MASSACHUSETTS

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Medical Policy

Intravitreal and Punctum Corticosteroid Implants

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Policy Number: 272

BCBSA Reference Number: 9.03.23 (For Plan internal use only)
NDC/LCD: N/A

Related Policies

Aqueous Shunts and Stents for Glaucoma, #223

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

A fluocinolone acetonide intravitreal implant 0.59 mg (Retisert®) may be **MEDICALLY NECESSARY** for the treatment of:

- Chronic noninfectious intermediate, posterior, or panuveitis.

A fluocinolone acetonide intravitreal implant 0.18mg (Yutiq®) may be **MEDICALLY NECESSARY** for the treatment of:

- Chronic noninfectious uveitis affecting the posterior segment of the eye in individuals who are contraindicated or unable to tolerate standard medical therapy.[1]

A fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien®) may be considered **MEDICALLY NECESSARY** for the treatment of:

- Diabetic macular edema in individuals who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure.

A dexamethasone intravitreal implant 0.7 mg (Ozurdex™) may be **MEDICALLY NECESSARY** for the treatment of:

- Non-infectious ocular inflammation, or uveitis, affecting the intermediate or posterior segment of the eye, **OR**
- Macular edema following branch or central retinal vein occlusion, **OR**
- Diabetic macular edema.

A punctum dexamethasone insert 0.4 mg (Dextenza®) may be considered **MEDICALLY NECESSARY** for the treatment of:

- Ocular inflammation and pain following ophthalmic surgery.

A fluocinolone acetonide intravitreal implant 0.59 mg (Retisert®) or 0.19 mg (Iluvien®) or dexamethasone intravitreal implant 0.7 mg (Ozurdex™) is considered **INVESTIGATIONAL** for the treatment of:

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

A fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq®) is considered **INVESTIGATIONAL** for all other conditions.

All other uses of a corticosteroid intravitreal implant are considered **INVESTIGATIONAL**.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT Codes	Description
67027	Implantation of intravitreal drug delivery system (eg, ganciclovir implant), includes concomitant removal of vitreous

67028	Intravitreal injection of a pharmacologic agent (separate procedure)

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
J7311	Injection, fluocinolone acetonide, intravitreal implant (retisert), 0.01 mg
J7312	Injection, dexamethasone, intravitreal implant, 0.1 mg
J7313	Injection, fluocinolone acetonide, intravitreal implant (iluvien), 0.01 mg

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
E08.311	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy with macular edema
E08.3211	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, right eye
E08.3212	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, left eye
E08.3213	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E08.3219	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye
E08.3311	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E08.3312	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E08.3313	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E08.3319	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye
E08.3411	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, right eye
E08.3412	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, left eye
E08.3413	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E08.3419	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye
E08.3511	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, right eye
E08.3512	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, left eye
E08.3513	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, bilateral

E08.3519	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, unspecified eye
E09.311	Drug or chemical induced diabetes mellitus with unspecified diabetic retinopathy with macular edema
E09.3211	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E09.3212	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E09.3213	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E09.3219	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye
E09.3311	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E09.3312	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E09.3313	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E09.3319	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye
E09.3411	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E09.3412	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E09.3413	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E09.3419	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye
E09.3511	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E09.3512	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E09.3513	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E09.3519	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye
E10.311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.3211	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E10.3212	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E10.3213	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3311	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E10.3312	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E10.3411	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E10.3412	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E10.3413	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral

E10.3511	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E10.3512	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E10.3513	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11.3211	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E11.3219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye
E11.3311	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E11.3312	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E11.3313	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E11.3319	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye
E11.3411	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E11.3412	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E11.3413	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E11.3419	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye
E11.3511	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E11.3512	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E11.3513	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E11.3519	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye
E13.311	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema
E13.3211	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E13.3212	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E13.3213	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E13.3219	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye
E13.3311	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E13.3312	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye

