Clinical Policy Bulletin:
Ozurdex (Dexamethasone Intravitreal Implant)

Number: 0795

Policy

Aetna considers Ozurdex (dexamethasone intravitreal implant) medically necessary for the treatment of the following indications:

- Macular edema secondary to branch or central retinal vein occlusion
- Non-infectious uveitis affecting the posterior segment of the eye
- Diabetic macular edema (DME)

Aetna considers Ozurdex experimental and investigational for the treatment of the following indications (not an all inclusive list) because of insufficient evidence of its effectiveness for these indications:

- Coats' disease
- Macular edema secondary to idiopathic retinal vasculitis, aneurysms, neuroretinitis (IRVAN) syndrome, or retinitis pigmentosa
- Pseudophakic macular edema (Irvine-Gass syndrome) except for pseudophakic persons with DME.

Ozurdex is contraindicated and considered unproven in individuals with advanced glaucoma and ocular or periocular infections.

See also CPB 0719 - Retisert (Fluocinolone Acetonide Intra-vitreal Implant).

Background

Retinal vein occlusion is a blockage of a portion of the venous circulation that drains the retina and is second only to diabetic retinopathy as the most common retinal vascular cause of visual loss. It generally does not occur until later in life and may have several causes, including: hypertension, atherosclerosis, diabetes,
and glaucoma. When a blockage occurs, pressure builds up in the capillaries causing hemorrhages and leakage of fluid and blood. This can lead to macular edema (ME) and ischemia of the macula. There are 2 basic types of retinal vein occlusion: central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). Central retinal vein occlusion is obstruction of the retinal vein at the optic nerve and BRVO is obstruction of a portion of the venous circulation that drains the retina. Central vein occlusion can also be further categorized as either ischemic or non-ischemic. Most individuals with ischemic CRVO develop the complications of ME that ultimately lead to blindness. The non-ischemic type maintains better blood flow to the retina through collateral circulation, thus, preventing the dreaded complications of the ischemic type. Branch retinal vein occlusion occurs 3 times more often than CRVO and may include both systemic factors (e.g., hypertension) as well as local anatomic factors (e.g., arterio-venous crossings).

While there are similarities in the pathogenesis and clinical nature of both forms of retinal vein occlusion, each has unique etiologies, differential diagnosis, management and prognosis. Central retinal vein occlusion is difficult to treat. No known effective treatment is available for either the prevention or treatment of CRVO. Pan-retinal photocoagulation (PRP) has been used in the treatment of neovascular complications of CRVO, however, no definite guidelines exist regarding the exact indication and timing of PRP. Other treatments with varying degrees of success include: aspirin, anti-inflammatory agents, isovolemic hemodilution, plasmapheresis, systemic anti-coagulation, fibrinolytic agents, systemic corticosteroids, local anti-coagulation with intravitreal injection of alteplase, intravitreal injection of triamcinolone, and intravitreal injection of bevacizumab.

Mohamed et al (2007) assessed the evidence for the effectiveness of interventions to improve visual acuity (VA) and prevent or treat neovascularization secondary to CRVO. Randomized controlled trials (RCTs) of more than 3 months’ follow-up comparing intervention with a control group were included for review. The authors reviewed 17 RCTs that met their inclusion criteria. They evaluated 4 RCTs on laser photocoagulation and reported that grid macular laser photocoagulation did not improve VA in CRVO with ME. Prophylactic PRP did not prevent angle and iris neovascularization in ischemic CRVO, but resulted in regression of angle and iris neovascularization and reduced progression to neovascular glaucoma. Four RCTs reported improvement in VA with in-patient hemodilution, 2 RCTs demonstrated no significant improvement, and 1 RCT showed deterioration in VA after out-patient hemodilution. Randomized clinical trials evaluating ticlodipine, troxerutin, and streptokinase showed limited or no benefit. The authors concluded that (i) there is limited level I evidence for any intervention to improve VA in patients with CRVO, (ii) PRP resulted in regression of neovascularization, and (iii) hemodilution may improve vision in some patients, but data are conflicting. The authors stated in their conclusion that more robust RCTs evaluating current treatments for CRVO are needed.

