakic than in those who were phakic (difference in mean change in number of letters at 39 months from baseline was 4.2 letters in pseudophakic patients vs 0.3 letters in phakic patients).

 Table 5. Summary of 39-Month Results From the FDA Pivotal Trials in Diabetic Macular

 Edema

Outcome	Study 1 (N=328)			Study 2 (N=328)		
	Implant	Sham	Difference	Implant	Sham	Difference
	(n=163)	(n=165)	(95% CI)	(n=165)	(n=163)	(95% CI)
↑ 15	34 (21%)	19	9.3% (1.4% to	30	16	13.0% (2.7% to
letters		(12%)	17.3%)	(18%)	(10%)	23.4%)
$\downarrow 15$	15 (9%)	17	-1.1% (-7.5% to	30	18	7.1% (-0.5% to
letters		(10%)	5.3%)	(18%)	(11%)	14.7%)

CI: confidence interval ; FDA: Food and Drug Administration.

Subsequent to the 2014 pivotal trials and FDA approval, several small and/or short-term trials have been published that evaluate the comparative effects of intravitreal dexamethasone implant (0.7 mg) versus other treatments – primarily anti-VEGF in various subgroups of patients with diabetic macular edema. In general, compared with primarily anti-VEGF treatments, intravitreal dexamethasone implant (0.7 mg) was consistently associated with larger reductions in retinal thickness, but visual acuity changes were similar between treatment groups. While promising, as these findings are based on single small studies, several of which are nonrandomized, adequately powered and longer-term randomized trials are still needed to confirm these findings.

Table 6. Summary of Additional Studies of Intravitreal Dexamethasone Implant (0.7 mg) in Diabetic Macular Edema

Author, Year, study design, sample size	Population	Comparator	Summary of findings
Gillies et al (2014) , BEVORDEX RCT, N=88	Patients with DME	Bevacizumab	Dexamethasone had greater reduction in 12-mo retinal thickness and similar for BCVA improvement of \geq 10 letters. But, dexamethasone resulted in greater risk of

Policy #	00549	
Original E	Effective Date:	04/19/2017
Current Ef	ffective Date:	06/01/2025

			vision loss > 10 letters and more adverse events.
Callanan et al (2017), RCT, N=363	Patients with DME	Ranibizumab 0.5 mg	Dexamethasone was noninferior to ranibizumab in mean average BCVA change based on the prespecified noninferiority margin of 5 letters, similar in retinal thickness reduction, but ocular adverse events were more frequent for dexamethasone.
Sharma et al (2019), RCT, N=40	Centre involved DME	Bevacizumab 1.25 mg or ranibizumab 0.5 mg	Dexamethasone had greater improvements in 3-mo retinal thickness, but similar visual acuity
Unpublished RCT, NCT02471651, N=40	Persistent DME following anti-VEGF therapy	Continue on various anti- VEGF therapy	Treatments similar in 9-mo retinal thickness and visual acuity improvements

BCVA: best-corrected visual acuity; DME: Diabetic Macular Edema; NCT02471651: Dexamethasone Intravitreal Implant (0.7mg) for the Treatment of Persistent Diabetic Macular Edema Following Intravitreal Anti-Vascular Endothelial Growth Factor Therapy; RCT: randomized controlled trial; VEGF: vascular endothelial growth factor.

Cornish et al (2023) reported on 5-year outcomes of the BEVORDEX trial in patients with diabetic macular edema. Patients were randomized to receive either intravitreal dexamethasone implant (0.7 mg) or intravitreal bevacizumab. Data was available for 82% (n = 72) of eyes 3 years after enrollment, 72% (n = 63) at 4 years, and 59% (n = 52) at 5 or more years of follow-up. Baseline characteristics of the eyes from both study arms were similar. Table 7 summarizes the trial's results.

Table 7. Summary of Key Nonrandomized Trials Study Results

v	v	v		
Study	Mean VA at	Proportion of	Mean change	Proportion of
	5 years,	eyes who gained	in CMT, µm	eyes that had
	letters (95%	\geq 10 letters from		cataract
	CI)	baseline to 5		surgery by 5
		years, n (%)		years (%)
Cornish et al			From baseline	
(2023)			to 5 years	
			(95% CI)	

Po Or Cu	blicy # 00549 riginal Effective Date: arrent Effective Date:	04/19/2017 06/01/2025			
	Dexamethasone	58.5 (95% CI, 55.1 to 61.9)	14 (30.4%)	-150 (95% CI, -199 to -100)	84%
	Bevacizumab	59.5 (95% CI, 57.4 to 63.6)	14 (33.3%)	-173 (95% CI, -232 to -121)	68%
	Chakraborty et al (2024	Mean BCVA at 12 months		CMT (µm) at 12 months	Need for IOP lowering surgery, n (%)
	Dexamethasone	0.50 + 0.07 logMAR		293 + 15.9	5 (13)
	Aflibercept	0.47 + 0.12 logMAR		292 + 10.8	0
	P-value	0.58		0.95	0.02
	Bolukbasi et al (2019)	Mean BCVA at 3 months		Mean change in CMT (+/- SD), μm	
	Dexamethasone	0.4 ± 0.2 LogMAR	NR	228.6 ± 109.8	NR
	Aflibercept	0.3 ± 0.2 LogMAR	NR	168.5 ± 106.4	NR
	Cakir et al (2019)	Mean BCVA at 4 months	Mean change in CMT (+/- SD), µm at 1 month	Mean change in CMT (+/- SD), μm at 4 months	Proportion of eyes that had cataract surgery by end of study
	Dexamethasone	1.0 ± 0.5 LogMAR	188.2 ± 142.7	-63 ± 67.3	0
	Ranibizumab	0.7 ± 0.5 LogMAR	95.7 ± 110.7	-5.8 ± 43.9	0
	Coelho et al (2019)		Letter improvement on ETDRS chart	CFT reduction, µm	
	Dexamethasone	NR	> 5-letter improvement on the ETDRS chart at months 1 and 3	> 100 µm CFT reduction at month 1	NR
	Fluocinolone acetonide	NR	> 10-letter improvement on the ETDRS chart over months 3 to 24	Sustained ~200 µm over 1 to 24 months	NR