E13.3313	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E13.3319	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye
E13.3411	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E13.3412	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E13.3413	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E13.3419	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye
E13.3511	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E13.3512	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E13.3513	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E13.3519	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye
H05.00	Unspecified acute inflammation of orbit
H05.10	Unspecified chronic inflammatory disorders of orbit
H20.9	Unspecified iridocyclitis
H30.001	Unspecified focal chorioretinal inflammation, right eye
H30.002	Unspecified focal chorioretinal inflammation, left eye
H30.003	Unspecified focal chorioretinal inflammation, bilateral
H30.011	Focal chorioretinal inflammation, juxtapapillary, right eye
H30.012	Focal chorioretinal inflammation, juxtapapillary, left eye
H30.013	Focal chorioretinal inflammation, juxtapapillary, bilateral
H30.021	Focal chorioretinal inflammation of posterior pole, right eye
H30.022	Focal chorioretinal inflammation of posterior pole, left eye
H30.023	Focal chorioretinal inflammation of posterior pole, bilateral
H30.029	Focal chorioretinal inflammation of posterior pole, unspecified eye
H30.031	Focal chorioretinal inflammation, peripheral, right eye
H30.032	Focal chorioretinal inflammation, peripheral, left eye
H30.033	Focal chorioretinal inflammation, peripheral, bilateral
H30.041	Focal chorioretinal inflammation, macular or paramacular, right eye
H30.042	Focal chorioretinal inflammation, macular or paramacular, left eye
H30.043	Focal chorioretinal inflammation, macular or paramacular, bilateral
H30.101	Unspecified disseminated chorioretinal inflammation, right eye
H30.102	Unspecified disseminated chorioretinal inflammation, left eye
H30.103	Unspecified disseminated chorioretinal inflammation, bilateral
H30.111	Disseminated chorioretinal inflammation of posterior pole, right eye
H30.112	Disseminated chorioretinal inflammation of posterior pole, left eye
H30.113	Disseminated chorioretinal inflammation of posterior pole, bilateral
H30.119	Disseminated chorioretinal inflammation of posterior pole, unspecified eye
H30.121	Disseminated chorioretinal inflammation, peripheral right eye
H30.122	Disseminated chorioretinal inflammation, peripheral, left eye
H30.123	Disseminated chorioretinal inflammation, peripheral, bilateral
H30.141	Acute posterior multifocal placoid pigment epitheliopathy, right eye
H30.142	Acute posterior multifocal placoid pigment epitheliopathy, left eye
H30.143	Acute posterior multifocal placoid pigment epitheliopathy, bilateral

H30.21	Posterior cyclitis, right eye
H30.22	Posterior cyclitis, left eye
H30.23	Posterior cyclitis, bilateral
H30.811	Harada's disease, right eye
H30.812	Harada's disease, left eye
H30.813	Harada's disease, bilateral
H30.891	Other chorioretinal inflammations, right eye
H30.892	Other chorioretinal inflammations, left eye
H30.893	Other chorioretinal inflammations, bilateral
H30.899	Other chorioretinal inflammations, unspecified eye
H30.90	Unspecified chorioretinal inflammation, unspecified eye
H30.91	Unspecified chorioretinal inflammation, right eye
H30.92	Unspecified chorioretinal inflammation, left eye
H30.93	Unspecified chorioretinal inflammation, bilateral
H34.8110	Central retinal vein occlusion, right eye, with macular edema
H34.8120	Central retinal vein occlusion, left eye, with macular edema
H34.8130	Central retinal vein occlusion, bilateral, with macular edema
H34.8310	Tributary (branch) retinal vein occlusion, right eye, with macular edema
H34.8320	Tributary (branch) retinal vein occlusion, left eye, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.9	Unspecified retinal vascular occlusion
H35.81	Retinal edema
H44.111	Panuveitis, right eye
H44.112	Panuveitis, left eye
H44.113	Panuveitis, bilateral
H44.119	Panuveitis, unspecified eye

The above <u>medical necessity criteria MUST</u> be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
J7314	Injection, fluocinolone acetonide, intravitreal implant (Yutiq), 0.01 mg