A Cochrane systematic review on the use of intravitreal steroids versus observation for CRVO-ME (Gewaily and Greenberg, 2009) found no relevant RCTs and concluded that "[t]here is inadequate evidence for the use of intravitreal
steroids for CRVO-ME due to a paucity of RCTs and well-designed observational studies on the topic; therefore, it is still an experimental procedure."

The Standard Care versus Corticosteroid for Retinal Vein Occlusion (SCORE) study, a phase III clinical trial conducted at 84 clinical sites and supported by the National Eye Institute (NEI) at the National Institutes of Health (NIH), included participants with CRVO (n = 271) and BRVO (n = 411) in 2 separate trials. The SCORE study reported that intravitreal injections of a corticosteroid medication could reduce vision loss due to CRVO-ME and that treated patients were also 5 times more likely to regain vision after 1 year than patients who were under observation. The study compared intravitreal triamcinolone (1 mg and 4 mg doses) versus observation for eyes with vision loss associated with CRVO-ME. Of those participants in the observation, 1 mg, and 4 mg groups, 7 %, 27 %, and 26 % achieved the primary outcome measure of a gain in VA letter score of 15 or more from baseline to month 12, respectively. The odds of achieving the primary outcome were 5.0 times greater in the 1 mg group than the observation group (odds ratio [OR], 5.0; 95 % confidence interval [CI]: 1.8 to 14.1; p = 0.001) and 5.0 times greater in the 4 mg group than the observation group (OR, 5.0; 95 % CI: 1.8 to 14.4; p = 0.001); there was no difference identified between the 1 mg and 4 mg groups (OR, 1.0; 95 % CI: 0.5 to 2.1; p = 0.97). The rates of elevated intra-ocular pressure and cataract were similar for the observation and 1 mg groups, but higher in the 4 mg group. The authors concluded that intra-vitreal triamcinolone is superior to observation for treating vision loss associated with CRVO-ME in patients who have characteristics similar to those in the SCORE-CRVO trial. The 1-mg dose has a safety profile superior to that of the 4-mg dose. The authors concluded that intra-vitreal triamcinolone in a 1-mg dose, following the re-treatment criteria applied in the SCORE study should be considered for up to 1 year, and possibly 2 years, for patients with characteristics similar to those in the SCORE-CRVO trial (Ip et al, 2009).

In general, BRVO has a good prognosis. Between 50 to 60 % of patients report a final VA of 20/40 or better without treatment. Thus, comparative studies are necessary to determine whether improvements in VA are a result of the procedure or simply the natural course of the condition. Laser photocoagulation, as demonstrated by the Branch Vein Occlusion Study (BVOS; Scott et al, 2009), is the gold standard for the treatment of ME and ocular neovascularization following BRVO. However, the limited functional outcomes achievable by means of laser treatment have prompted researchers to try alternative options.

McIntosh et al (2007) assessed the evidence for the effectiveness of interventions to improve VA and to treat neovascularization secondary to BRVO and/or BRVO-ME. Randomized clinical trials with more than 3 months’ follow-up were included for review. The authors reviewed 12 RCTs that met their inclusion criteria. The authors evaluated 5 RCTs on laser photocoagulation and reported that grid macular laser photocoagulation was effective in improving VA in 1 large multi-center RCT (the BVOS study, Scott et al, 2009), but 2 smaller RCTs found no significant difference. The BVOS study found that scatter retinal laser photocoagulation was effective in preventing neovascularization and vitreous hemorrhage in patients with neovascularization, but a subsequent RCT found no significant effect. Randomized clinical trials evaluating intravitreal steroids (n = 2), hemodilution (n = 3), ticlopidine (n = 1), and troxerutin (n = 1) showed limited or no
benefit. The authors concluded that (i) there is limited level I evidence for any interventions for BRVO, (ii) the BVOS study showed that macular grid laser photocoagulation is an effective treatment for ME and improved vision in eyes with VA of 20/40 to 20/200, and (iii) scatter laser photocoagulation can effectively treat neovascularization. The authors concluded that the effectiveness of many new treatments is not supported by current evidence.