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

BCVA, best corrected visual acuity; CI: confidence interval; CFT: central foveal thickness; CMT, central macular thickness; CI: confidence interval; ETDRS: Early Treatment Diabetic Retinopathy Study; NR: not reported; SD, standard deviation; VA: visual acuity.

Subsection Summary: Intravitreal Dexamethasone Implant (0.7 mg) for Diabetic Macular Edema

Two identical RCTs have established the efficacy of dexamethasone intravitreal implants (0.7 mg) for patients with DME. The 2 RCTs compared 2 doses of implants with a sham control. Compared to sham, both doses of the dexamethasone implant resulted in clinically meaningful improvements in visual acuity at 39 months post-implantation. The visual acuity improvement peaked at 3 months posttreatment but diminished thereafter, possibly due to development of cataracts. Subgroup analysis showed greater improvements in visual acuity in patients who were pseudophakic than in those who were phakic. Evidence from various small and/or short-term trials have found that, compared with primarily anti-VEGF treatments, intravitreal dexamethasone implant (0.7 mg) was consistently associated with larger reductions in retinal thickness, but visual acuity changes were similar between treatment groups.

AGE-RELATED MACULAR DEGENERATION

Intravitreal Dexamethasone Implant (0.7 mg) Plus Anti-VEGF Therapy- Ozurdex

Kuppermann et al (2015) reported the results of industry-sponsored, single-masked, shamcontrolled, randomized trial in which 243 patients with choroidal neovascularization secondary to AMD were allocated to dexamethasone implants (n = 123) or a sham procedure (n = 120). All patients received 2 protocol-mandated intravitreal ranibizumab injections with the next injection given as needed based on established study criteria. The primary efficacy end point was the ranibizumab injection-free interval at 6 months. The median injection-free survival was 34 days in the implant group and 29 days in the sham control group. Though this difference was statistically significant (p = 0.016), the effect size was small and clinically insignificant. The proportions of patients who did not require rescue ranibizumab over the 6-month study period were 8.3% the implant group and 2.5% in the sham group (p = 0.048). There were no significant differences between groups in mean change from baseline BCVA. More patients in the dexamethasone implant group had increased IOP (13.2% vs 4.2%; p = 0.014), but there were no differences between groups in cataracts-related events. Notably, the trial had a short follow-up (6 months).

Section Summary: Intravitreal Dexamethasone Implant (0.7 mg) Plus Anti-VEGF Therapy for Age-Related Macular Degeneration

One RCT evaluated the impact of adding implants to a standard VEGF inhibitor for patients with AMD. Results of this trial failed to demonstrate clinically meaningful reductions in the ranibizumab injection-free interval. Further, there was an IOP elevation in greater proportion of patients receiving implants without any additional clinical benefit.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

OTHER CONDITIONS Birdshot Retinochoroidopathy

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 corticosteroids 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). 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% 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 post-implant. Another retrospective cohort study (2015) that included 11 eyes with birdshot chorioretinitis reported improved control of inflammation and decreased reliance on adjunctive therapy with fluocinolone acetonide implants (0.59 mg). Authors observed a more robust increase in IOP compared to the observed elevation in patients with other types of posterior uveitis and panuveitis. Results of another retrospective study by Rush et al (2011), which included 32 eyes with birdshot chorioretinopathy who received fluocinolone acetonide implant (0.59 mg) with 12-month followup, also reported decrease in vitreous haze from 26% at baseline to 100% at 12 months. In 2 small retrospective studies with 6 eyes in 3 patients and 6 eyes in 4 patients, 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 BCVA of at least 20/25 during treatment. In the second, there was a mean improvement of 70 letters on BCVA using the EDTRS chart.

Section Summary: Birdshot Retinochoroidopathy

No RCTs were identified on the treatment of birdshot retinochoroidopathy with any corticosteroids intravitreal implants. Available evidence includes multiple observational studies that noted improvements in anatomic and visual acuity outcomes in patients refractory or intolerant to 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 retinopathy.