The following ICD Diagnosis Codes are considered medically necessary when submitted with the HCPCS code above if <u>medical necessity criteria</u> are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
H30.021	Focal chorioretinal inflammation of posterior pole, right eye
H30.022	Focal chorioretinal inflammation of posterior pole, left eye
H30.023	Focal chorioretinal inflammation of posterior pole, bilateral
H30.111	Disseminated chorioretinal inflammation of posterior pole, right eye
H30.112	Disseminated chorioretinal inflammation of posterior pole, left eye
H30.113	Disseminated chorioretinal inflammation of posterior pole, bilateral

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
J7314	Injection, fluocinolone acetonide, intravitreal implant (Yutiq), 0.01 mg

CPT Codes

CPT codes:	Code Description
0356T	Insertion of drug-eluting implant (including punctal dilation and implant removal when performed) into lacrimal canaliculus, each

HCPCS Codes

HCPCS codes:	Code Description
J1096	Dexamethasone, lacrimal ophthalmic insert, 0.1 mg

Description

Eye Conditions

Uveitis

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

The classification scheme recommended by the Uveitis Study Group and the Standardization of Uveitis Nomenclature Working Group is based on anatomic location. Individuals 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). Individuals with intermediate or posterior uveitis typically experience minimal pain, decreased visual acuity, and the presence of floaters (bits of vitreous debris or cells that cast shadows on the retina). Chronic inflammation associated with posterior segment uveitis can lead to cataracts, glaucoma, and structural damage to the eye, resulting in severe and permanent vision loss.

Treatment

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

Macular Edema After Retinal Vein Occlusion

Retinal vein occlusions are classified by whether the central retinal vein or one of its branches is obstructed. Central retinal vein occlusion and branch retinal vein occlusion differ in pathophysiology, clinical course, and therapy. Central retinal vein occlusions are categorized as ischemic or nonischemic. Ischemic central retinal vein occlusions are referred to as severe, complete, or total vein obstruction, and

account for 20% to 25% of all central retinal vein occlusions. Macular edema and permanent macular dysfunction occur in virtually all individuals with ischemic central retinal vein occlusion, and in many individuals with nonischemic central retinal vein occlusion. Branch retinal vein occlusion is a common retinal vascular disorder in adults between 60 and 70 years of age and occurs approximately 3 times more often than central retinal vein occlusion.

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

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

Diabetic Macular Edema
Diabetic retinopathy is a common microvascular complication of diabetes and a leading cause of blindness in adults. The 2 most serious complications for vision are diabetic macular edema and proliferative diabetic retinopathy. At its earliest stage (nonproliferative retinopathy), microaneurysms occur. As the disease progresses, blood vessels that nourish the retina are blocked, triggering the growth of new and fragile blood vessels (proliferative retinopathy). Severe vision loss with proliferative retinopathy arises from leakage of blood into the vitreous. Diabetic macular edema is characterized by swelling of the macula due to gradual leakage of fluids from blood vessels and breakdown of the blood-retinal barrier. Moderate vision loss can arise from the fluid accumulating in the center of the macula (macular edema) during the proliferative or nonproliferative stages of the disease. Although proliferative disease is the main blinding complication of diabetic retinopathy, macular edema is more frequent and is the leading cause of moderate vision loss in people with diabetes.

Treatment
Tight glycemic and blood pressure control is the first line of treatment to control diabetic retinopathy, followed by laser photocoagulation for individuals whose retinopathy is approaching the high-risk stage. Although laser photocoagulation is effective at slowing the progression of retinopathy and reducing visual loss, it does not restore lost vision. Alternatives to intravitreal implants include intravitreal injection of triamcinolone acetonide, which is used as off-label adjunctive therapy for diabetic macular edema. 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 diabetic macular edema.