The SCORE-BRVO trial evaluated the use of 2 different dosages of intravitreal triamcinolone for treating vision loss from BRVO-ME and reported that laser treatment is safer than corticosteroid injections and is equally effective. The study compared intravitreal triamcinolone (1-mg and 4-mg doses) with standard of care (i.e., grid photocoagulation in eyes without dense macular hemorrhage and deferral of photocoagulation until hemorrhage clears in eyes with dense macular hemorrhage) for eyes with vision loss associated with BRVO-ME (n = 411). Of those participants in the standard care, 1-mg, and 4-mg groups, 29 %, 26 %, and 27 % achieved the primary outcome measure of a gain in VA letter score of 15 or more from baseline to month 12, respectively. None of the pair-wise comparisons between the 3 groups was statistically significant at month 12. The rates of elevated intraocular pressure and cataract were similar for the standard care and 1 mg groups, but higher in the 4 mg group. The authors found no difference in VA at 12 months for the standard care group compared with the triamcinolone groups; however, rates of adverse events (particularly elevated intraocular pressure and cataract) were highest in the 4 mg group. The authors concluded that photocoagulation as applied in the SCORE study remains the standard of care for patients with vision loss associated with BRVO-ME who have characteristics similar to participants in the SCORE-BRVO trial and that grid photocoagulation should remain the benchmark against which other treatments are compared in clinical trials for eyes with vision loss associated with BRVO-ME (Scott et al, 2009).

Several processes have been implicated in the breakdown of the blood-retinal barrier that leads to ME, including the production of inflammatory mediators (e.g., prostaglandins and interleukin-6), increased amounts of vascular permeability factors (e.g., vascular endothelial growth factor) and the loss of endothelial tight junction proteins. Corticosteroids are thought to have beneficial effects on these processes, but delivering therapeutic concentrations of any medication to the retina while limiting systemic exposure presents a challenge. Intra-vitreal injections of the corticosteroid triamcinolone have shown promise in the treatment of ME. Dexamethasone, a more potent corticosteroid than triamcinolone, has been shown to produce high intra-vitreal levels of the drug, however, a short intraocular half-life after intra-vitreal injection (approximately 3 hours) has led to the investigation of other delivery methods.

Ozurdex (dexamethasone intra-vitreal implant) (Allergan, Irvine, CA) was approved by the U.S. Food and Drug Administration (FDA) in June 2009 for the treatment of ME associated with CRVO or BRVO. The rod-shaped biodegradable intra-vitreal implant contains 0.7 mg of dexamethasone and is injected directly into the eye (vitreous) through a small pars plana incision or puncture. A solid polymer drug delivery system called Novadur (Allergan, Irvine, CA) gradually releases dexamathasone for up to 6 months. Biodegradable polymers release the drug as they themselves degrade and are finally absorbed within the body.
The FDA's approval of Ozurdex was based on results from 2 randomized, double-masked, multi-center clinical studies (n = 853). The studies demonstrated a statistically significant improvement in 3 or more lines of VA in approximately 20 to 30 % of treated patients within 60 days post-implantation compared to sham. The duration of improvement continued for approximately 30 to 90 days and was effective in both CRVO and BRVO. The most significant adverse effect was an increase in intra-ocular pressure that occurred in 106 patients (25 %), which peaked at 60 days and returned to baseline levels by day 180. Three patients (0.7 %) required laser or surgical procedures as a result. Conjunctival hemorrhage occurred in 85 patients (20 %). Ozurdex is the first FDA-approved therapy for ME related to retinal vein occlusion. The proposed benefit of a sustained-release intra-vitreal corticosteroid insert such as Ozurdex is the potential for fewer injections. Intra-vitreal injections have been associated with endophthalmitis, eye inflammation, increased intra-ocular pressure, and retinal detachments.