Cystoid Macular Edema Related to Retinitis Pigmentosa

Retinitis pigmentosa is a degenerative process of the retina affecting primarily the rod photoreceptors and retinal pigment epithelium. Cystoid macular edema results from cystic accumulation of fluid in multiple layers of the retina following the breakdown of the blood-retinal barriers. It is a sub-type of macular edema which can be caused by many underlying conditions, including uveitis, retinal vein occlusion, diabetic macular edema, retinitis pigmentosa, as well as following procedures such as cataract extraction.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

No large, multi-center, sham-controlled RCTs were identified on the treatment of this indication for any corticosteroids 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. 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 (-147.5 μ m vs. -14 μ m, p < 0.001) and median change of best-corrected visual acuity (+6 vs. +1; p < 0.001). 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.

Section Summary: Cystoid Macular Edema Related to Retinitis Pigmentosa

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 lacked responder analysis of the proportion of patients with a 15-ormore 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

Type 1 macular telangiectasia is a rare congenital and unilateral condition of the eye in which a focal expansion or outpouching and dilation of capillaries in the parafoveal region leads to vascular incompetence, atrophy, and central loss of vision. It is also considered a variant of Coats disease. No RCTs were identified on the treatment of macular telangiectasia with any corticosteroids intravitreal implants. Three case reports with a total 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.

Section Summary: Idiopathic Macular Telangiectasia Type 1

No RCTs were identified on the treatment of idiopathic macular telangiectasia type 1 with any corticosteroids intravitreal implants. Available evidence includes multiple case reports, which have

Policy #	00549	
Original E	Effective Date:	04/19/2017
Current E	ffective Date:	06/01/2025

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 in patients with this indication.

Postoperative Chronic Macular Edema

Postoperative chronic macular edema, also called as pseudophakic cystoid macular edema or Irvine-Gass syndrome, is one of the most common causes of visual loss after cataract surgery. It is thought to occur as a consequence of inflammatory mediators that are upregulated in the aqueous and vitreous humors after surgical manipulation; it can lead to permanent visual loss.

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. 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. Key results are reported in Table 8.

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

Table 8. Summary of Key RCT Results

IOP: intraocular pressure; RCT: randomized controlled trial; SD: standard deviation.

Multiple case series have assessed improvements in visual acuity and anatomic changes. 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. EPISODIC, a 2017 observational retrospective study conducted in France, included 100 patients with postsurgical macular edema who received dexamethasone implants between April

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

2011 and June 2014 and who had a minimum of 1-year follow-up. Mean improvement in BCVA was 9.6 EDTRS letters at month 6 and 10.3 at month 12. The proportion of eyes with gains in BCVA of 15 or more letters was 32.5% and 37.5% at months 6 and 12, respectively. Average reduction in central subfield macular thickness was 135.2 and 160.9 μ m 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 (ie, 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

Circumscribed choroidal hemangiomas are benign vascular hamartomas without systemic associations. No RCTs were identified on the treatment of circumscribed choroidal hemangiomas with any corticosteroids intravitreal implants. A single case report 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.

Section Summary: Circumscribed Choroidal Hemangiomas

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

Proliferative Vitreoretinopathy

Proliferative vitreoretinopathy develops as a complication of rhegmatogenous retinal detachment. Proliferative vitreoretinopathy occurs in 8% to 10% of patients undergoing primary retinal detachment surgery and prevents the successful surgical repair of rhegmatogenous retinal detachment. No RCTs were identified on the treatment of proliferative vitreoretinopathy with any corticosteroids intravitreal implants. A case series (2017) of 5 patients with proliferative vitreoretinopathy has described combined use of surgery, endolaser, and dexamethasone implants.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

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.

Section Summary: Proliferative Vitreoretinopathy

No RCTs were identified on the treatment of proliferative vitreoretinopathy with any corticosteroids intravitreal implants. Available evidence includes 1 case series and 1 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

Radiation retinopathy is delayed-onset damage to the retina due to exposure to ionizing radiation, typically after months and is slowly progressive. No RCTs were identified on the treatment of radiation retinopathy with any corticosteroids intravitreal implants. In a retrospective study (2015), 12 eyes diagnosed with radiation maculopathy secondary to plaque brachytherapy were treated with dexamethasone implants. 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. They had limited responses to bevacizumab and intravitreal triamcinolone. Dexamethasone implants provided a prolonged period of anatomic stabilization. In another retrospective chart review (2013) of 5 patients with choroidal melanoma treated with dexamethasone implants for radiation macular edema, mix improvements in visual acuity were reported. The mean improvement in EDTRS 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 corticosteroids 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.

SUPRACHOROIDAL INJECTIONS MACULAR EDEMA ASSOCIATED WITH UVEITIS Suprachoroidal triamcinolone injection (4 mg) - Xipere

The efficacy of Xipere was assessed in a 6-month, randomized, multicenter, double-masked, shamcontrolled study in patients with macular edema associated with anterior-, intermediate-, posterior-, or pan-uveitis. Patients were treated at baseline and week 12. The primary efficacy endpoint was the proportion of patients in whom best corrected visual acuity (BCVA) had improved by \geq 15 letters

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

from baseline after 24 weeks of follow-up. A statistically significantly greater proportion of patients treated with Xipere achieved a \geq 15-letter improvement in BCVA than control patients (p < 0.01) at week 24 (47% vs. 16%, respectively).