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

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

Intravitreal and Punctum Implants

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

Selection of the route of corticosteroid administration (topical, systemic, periocular, or intraocular injection) is based on the cause, location, and severity of the disease. Each therapeutic approach has drawbacks. For example, topical corticosteroids require frequent (eg, hourly) administration and may not adequately penetrate the posterior segment of the eye due to their poor ability to penetrate ocular tissues. Systemically administered drugs penetrate poorly into the eye because of the blood-retinal barrier, and high-dose or long-term treatments may be necessary. Long-term systemic therapies can be associated with substantial adverse events such as hypertension and osteoporosis, while repeated (every 4-6 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 increase ocular toxicity due to increased corticosteroid concentrations in the eye over a longer duration. With any route of administration, cataracts are a frequent complication of long-term corticosteroid therapy.

Intraocular corticosteroid implants being evaluated include:

- Retisert (nonbiodegradable fluocinolone acetonide intravitreal implant; Bausch & Lomb) is a sterile implant that consists of a tablet containing fluocinolone acetonide 0.59 mg, a synthetic corticosteroid that is less soluble in aqueous solution than dexamethasone. The tablet is encased in a silicone elastomer cup with a release orifice and membrane; the entire elastomer cup assembly is attached to a suture tab. Following implantation (via pars plana incision and suturing) in the vitreous, the implant releases the active drug at a rate of 0.3 to 0.4 µg/d over 2.5 years.
- ILUVIEN (nonbiodegradable injectable intravitreal implant with fluocinolone acetonide; Alimera Sciences) is a rod-shaped device made of polyimide and polyvinyl alcohol. It is small enough to be placed using a 25-gauge applicator. It is expected to provide sustained delivery of fluocinolone acetonide for up to 3 years.
- Ozurdex (previously known as Posurdex; biodegradable dexamethasone intravitreal implant; Allergan, Irvine, CA) is composed of a biodegradable copolymer of lactic acid and glycolic acid with micronized dexamethasone. This implant is placed into the vitreous cavity through the pars plana using a customized, single-use, 22-gauge applicator. The implant provides intravitreal dexamethasone for up to 6 months. The mean number of Ozurdex injections reported in the literature is 4.2 injections per year, and more than 6 consecutive injections have been reported.[1,2]
- Dextenza® (biodegradable dexamethasone intracanalicular insert; Ocular Therapeutix™) is a rod-shaped hydrogel device that is designed to deliver a sustained and tapered release of 0.4 mg of dexamethasone over 4 weeks. Following ophthalmic surgery, it is inserted through the inferior punctum into the canaliculus of the operative eye. To allow for visualization and retention monitoring, the hydrogel device is conjugated with fluorescein. No removal is required as the device is designed to resorb and exit the nasolacrimal system independently.
- Yutiq (non-biodegradable fluocinolone acetonide intravitreal implant; EyePoint Pharmaceuticals U.S., Inc.) is a sterile 3.3 mm-long implant consisting of fluocinolone acetonide 0.18 mg that is preloaded into a single-dose applicator and injected directly into the vitreous. It is designed to provide a sustained release of fluocinolone acetonide at an initial rate of 0.25 mcg/day within over a 36-month period.

Summary

An intravitreal implant is a drug delivery system, injected or surgically implanted in the vitreous of the eye, for sustained release of a pharmacologic agent to the posterior and intermediate segments of the eye.

Four intravitreal corticosteroid implants, ie, fluocinolone acetonide 0.59 mg (Retisert), fluocinolone acetonide 0.18 mg (Yutiq), fluocinolone acetonide 0.19 mg (Iluvien), and dexamethasone 0.7 mg (Ozurdex), are reviewed herein. Fluocinolone acetonide implants are nonerodible and deliver drug up to 30 to 36 months while dexamethasone implants are bioerodible and last up to 6 months.