Williams et al (2009) evaluated the effects of a dexamethasone intravitreous drug delivery system (dexamethasone DDS) in a randomized, prospective, single-masked, controlled trial of patients with persistent (90 days or more) ME from uveitis or Irvine-Gass syndrome (n = 41). Patients were randomized to surgical placement of 0.35 mg or 0.7 mg dexamethasone DDS or observation. At day 90, the primary outcome measure of a 10-letter or more best corrected visual acuity (BCVA) improvement was achieved in the 0.35 mg group, 0.7 mg group, and the observation group (p = 0.029 versus the 0.7 mg group) in 41.7 % (5/12), 53.8 % (7/13) and 14.3 % (2/14) of patients, respectively. Improvement in VA persisted to day 180. A 15-letter or more improvement was achieved in 53.8 % (7/13) of 0.7 mg patients versus 7.1 % (1/14) of observed patients (p = 0.008). There were significantly greater reductions in fluorescein leakage in treated patients than in observed patients. Dexamethasone DDS was well-tolerated. Throughout the study, an increase in intra-ocular pressure of 10 mm Hg or more was observed in 5 of 13 patients in the 0.7 mg group, in 1 of 12 patients in the 0.35 mg group, and in no patients in the observation group. There were no reports of endophthalmitis. The authors concluded that dexamethasone DDS may be a promising new treatment option for patients with persistent ME resulting from uveitis or Irvine-Gass syndrome, however, further investigation of its clinical value in this patient population is warranted.

In June 2014, Ozurdex sustained-release, biodegradable dexamethasone intravitreal implant 0.7 mg was approved by the FDA for adult patients with diabetic macular edema who have artificial lens implants or are scheduled for cataract surgery (Allergan, 2014). The approval was based on the MEAD trial, which included two multicenter, 3-year, sham-controlled, masked, randomized clinical studies of patients with 15 or more letters improvement in best corrected visual acuity from baseline. The sustained-release biodegradable steroid implant uses a solid polymer to suppress the inflammation that causes diabetic macular edema by releasing the steroid over an extended period, without the need for monthly steroid injections. In September 2014, the FDA approved expanded indications for Ozurdex for the treatment of the general population of patients with diabetic macular edema (DME), based on ongoing review of clinical data demonstrating efficacy and safety.
The Ozurdex implant uses a biodegradable polymer implant that releases dexamethasone over an extended period of time to suppress inflammation, which plays a key role in the development of DME (Allergan, 2014). The most common adverse events in the studies of Ozurdex for DME included cataracts and elevated intraocular pressure. An increase in mean intraocular pressure was seen with each treatment cycle; mean pressure generally returned to baseline between treatment cycles. The labeling states that Ozurdex should not be used in persons with glaucoma.

Injections into the vitreous in the eye, including those with Ozurdex, are associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments (Allergan, 2014). Use of corticosteroids may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may increase the establishment of secondary eye infections due to bacteria, fungi, or viruses. The labeling for Ozurdex states that it should not be used in patients that have any infections or diseases in the eye, or surrounding eye area, including most viral diseases of the cornea and conjunctiva, including active herpes viral infection of the eye, vaccinia, varicella, mycobacterial infections, and fungal diseases.

Other adverse effects among patients with diabetic macular edema included conjunctival blood spot, reduced vision, conjunctival swelling and/or inflammation, floaters, dry eye, vitreous detachment, vitreous opacities, retinal aneurysm, foreign body sensation, corneal erosion, inflammation of the cornea, anterior chamber inflammation, retinal tear, drooping eyelid, and high blood pressure (Allergan, 2014).