Section Summary: Macular Edema Associated With Uveitis

One RCT demonstrated that a triamcinolone suprachoroidal 4 mg injection (Xipere) was better than placebo for the treatment of macular edema associated with uveitis.

References

- 1. 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
- 2. 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
- Bausch & Lomb Incorporated. Retisert

 (fluocinolone acetonide intravitreal implant) 0.59 mg: Prescribing Label. 2012; http://www.bausch.com/Portals/107/

/m/BL/United%20States/USFiles/Package%20Inserts/Pharma/retisert-prescribing-information.pdf.

- 4. Jaffe GJ, Martin D, Callanan D, et al. Fluocinolone acetonide implant (Retisert) for noninfectious posterior uveitis: thirty-four-week results of a multicenter randomized clinical study. Ophthalmology. Jun 2006;113(6):1020-1027. PMID 16690128
- U.S. Food and Drug Administration. Center for Drug Evaluation and Research, Application number 21-737, Medical Review. 2005; http://www.accessdata.fda.gov/drugsatfda_docs/nda/2005/021737s000_MedR.pdf.
- 6. Pavesio C, Zierhut M, Bairi K, et al. Evaluation of an intravitreal fluocinolone acetonide implant versus standard systemic therapy in non-infectious posterior uveitis. Ophthalmology. Mar 2010;117(3):567-575, 575 e561. PMID 20079922
- 7. Brady CJ, Villanti AC, Law HA, et al. Corticosteroid implants for chronic non-infectious uveitis. Cochrane Database Syst Rev. Feb 12 2016;2:CD010469. PMID 26866343
- 8. Kempen JH, Altaweel MM, Holbrook JT, et al. The multicenter uveitis steroid treatment trial: rationale, design, and baseline characteristics. Am J Ophthalmol. Apr 2010;149(4):550-561 e510. PMID 20097325
- 9. Kempen JH, Altaweel MM, Holbrook JT, et al. Randomized comparison of systemic antiinflammatory therapy versus fluocinolone acetonide implant for intermediate, posterior, and panuveitis: the multicenter uveitis steroid treatment trial. Ophthalmology. Oct 2011;118(10):1916-1926. PMID 21840602
- 10. Jaffe GJ, Branchaud B, Hahn P, et al. Quality of Life and Risks Associated with Systemic Antiinflammatory Therapy versus Fluocinolone Acetonide Intraocular Implant for Intermediate Uveitis, Posterior Uveitis, or Panuveitis: Fifty-four-Month Results of the Multicenter Uveitis

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Steroid Treatment Trial and Follow-up Study. Ophthalmology. Oct 2015; 122(10): 1976-86. PMID 26298718

- Holbrook JT, Sugar EA, Burke AE, et al. Dissociations of the Fluocinolone Acetonide Implant: The Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study. Am J Ophthalmol. Apr 2016;164:29-36. PMID 26748056
- Lowder C, Belfort R, Jr., Lightman S, et al. Dexamethasone intravitreal implant for noninfectious intermediate or posterior uveitis. Arch Ophthalmol. Jan 10 2011;129(5):545-553. PMID 21220619
- Lightman S, Belfort R, Jr., Naik RK, et al. Vision-related functioning outcomes of dexamethasone intravitreal implant in non-infectious intermediate or posterior uveitis. Invest Ophthalmol Vis Sci. Jul 2013;54(7):4864-4870. PMID 23761087
- Gillespie BW, Musch DC, Niziol LM, et al. Estimating minimally important differences for two vision-specific quality of life measures. Invest Ophthalmol Vis Sci. Jun 06 2014;55(7):4206-4212. PMID 24906863
- 15. Allergan Inc. Ozurdex (dexamethasone intravitreal implant): Prescribing Label 2014; http://www.allergan.com/assets/pdf/ozurdex_pi.pdf.
- 16. U.S. Food and Drug Administration. Center for Drug Evaluation and Research, Application number 210331, Medical Review. 2018; https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210331Orig1s000MedR.pdf. Accessed January 12, 2023.
- Jaffe GJ, Foster CS, Pavesio CE, et al. Effect of an Injectable Fluocinolone Acetonide Insert on Recurrence Rates in Chronic Noninfectious Uveitis Affecting the Posterior Segment: Twelve-Month Results. Ophthalmology. Apr 2019; 126(4): 601-610. PMID 30367884
- Jaffe GJ, Pavesio CE. Effect of a Fluocinolone Acetonide Insert on Recurrence Rates in Noninfectious Intermediate, Posterior, or Panuveitis: Three-Year Results. Ophthalmology. Oct 2020; 127(10): 1395-1404. PMID 32624244
- 19. Yeh S, Kim SJ, Ho AC, et al. Therapies for macular edema associated with central retinal vein occlusion: a report by the American Academy of Ophthalmology. Ophthalmology. Apr 2015;122(4):769-778. PMID 25576994
- 20. U.S. Food and Drug Administration. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2009/022315s000_SumR.pdf.
- 21. Kuppermann BD, Blumenkranz MS, Haller JA, et al. Randomized controlled study of an intravitreous dexamethasone drug delivery system in patients with persistent macular edema. Arch Ophthalmol. Mar 2007;125(3):309-317. PMID 17353400
- 22. Kumar P, Sharma YR, Chandra P, et al. Comparison of the Safety and Efficacy of Intravitreal Ranibizumab with or without Laser Photocoagulation Versus Dexamethasone Intravitreal Implant with or without Laser Photocoagulation for Macular Edema Secondary to Branch Retinal Vein Occlusion. Folia Med (Plovdiv). Jun 01 2019; 61(2): 240-248. PMID 31301668
- 23. Ji K, Zhang Q, Tian M, et al. Comparison of dexamethasone intravitreal implant with intravitreal anti-VEGF injections for the treatment of macular edema secondary to branch retinal vein occlusion: A meta-analysis. Medicine (Baltimore). May 2019; 98(22): e15798. PMID 31145307