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

Uveitis

For individuals with chronic noninfectious intermediate or posterior uveitis who receive an intravitreal fluocinolone acetonide implant (0.59 mg), the evidence includes 4 randomized controlled trials (RCTs). Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. 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 intravitreal fluocinolone acetonide implants in preventing recurrence and improving visual acuity over 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. After 24 and 54 months of follow-up, visual acuity improved from baseline in the implant groups compared with the systematic therapy groups by +6.0 and +3.2 letters (p=0.16) and +2.4 and 3.1 letters (p=0.073), respectively. However, nearly all phakic individuals receiving implants developed cataracts and required cataract surgery. Further, most also developed glaucoma, with 75% of individuals requiring intraocular pressure lowering medications and 35% requiring filtering surgeries. Systemic adverse events such as hyperlipidemia, diabetes, osteoporosis, fractures, and blood count/chemistry abnormalities were infrequent and not statistically distinguishable between groups. The incidence of hypertension was greater in the systemic therapy group (27%) than in the implant group (13%), but rates of antihypertensive treatment initiation did not differ. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with noninfectious intermediate or posterior uveitis who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes an RCT. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Results of this trial at 8 weeks showed that the implant was effective in reducing inflammation (the proportion of eyes with no inflammation was 47% and 12% with implant and sham, respectively) and resulted in clinically meaningful improvement in vision at week 8 compared with sham controls (the proportion of individuals with a gain of ≥15 letters in best-corrected visual acuity from baseline was »40% with implants and 10% with sham). Further, at week 26, individuals treated with implants reported meaningful increases in vision-related functioning. The major limitation of this trial was its lack of long-term follow-up. Use of implants resulted in higher incidences of cataracts and elevated intraocular pressure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with chronic noninfectious posterior uveitis affecting the posterior segment of the eye and who receive intravitreal fluocinolone acetonide implant (0.18 mg, Yutiq), the evidence includes 3 pivotal RCTs. Relevant outcomes are symptom improvement, change in disease status, functional status, and quality of life. Harmful outcomes of interest are treatment related adverse events and treatment-related morbidity. RCTs consistently found statistically significantly lower uveitis recurrence rates for intravitreal fluocinolone acetonide implant (0.18 mg, Yutiq) at both 6 and 12 months in 2 pivotal trials. Clinical outcomes from Jaffe et. all, demonstrated lower rates of recurrence compared to shame, longer periods of time to first recurrence and less adjunctive therapy. When compared to alternative treatment options, the benefits of Yutiq include in office implantation, faster recovery periods, and sustained treatment effect for up to 36 months. Yutiq is also associated with decreased adverse events, such as cataracts and intraocular pressure, compared other forms of fluocinolone acetonide implants due to lower implant dose. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Macular Edema
For individuals with macular edema after retinal vein occlusion who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Compared with sham controls, implants resulted in clinically meaningful improvements in visual acuity within 1 to 3 months postimplant and improvement in vision occurred faster. The difference in the proportion of individuals with gain of 15 or more letters in best-corrected visual acuity from baseline was more than 10% in favor implants versus sham in both studies at 30, 60 and 90 days, but not at 180 days postimplant. Use of implants resulted in higher incidences of cataracts and elevated intraocular pressure. Several additional RCTs and a meta-analysis have evaluated the comparative effects of dexamethasone intravitreal implants versus other therapies and found mixed results. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with macular edema after retinal vein occlusion who receive an intravitreal fluocinolone acetonide implant (0.59 mg), no studies were identified. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Diabetic Macular Edema
For individuals with refractory (persistent or recurrent) diabetic macular edema who receive an intravitreal fluocinolone acetonide implant (0.59 mg), the evidence includes an RCT. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Compared with the standard of care (as needed laser or observation), a greater proportion of individuals with implants reported clinically significant improvement in vision at 6 months (1.4% vs. 16.8% respectively) and subsequent time points assessed but not at or beyond 30 months of follow-up. Ninety percent of individuals with phakic eyes who received implants required cataract surgery, and 60% developed elevated intraocular pressure. Due to the substantial increase in adverse events and availability of agents with better tolerability profiles (eg, antivascular endothelial growth factor inhibitors), implant use in diabetic macular edema is questionable. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with diabetic macular edema who receive an intravitreal fluocinolone acetonide implant (0.19 mg), the evidence includes 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Implant-treated eyes showed clinically meaningful improvements in the vision at 2 and 3 years postimplant. The percentage of individuals who gained 15 letters or more was 28.7% in the implant group versus 18.9% in the sham group at 3 years. Subgroup analysis showed greater improvements in visual acuity in individuals who were pseudophakic compared with those who were phakic (difference in mean change in number of letters at 2 years from baseline was 5.6 letters in pseudophakic individuals vs. 1 letter in phakic individuals). A major limitation of these implants is that nearly 80% of all phakic individuals will develop cataracts and will require cataract surgery. Further, intraocular pressure was elevated in 34% of individuals who received this implant compared with 10% of controls. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with diabetic macular edema who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes 3 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Compared with sham control, 2 identically designed RCTs showed clinically meaningful improvements in vision with dexamethasone implants that peaked at 3 months and maintained 39 months (with retreatment). The difference in the proportion of individuals with a gain of 15 or more letters in best-corrected visual acuity from baseline was 9.3% and 13.0% in the 2 trials, respectively, favoring implant versus sham at 39 months postimplant. Subgroup analysis of these trials showed greater improvements in visual acuity in individuals who were pseudophakic compared with those who were phakic. Additionally, evidence from various small and/or short-term trials and retrospective studies have found that, compared with primarily antivascular endothelial growth factor 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. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with diabetic macular edema who receive an intravitreal dexamethasone implant (0.7 mg) plus antivascular endothelial growth factor therapy, the evidence includes 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Findings from both RCTs were consistent in demonstrating that although adding dexamethasone to an antivascular endothelial growth factor treatment can lead to a greater mean reduction in central subfield thickness, it does not improve visual acuity and can lead to a higher risk of intraocular pressure elevation.Based on the consistent lack of improvement in visual acuity, increased risk of intraocular pressure elevation, and imprecision, these RCTs provide insufficient evidence to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with diabetic macular edema who receive an intravitreal dexamethasone implant (0.7 mg) plus laser photocoagulation, the evidence includes an RCT. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. One RCT with 1-year follow-up demonstrated that combination implants plus laser photocoagulation compared with laser photocoagulation alone resulted in better visual acuity (as measured by a gain of ≥10 letters) at 9 months but not at 12 months. However, the generally accepted standard outcome measure for change is 15 or more letters, and this standard was not used in this trial. The use of dexamethasone implants resulted in higher incidences of cataracts and elevated intraocular pressure. Further, a differential loss to follow-up, lack of power calculations for sample size estimation, and lack of intention-to-treat analysis preclude interpretation of results. A larger RCT with adequate power is needed to confirm these findings. The evidence is insufficient to determine the effects of the technology on health outcomes.