Boyer, et al. (2013) reported on the results of two randomized controlled clinical studies to evaluate the safety and efficacy of Ozurdex dexamethasone intravitreal implant (DEX) 0.7 and 0.35 mg in the treatment of patients with diabetic macular edema (DME). Two randomized, multicenter, masked, sham-controlled, phase III clinical trials with identical protocols were conducted. Data were pooled for analysis. Study subjects were 1048 patients with DME, best-corrected visual acuity (BCVA) of 20/50 to 20/200 Snellen equivalent, and central retinal thickness (CRT) of ≥300 μm by optical coherence tomography. Patients were randomized in a 1:1:1 ratio to study treatment with DEX implant 0.7 mg, DEX implant 0.35 mg, or sham procedure and followed for 3 years (or 39 months for patients treated at month 36) at ≤40 scheduled visits. Patients who met retreatment eligibility criteria could be retreated no more often than every 6 months. The predefined primary efficacy endpoint was achievement of ≥15-letter improvement in BCVA from baseline at study end. Safety measures included adverse events and intraocular pressure (IOP). Mean number of treatments received over 3 years was 4.1, 4.4, and 3.3 with DEX implant 0.7 mg, DEX implant 0.35 mg, and sham, respectively. The percentage of patients with ≥15-letter improvement in BCVA from baseline at study end was greater with DEX implant 0.7 mg (22.2%) and DEX implant 0.35 mg (18.4%) than sham (12.0%; p ≤ 0.018). Mean average reduction in CRT from baseline was greater with DEX implant 0.7 mg (-111.6 μm) and DEX implant 0.35 mg (-107.9 μm) than sham (-41.9 μm; p < 0.001). Rates of cataract-related adverse events in phakic eyes were 67.9%, 64.1%, and 20.4% in the DEX implant 0.7 mg, DEX implant 0.35 mg, and sham groups, respectively. Increases in IOP...
were usually controlled with medication or no therapy; two patients (0.6%) in the DEX implant 0.7 mg group and 1 (0.3%) in the DEX implant 0.35 mg group required trabeculectomy. The investigators concluded that the DEX implant 0.7 mg and 0.35 mg met the primary efficacy endpoint for improvement in BCVA. The investigators stated that the safety profile was acceptable and consistent with previous reports.

In a randomized, controlled, multi-center, double-masked, parallel-group, 12-month trial, Callanan et al (2013) evaluated Ozurdex (dexamethasone intravitreal implant [DEX implant]) 0.7 mg combined with laser photocoagulation compared with laser alone for treatment of diffuse DME. A total of 253 patients with retinal thickening and impaired vision resulting from diffuse DME in at least 1 eye (the study eye) were enrolled. Patients were randomized to treatment in the study eye with DEX implant at baseline plus laser at month 1 (combination treatment; n = 126) or sham implant at baseline and laser at month 1 (laser alone; n = 127) and could receive up to 3 additional laser treatments and 1 additional DEX implant or sham treatment as needed. The primary efficacy variable was the percentage of patients who had a 10-letter or more improvement in BCVA from baseline at month 12. Other key efficacy variables included the change in BCVA from baseline and the area of vessel leakage evaluated with fluorescein angiography. Safety variables included adverse events and IOP. The percentage of patients who gained 10 letters or more in BCVA at month 12 did not differ between treatment groups, but the percentage of patients was significantly greater in the combination group at month 1 (p < 0.001) and month 9 (p = 0.007). In patients with angiographically verified diffuse DME, the mean improvement in BCVA was significantly greater with DEX implant plus laser treatment than with laser treatment alone (up to 7.9 versus 2.3 letters) at all time-points through month 9 (p ≤ 0.013). Decreases in the area of diffuse vascular leakage measured angiographically were significantly larger with DEX implant plus laser treatment through month 12 (p ≤ 0.041). Increased IOP was more common with combination treatment. No surgeries for elevated IOP were required. The authors concluded that there was no significant between-group difference at month 12. However, significantly greater improvement in BCVA, as demonstrated by changes from baseline at various time points up to 9 months and across time based on the area under the curve analysis, occurred in patients with diffuse DME treated with DEX implant plus laser than in patients treated with laser alone.