- 24. Tang HX, Li JJ, Yuan Y, et al. Comparing the efficacy of dexamethasone implant and anti-VEGF for the treatment of macular edema: A systematic review and meta-analysis. PLoS One. 2024; 19(7): e0305573. PMID 38985778
- 25. Thorne JE, Sugar EA, Holbrook JT, et al. Periocular Triamcinolone vs. Intravitreal Triamcinolone vs. Intravitreal Dexamethasone Implant for the Treatment of Uveitic Macular Edema: The PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) Trial. Ophthalmology. Feb 2019; 126(2): 283-295. PMID 30269924
- 26. Pichi F, Specchia C, Vitale L, et al. Combination therapy with dexamethasone intravitreal implant and macular grid laser in patients with branch retinal vein occlusion. Am J Ophthalmol. Mar 2014;157(3):607-615 e601. PMID 24528934
- 27. Gado AS, Macky TA. Dexamethasone intravitreous implant versus bevacizumab for central retinal vein occlusion-related macular oedema: a prospective randomized comparison. Clin Experiment Ophthalmol. Sep-Oct 2014;42(7):650-655. PMID 24612095
- 28. Maturi RK, Chen V, Raghinaru D, et al. A 6-month, subject-masked, randomized controlled study to assess efficacy of dexamethasone as an adjunct to bevacizumab compared with bevacizumab alone in the treatment of patients with macular edema due to central or branch retinal vein occlusion. Clin Ophthalmol. 2014;8:1057-1064. PMID 24940042
- 29. Fraser-Bell S, Kang HK, Mitchell P, et al. Dexamethasone intravitreal implant in treatment-naïve diabetic macular oedema: findings from the prospective, multicentre, AUSSIEDEX study. Br J Ophthalmol. Jan 2023; 107(1): 72-78. PMID 34433549
- 30. Zhang M, Liu Y, Song M, et al. Intravitreal dexamethasone implant has better retinal perfusion than anti-vascular endothelial growth factor treatment for macular edema secondary to retinal vein occlusion: a five-year real-world study. Ophthalmic Res. Oct 10 2022. PMID 36215955
- 31. Garay-Aramburu G, Hunt A, Arruabarrena C, et al. Initial response and 12-month outcomes after commencing dexamethasone or vascular endothelial growth factor inhibitors for retinal vein occlusion in the FRB registry. Sci Rep. Mar 13 2024; 14(1): 6122. PMID 38480837
- 32. Rittiphairoj T, Mir TA, Li T, et al. Intravitreal steroids for macular edema in diabetes. Cochrane Database Syst Rev. Nov 17 2020; 11(11): CD005656. PMID 33206392
- 33. Grover D, Li TJ, Chong CC. Intravitreal steroids for macular edema in diabetes. Cochrane Database Syst Rev. 2008(1):CD005656. PMID 18254088
- 34. Pearson PA, Comstock TL, Ip M, et al. Fluocinolone acetonide intravitreal implant for diabetic macular edema: a 3-year multicenter, randomized, controlled clinical trial. Ophthalmology. Aug 2011;118(8):1580-1587. PMID 21813090
- 35. Campochiaro PA, Brown DM, Pearson A, et al. Long-term benefit of sustained-delivery fluocinolone acetonide vitreous inserts for diabetic macular edema. Ophthalmology. Apr 2011;118(4):626-635 e622. PMID 21459216
- 36. Alimera Sciences Inc. Iluvien® (fluocinolone acetonide intravitreal implant) 0.19 mg for Intravitreal Injection: Prescribing Label. http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/201923s000lbl.pdf.
- 37. Campochiaro PA, Brown DM, Pearson A, et al. Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema. Ophthalmology. Oct 2012;119(10):2125-2132. PMID 22727177