Age-Related Macular Degeneration
For individuals with age-related macular degeneration who receive an intravitreal dexamethasone implant (0.7 mg) plus antivascular endothelial growth factor inhibitor, the evidence includes an RCT. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Results of this trial did not demonstrate clinically meaningful reductions in the ranibizumab injection-free interval between combined treatments (34 days) and antivascular endothelial growth factor alone (29 days; p=0.016). Further, intraocular pressure was elevated in a greater proportion of individuals receiving implants without any additional clinical benefit. The evidence is insufficient to determine the effects of the technology on health outcomes.

Other Conditions
For individuals with birdshot retinochoroidopathy refractory or intolerant to standard therapy who receive an intravitreal fluocinolone acetonide implant (0.59 mg) or intravitreal dexamethasone implant (0.7 mg), the evidence includes multiple observational studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Multiple observational studies have noted improvements in anatomic and visual acuity outcomes. Long-term follow-up for efficacy and safety is limited. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in individuals with refractory or intolerant birdshot retinopathy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with cystoid macular edema related to retinitis pigmentosa who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes a small observation-controlled RCT, a small prospective, oral acetazolamide-controlled cohort study, and multiple case reports. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Studies have noted mixed results for anatomic and visual acuity outcomes. Long-term follow-up for efficacy and safety is limited. Larger RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in individuals with cystoid macular edema related to retinitis pigmentosa. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with idiopathic macular telangiectasia type 1 who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes multiple case reports. Relevant outcomes are symptoms, change