Pacella et al (2013) evaluated the safety and effectiveness of Ozurdex in patients with persistent DME over a 6-month follow-up period. A total of 17 patients (20 eyes) affected by DME were selected. The mean age was 67 + 8 years, and the mean duration of DME was 46.3 + 18.6 months. The eligibility criteria were: age greater than or equal to 18, a BCVA between 5 and 40 letters, and macular edema with a thickness of greater than or equal to 275 μm; 13 patients had also previously been treated with anti-VEGF medication. The mean ETDRS (Early Treatment Diabetic Retinopathy Study) value went from 18.80 + 11.06 (T0) to 26.15 + 11.03 (p = 0.04), 28.15 + 10.29 (p = 0.0087), 25.95 + 10.74 (p = 0.045), 21.25 + 11.46 (p = 0.5) in month 1, 3, 4, and 6, respectively. The mean logMAR (logarithm of the minimum angle of resolution) value went from 0.67 + 0.23 (at T0) to 0.525 + 0.190 (p = 0.03), 0.53 + 0.20 (p = 0.034), and 0.56 + 0.22 (p = 0.12) in month 1, 3, and 4, respectively, to finally reach 0.67 + 0.23 in month 6. The mean CMT value improved from 518.80 + 224.75 μm (at T0) to 412.75 + 176.23 μm,


292.0 + 140.8 μm (p < 0.0001), and 346.95 + 135.70 (p = 0.0018) on day 3 and in month 1 and 3, respectively, to then increase to 476.55 + 163.14 μm (p = 0.45) and 494.25 + 182.70 μm (p = 0.67) in month 4 and 6. The authors concluded that Ozurdex produced significant improvements in BCVA and CMT from the third day of implant in DME sufferers, and this improvement was sustained until the third month.

In a retrospective, interventional case-series study, Rishi, et al. (2013) evaluated the safety and effectiveness of Ozurdex in patients with recalcitrant DME. Inclusion criteria comprised patients presenting with recalcitrant DME, 3 or more months after 1 or more treatments of macular laser photocoagulation and/or intravitreal anti-vascular endothelial growth factor (VEGF) injections. Exclusion criteria included history of corticosteroid-responsive intra-ocular pressure (IOP) rise, cataract extraction, or other intra-ocular surgery within 3 months. The main outcome measure was VA at 1 and 4 months after Ozurdex injection. Secondary outcome measures included change in central macular thickness (CMT) on Optical coherence tomography (OCT) and changes in IOP following Ozurdex implant. Of 18 eyes (17 patients) with recalcitrant DME that underwent Ozurdex implant, 3 eyes (2 patients) had follow-up of more than 3 months post-injection. Mean age of patients was 56 years. Mean duration of diabetes mellitus was 16.6 years. Systemic control of diabetes mellitus was good as assessed by FBS/PPBS and HbA1c. The pre-operative mean CMT was 744.3 μm and improved to 144 and 570 μm at months 1 and 4, respectively. Pre-operative mean BCVA was 0.6 logMAR units and improved to 0.3 and 0.46 logMAR units at month 1 and 4, respectively. The mean follow-up was 4.3 months (range of 4 to 5 months). The authors concluded that Ozurdex appears effective in management of recalcitrant DME. Moreover, they stated that the results of the ongoing POSURDEX study will elaborate these effects better.

In a review on new developments in corticosteroid therapy for uveitis, Taylor et al (2010) stated that corticosteroids remain the mainstay of the management of patients with uveitis. Topical corticosteroids are effective in the control of anterior uveitis, but vary in strength, ocular penetration and side effect profile. Systemic corticosteroids are widely used for the management of posterior segment inflammation that requires treatment, particularly when it is associated with systemic disease or when bilateral ocular disease is present. However, when ocular inflammation is unilateral, or is active in 1 eye only, local therapy has considerable advantages, and peri-ocular injections of corticosteroid are a useful alternative to systemic medication and are very effective in controlling mild or moderate intra-ocular inflammation. More recently, the injection of intra-ocular corticosteroids such as triamcinolone have been found to be effective in reducing ME and improving vision in uveitic eyes that have proved refractory to systemic or peri-ocular corticosteroids. The effect is usually transient, lasting around 3 months, but can be repeated although the side effects of cataract and raised intra-ocular pressure are increased in frequency with intra-ocular versus peri-ocular corticosteroid injections. This has led to the development of new intra-ocular corticosteroid devices, which are designed to deliver sustained-release drugs and obviate the need for systemic immuno-suppressive treatment. The first such implant was Retisert, which is surgically implanted (in the operating theater) and is designed to release fluocinolone over a period of about 30 months. More recently, Ozurdex, a "bioerodible" dexamethasone implant, which can be inserted in an
office setting, has completed phase III clinical trials in patients with intermediate and posterior uveitis. This implant lasts approximately 6 months, and has been found to be effective with a much better side effect profile than Retisert or intra-vitreal triamcinolone injection, at least for 1 injection.