- Cunha-Vaz J, Ashton P, Iezzi R, et al. Sustained delivery fluocinolone acetonide vitreous implants: long-term benefit in patients with chronic diabetic macular edema. Ophthalmology. Oct 2014;121(10):1892-1903. PMID 24935282
- 39. Massin P, Erginay A, Dupas B, et al. Efficacy and safety of sustained-delivery fluocinolone acetonide intravitreal implant in patients with chronic diabetic macular edema insufficiently responsive to available therapies: a real-life study. Clin Ophthalmol. 2016;10:1257-1264. PMID 27468222
- Morozova C, Humayun LL, Kasper J, et al. Real-World Outcomes of the 0.19 mg Fluocinolone Acetonide Intravitreal Implant for Diabetic Macular Edema. J Vitreoretin Dis. 2024; 8(4): 394-400. PMID 39148560
- 41. Capone L, Airaghi P, Aragona P, et al. Real-world experience with fluocinolone acetonide intravitreal implant in patients with diabetic macular edema. Eur J Ophthalmol. Nov 2024; 34(6): 1837-1842. PMID 38396370
- 42. Boyer DS, Yoon YH, Belfort R, Jr., et al. Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. Ophthalmology. Oct 2014;121(10):1904-1914. PMID 24907062
- 43. Gillies MC, Lim LL, Campain A, et al. A randomized clinical trial of intravitreal bevacizumab versus intravitreal dexamethasone for diabetic macular edema: the Bevordex study. Ophthalmology. Dec 2014; 121(12): 2473-81. PMID 25155371
- 44. U.S. National Library of Medicine. Dexamethasone Intravitreal Implant for the Treatment of Persistent Diabetic Macular Edema (DIME) NCT02471651. 2019. https://clinicaltrials.gov/ct2/show/results/NCT02471651?term=NCT02471651&draw=2&rank =1 Accessed January 18, 2023.
- 45. Callanan DG, Loewenstein A, Patel SS, et al. A multicenter, 12-month randomized study comparing dexamethasone intravitreal implant with ranibizumab in patients with diabetic macular edema. Graefes Arch Clin Exp Ophthalmol. Mar 2017; 255(3): 463-473. PMID 27632215
- 46. Sharma A, Bellala K, Dongre P, et al. Anti-VEGF versus dexamethasone implant (Ozurdex) for the management of Centre involved Diabetic Macular Edema (CiDME): a randomized study. Int Ophthalmol. Jan 2020; 40(1): 67-72. PMID 31377905
- 47. U.S. National Library of Medicine. Dexamethasone Intravitreal Implant for the Treatment of Persistent Diabetic Macular Edema (DIME) NCT02471651. 2019. https://clinicaltrials.gov/ct2/show/results/NCT02471651?term=NCT02471651&draw=2&rank =1 Accessed January 18, 2023.
- 48. Cornish EE, Teo KY, Gillies MC, et al. Five-year outcomes of eyes initially enrolled in the 2year Bevordex trial of bevacizumab or dexamethasone implants for diabetic macular oedema. Br J Ophthalmol. Jan 2023; 107(1): 79-83. PMID 34340975
- 49. Chakraborty D, Mondal S, Sengupta S, et al. Aflibercept vs. dexamethasone implant for recalcitrant diabetic macular edema in pseudophakic eyes 1-year outcomes from a quazi-randomized study in India. Indian J Ophthalmol. Jul 01 2024; 72(7): 1001-1006. PMID 38622856

- 50. Bolukbasi S, Cakir A, Erden B, et al. Comparison of the short-term effect of aflibercept and dexamethasone implant on serous retinal detachment in the treatment of naive diabetic macular edema. Cutan Ocul Toxicol. Dec 2019; 38(4): 401-405. PMID 31438736
- 51. Cakir A, Erden B, Bolukbasi S, et al. Comparison of the effect of ranibizumab and dexamethasone implant in diabetic macular edema with concurrent epiretinal membrane. J Fr Ophtalmol. Sep 2019; 42(7): 683-689. PMID 31088741
- 52. Coelho J, Malheiro L, Melo Beirão J, et al. Real-world retrospective comparison of 0.19 mg fluocinolone acetonide and 0.7 mg dexamethasone intravitreal implants for the treatment of diabetic macular edema in vitrectomized eyes. Clin Ophthalmol. 2019; 13: 1751-1759. PMID 31571814
- 53. Maturi RK, Bleau L, Saunders J, et al. A 12-month, single-masked, randomized controlled study of eyes with persistent diabetic macular edema after multiple anti-VEGF injections to assess the efficacy of the dexamethasone-delayed delivery system as an adjunct to bevacizumab compared with continued bevacizumab monotherapy. Retina. Mar 30 2015;35(8):1604-1614. PMID 25829346
- 54. Callanan DG, Gupta S, Boyer DS, et al. Dexamethasone intravitreal implant in combination with laser photocoagulation for the treatment of diffuse diabetic macular edema. Ophthalmology. Sep 2013;120(9):1843-1851. PMID 23706947
- 55. Kuppermann BD, Goldstein M, Maturi RK, et al. Dexamethasone intravitreal implant as adjunctive therapy to ranibizumab in neovascular age-related macular degeneration: a multicenter randomized controlled trial. Ophthalmologica. Sep 2015;234(1):40-54. PMID 26088793
- 56. 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
- 57. 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
- 58. 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
- 59. 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
- 60. Erdogan G, Aydogan T, Unlu 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
- 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
- 62. Spaide RF. Retinal Vascular Cystoid Macular Edema: Review and New Theory. Retina. Oct 2016; 36(10): 1823-42. PMID 27328171