in disease status, functional outcomes, quality of life, and treatment-related morbidity. Case reports have noted mixed results for visual acuity and inflammation-related outcomes. Long-term follow-up for 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 individuals with idiopathic macular telangiectasia type 1. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with postoperative chronic macular edema who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes multiple observational studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Among the multiple observational studies, a large retrospective analysis of 100 individuals showed that 2 of every 5 individuals experienced clinically meaningful improvements in the vision at 1-year follow-up. An RCT is needed to confirm the efficacy of corticosteroid implants in individuals with postoperative chronic macular edema. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with circumscribed choroidal hemangiomas who receive an intravitreal dexamethasone implant (0.7 mg) plus photodynamic therapy, the evidence includes a case report. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Results of the case report do not permit conclusions about the efficacy or safety of adding dexamethasone implants for circumscribed choroidal hemangiomas to photodynamic therapy. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in this population. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with proliferative vitreoretinopathy who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes a case series and a case report. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. These studies have 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 individuals with proliferative retinopathy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with radiation retinopathy who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes multiple observational studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Multiple observational studies have noted improvements in anatomic and visual acuity outcomes. Long-term follow-up for efficacy and safety is limited. RCTs are needed to permit conclusions on the efficacy of corticosteroid implants in individuals with radiation retinopathy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals scheduled to undergo clear corneal cataract surgery who receive punctum dexamethasone insert (0.4 mg), the evidence includes 3 RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. All 3 trials noted significant improvements with the punctum dexamethasone insert (0.4 mg) across both coprimary efficacy endpoints of absence of pain at 8 days and absence of anterior chamber cells at day 14. Adverse events were generally similar between punctum dexamethasone insert (0.4 mg) and sham. Based on the consistent benefits and lack of important increases in adverse event risk, evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery who receive prophylaxis with intravitreal dexamethasone 0.7 mg (Ozurdex), the best evidence includes 1 single-center, open-label RCT of 43 individuals in India. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Compared with oral corticosteroids, intravitreal dexamethasone 0.7 mg had similar benefits and avoided need for early steroid taper due to adverse effects on blood glucose, but potentially increased risk of developing intraocular pressure. Due to important study limitations including its small sample size, unclear allocation concealment methods and lack of blinding, evidence is insufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Policy History

Date	Action
5/2022	Annual policy review. Editorial refinement to policy statement. Policy intent unchanged.
1/2022	New medically necessary indications added for fluocinolone acetonide 0.18 mg (Yutiq) for noninfectious posterior uveitis. Clarified coding information. 1/2022.
4/2021	Annual policy review. References updated. Policy statements unchanged.
8/2020	Annual policy review. Added new policy statements for all 3 new indications – medically necessary for Dextenza for individuals with ocular inflammation and pain following ophthalmic surgery; investigational for Yutiq for treatment of chronic noninfectious posterior uveitis affecting the posterior segment of the eye, and investigational for prophylactic Ozurdex for individuals with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery. Policy title changed. Clarified coding information. Effective 8/1/2020.
1/2020	Clarified coding information.
10/2019	Clarified coding information.
4/2019	Annual policy review. Description, summary and references updated. Policy statements unchanged.
4/2018	Annual policy review. New references added.
3/2018	Clarified coding information.
10/2017	Clarified coding information.
8/2017	Annual policy review. New investigational indications described. Policy statements revised to include the dose of dexamethasone intravitreal implant and fluocinolone acetonide intravitreal implant. Clarified coding information. Effective 8/1/2017.
7/2016	Annual policy review. Minor corrections made to language for consistency throughout.
4/2016	Annual policy review. New references added.
1/2016	Annual policy review. New references added.
3/2015	Annual policy review. New medically necessary indications described. Clarified coding information. Effective 3/1/2015.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes. Effective 10/2015.
5/2014	Annual policy review. New references added.
5/2013	Annual policy review. New references added.
2/2013	Annual policy review. Changes to policy statement. Effective 2/4/2013.
11/2011 -4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/1/2011	Annual policy review. Changes to policy statement. Effective 12/1/2011.
3/1/2011	New Medical Policy 272 effective 3/1/2011describing covered and non-covered indications.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

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Endnotes

[1] Based on expert opinion