- 63. 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): 1393-400. PMID 25748280
- Csaky KG, Richman EA, Ferris FL. Report from the NEI/FDA Ophthalmic Clinical Trial Design and Endpoints Symposium. Invest Ophthalmol Vis Sci. Feb 2008; 49(2): 479-89. PMID 18234989
- 65. Park UC, Park JH, Ma DJ, et al. A Randomized Paired-Eye Trial of Intravitreal Dexamethasone Implant for Cystoid Macular edema in Retinitis Pigmentosa. Retina. Jul 2020; 40(7): 1359-1366. PMID 31166248
- 66. 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 3188670
- 67. 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
- 68. Loutfi M, Papathomas T, Kamal A. Macular oedema related to idiopathic macular telangiectasia type 1 treated with dexamethasone intravitreal implant (ozurdex). Case Rep Ophthalmol Med. 2014;2014:231913. PMID 25045562
- Holló G, Aung T, Cantor LB, et al. Cystoid macular edema related to cataract surgery and topical prostaglandin analogs: Mechanism, diagnosis, and management. Surv Ophthalmol. 2020; 65(5): 496-512. PMID 32092363
- 70. Grzybowski A, Sikorski BL, Ascaso FJ, et al. Pseudophakic cystoid macular edema: update 2016. Clin Interv Aging. 2016; 11: 1221-1229. PMID 27672316
- 71. 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. Apr 2017; 42(4): 648-652. PMID 27612922
- 72. 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: 1441-9. PMID 25258512
- 73. 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
- 74. Klamann A, Bottcher K, Ackermann P, et al. Intravitreal dexamethasone implant for the treatment of postoperative macular edema. Ophthalmologica. 2016;236(4):181-185. PMID 27915343
- 75. 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
- 76. 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

- 77. 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
- 78. Landre 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
- 79. 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
- 80. Dutra Medeiros M, Navarro R, Garcia-Arumi J, et al. Dexamethasone intravitreal implant for treatment of patients with recalcitrant macular edema resulting from Irvine-Gass syndrome. Invest Ophthalmol Vis Sci. May 07 2013;54(5):3320-3324. PMID 23599334
- 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
- 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. May 17 2016. PMID 27190126
- 83. Bazin L, Gambrelle J. [Combined treatment with photodynamic therapy and intravitreal dexamethasone implant (Ozurdex((R))) for circumscribed choroidal hemangioma]. J Fr Ophtalmol. Dec 2012;35(10):798-802. PMID 23040445
- 84. Sherif M, Wolfensberger TJ. Intraocular dexamethasone implant as adjunct to silicone oil tamponade for proliferative vitreoretinopathy. Klin Monbl Augenheilkd. Feb 01 2017. PMID 28147403
- 85. 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
- 86. 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
- Bui KM, Chow CC, Mieler WF. Treatment of recalcitrant radiation maculopathy using intravitreal dexamethasone (Ozurdex) implant. Retin Cases Brief Rep. Summer 2014;8(3):167-170. PMID 25372430
- 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. PMID 23652581
- 89. Yutiq [package insert]. EyePoint Pharmaceuticals. Watertown, Massachusetts. Updated 10/2018.
- 90. Uveitis: Etiology, clinical manifestations, and diagnosis. UpToDate. Accessed April 2022.
- 91. Xipere [package insert]. Clearside Biomedical, Inc. Alpharetta, Georgia. Updated October 2021.

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Policy History

Current Effective Date: 06/01/2025 04/06/2017 Medical Policy Committee review 04/19/2017 Medical Policy Implementation Committee approval. New Policy. 04/05/2018 Medical Policy Committee review 04/04/2019 Medical Policy Committee review 04/04/2019 Medical Policy Committee review 04/04/2019 Medical Policy Committee review 04/24/2019 Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. 04/02/2020 Medical Policy Committee review 04/08/2020 Medical Policy Committee review 04/01/2021 Medical Policy Committee review 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 05/05/2022 Medical Policy Committee review 05/05/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updat	Original Effectiv	ve Date: 04/19/2017
 04/06/2017 Medical Policy Committee review 04/19/2017 Medical Policy Implementation Committee approval. New Policy. 04/05/2018 Medical Policy Implementation Committee approval. No change to coverage. 04/04/2019 Medical Policy Implementation Committee approval. No change to coverage. 04/04/2019 Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. 04/02/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 05/05/2022 Medical Policy Committee review 05/05/2022 Medical Policy Committee review 05/05/2023 Medical Policy Committee review 05/04/2023 Medical Policy Committee review 05/04/2023 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 06/20/2024 Medical Policy Committee review 05/02/2024 Medical Policy Committee review 	Current Effectiv	e Date: 06/01/2025
 04/19/2017 Medical Policy Implementation Committee approval. New Policy. 04/05/2018 Medical Policy Committee review 04/08/2019 Medical Policy Committee review 04/24/2019 Medical Policy Implementation Committee approval. No change to coverage. 04/02/2020 Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. 04/02/2020 Medical Policy Committee review 04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/04/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 04/14/2021 Medical Policy Committee review 05/05/2022 Medical Policy Committee review 05/05/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Committee review 05/02/2024 Medical Policy Committee review 05	04/06/2017	Medical Policy Committee review
 04/05/2018 Medical Policy Committee review 04/18/2018 Medical Policy Implementation Committee approval. No change to coverage. 04/04/2019 Medical Policy Committee review 04/24/2019 Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. 04/02/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/01/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 05/04/2023 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligib	04/19/2017	Medical Policy Implementation Committee approval. New Policy.
 Medical Policy Implementation Committee approval. No change to coverage. Medical Policy Committee review Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update Update Update Coding Update Medical Policy Committee review <li< td=""><td>04/05/2018</td><td>Medical Policy Committee review</td></li<>	04/05/2018	Medical Policy Committee review
 Medical Policy Committee review Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. Medical Policy Committee review Medical Policy C	04/18/2018	Medical Policy Implementation Committee approval. No change to coverage.
 04/24/2019 Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to the policy. Updated background and rationale information. Removed summary section at the end of the policy. 04/02/2020 Medical Policy Committee review 04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/05/2022 Medical Policy Committee review 05/05/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update Rationale section with most recent literature. 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility 	04/04/2019	Medical Policy Committee review
 the policy. Updated background and rationale information. Removed summary section at the end of the policy. 04/02/2020 Medical Policy Committee review 04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Committee review 	04/24/2019	Medical Policy Implementation Committee approval. Added a new drug, Yutiq, to
 section at the end of the policy. 04/02/2020 Medical Policy Committee review 04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update Policy Implementation Committee approval. Coverage eligibility unchanged. Update Policy Implementation Committee approval. Coverage eligibility unchanged. Update Policy Committee review 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility 		the policy. Updated background and rationale information. Removed summary
 04/02/2020 Medical Policy Committee review 04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update Policy Implementation committee approval. Coverage eligibility unchanged. Update Policy Implementation committee approval. Coverage eligibility unchanged. Update Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 		section at the end of the policy.
 04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Committee review 05/10/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update Policy Committee review 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Committee review 	04/02/2020	Medical Policy Committee review
 unchanged. 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility 	04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility
 04/01/2021 Medical Policy Committee review 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Update 05/02/2024 Medical Policy Committee review 		unchanged.
 04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility 	04/01/2021	Medical Policy Committee review
 unchanged. 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility 	04/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility
 07/16/2021 Coding update 05/05/2022 Medical Policy Committee review 05/11/2022 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/02/2024 Medical Policy Implementation Committee approval. Coverage eligibility 		unchanged.
 Medical Policy Committee review Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. Coding Update Coding Update Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Coding Update Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility 	07/16/2021	Coding update
 Medical Policy Implementation Committee approval. Changed policy title from "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. Coding Update Coding Update Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility 	05/05/2022	Medical Policy Committee review
 "Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Committee review 05/10/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility 	05/11/2022	Medical Policy Implementation Committee approval. Changed policy title from
 Corticosteroid Products". Added a new product, Xipere, to the policy. Added information to the policy about suprachoroidal injections. 05/04/2023 Medical Policy Committee review 05/10/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility 		"Intravitreal Corticosteroid Implants" to "Intravitreal and Suprachoroidal
 information to the policy about suprachoroidal injections. Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature. Coding Update Coding Update Coding Update Medical Policy Committee review Medical Policy Committee review Medical Policy Committee review Medical Policy Implementation Committee approval. Coverage eligibility 		Corticosteroid Products". Added a new product, Xipere, to the policy. Added
05/04/2023Medical Policy Committee review05/10/2023Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature.06/20/2023Coding Update12/12/2023Coding Update05/02/2024Medical Policy Committee review05/08/2024Medical Policy Implementation Committee approval. Coverage eligibility		information to the policy about suprachoroidal injections.
05/10/2023Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated Rationale section with most recent literature.06/20/2023Coding Update12/12/2023Coding Update05/02/2024Medical Policy Committee review05/08/2024Medical Policy Implementation Committee approval. Coverage eligibility	05/04/2023	Medical Policy Committee review
 unchanged. Updated Rationale section with most recent literature. 06/20/2023 Coding Update 12/12/2023 Coding Update 05/02/2024 Medical Policy Committee review 05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility 	05/10/2023	Medical Policy Implementation Committee approval. Coverage eligibility
06/20/2023Coding Update12/12/2023Coding Update05/02/2024Medical Policy Committee review05/08/2024Medical Policy Implementation Committee approval. Coverage eligibility		unchanged. Updated Rationale section with most recent literature.
12/12/2023Coding Update05/02/2024Medical Policy Committee review05/08/2024Medical Policy Implementation Committee approval. Coverage eligibility	06/20/2023	Coding Update
05/02/2024Medical Policy Committee review05/08/2024Medical Policy Implementation Committee approval. Coverage eligibility	12/12/2023	Coding Update
05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility	05/02/2024	Medical Policy Committee review
	05/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility
unchanged.		unchanged.
05/01/2025 Medical Policy Committee review	05/01/2025	Medical Policy Committee review
05/13/2025 Medical Policy Implementation Committee approval. Updated literature review.	05/13/2025	Medical Policy Implementation Committee approval. Updated literature review.
Coverage eligibility unchanged.	N . G 1 1 1 1	Coverage eligibility unchanged.

Next Scheduled Review Date: 05/2026

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology $(CPT^{\$})^{\ddagger}$, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

<u></u>	
Code Type	Code
СРТ	67027, 67028, 67516 Delete code effective 01/01/2024: 0465T
HCPCS	J7311, J7312, J7313, J7314, J3299
ICD-10 Diagnosis	All Related Diagnoses

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

Policy # 00549 Original Effective Date: 04/19/2017 Current Effective Date: 06/01/2025

- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.