In September 2010, Allergan received FDA approval of its supplemental new drug application of Ozurdex for the treatment of non-infectious uveitis affecting the posterior segment of the eye. The approval was based on the findings of a single, multi-center, masked, randomized study of 153 patients with non-infectious uveitis affecting the posterior segment of the eye. After a single injection, the percent of patients reaching a vitreous haze score of 0 (where a score of 0 represents no inflammation) was statistically significantly greater for patients receiving Ozurdex versus sham at week 8 (primary time point) (47 % versus 12 %). The percent of patients achieving a 3-line improvement from baseline BCVA was 43 % for patients receiving Ozurdex versus 7 % for sham at week 8.

Bansal et al (2012) reported the behavior of intravitreal Ozurdex implant in eyes with post-lensectomy-vitrectomy (PLV) aphakia. These researchers carried out a retrospective chart review of 3 eyes with PLV aphakia (3 patients with uveitis) who received intravitreal injection of Ozurdex for cystoid macular edema (1 eye), persistent inflammation (1 eye), and ocular hypotony (1 eye). Final outcome was assessed in terms of effectiveness, stability, and tolerance of the implant. Following implantation of the Ozurdex, an initial improvement was seen in all 3 eyes. However, the implant migrated into the anterior chamber (AC) at 1 week in 2 eyes and at 5 weeks in 1 eye, and wandered between the AC and vitreous cavity with changing postures of the patient. Two eyes developed corneal edema, of which 1 eye underwent implant removal from the AC. The authors concluded that Ozurdex implant should be contraindicated in eyes with PLV aphakia to avoid its deleterious effect on the corneal endothelium.

Martinez-Castillo et al (2012) reported a case of Coats' disease managed with Ozurdex combined with retinal photocoagulation. A 46-year old female with 20/200 VA was diagnosed with Coats' disease with secondary retinal vaso-proliferative tumor. An initial approach was performed with an intra-vitreal injection of the sustained-release dexamethasone implant Ozurdex. After re-attachment of the retina, the telangiectatic vessels were treated with laser photocoagulation. The patient's VA improved to 20/25 after the intra-vitreal Ozurdex. No further recurrences of exudation were evident through the 12-month follow-up. The authors concluded that Ozurdex may be an effective initial therapeutic approach for Coats' disease with immediate anatomical response and visual improvement. The results of this case study need to be validated by well-designed studies.

Empeslidis et al (2013) presented the short-term favorable clinical results with Ozurdex in a patient with florid idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN) syndrome. The patient was a 26-year old man with significant bilateral deterioration of vision due to vitreous hemorrhage and neuroretinitis with a background of vasculitis and neovascularization. The patient was initially treated with high doses of oral steroids (80 mg prednisolone), which were gradually tapered, and also received extensive argon laser photocoagulation in ischemic areas in both eyes. Despite vigorous treatment and an initial positive
response to treatment, pars plana vitrectomy was eventually needed to address the recurrent vitreous hemorrhages in the left eye. Consequently, VA improved from 0.1 to 0.2 (Snellen) and there was no relapse of vitreous hemorrhage. Persistent ME was noted, however, and it was decided to treat with a dexamethasone 0.7 mg intravitreal implant. Following the dexamethasone implant OS, VA improved significantly from 0.2 to 0.5 (Snellen), the patient reported much less distortion, and there was marked reduction in central retinal thickness from 467 to 234 microns. The patient remained in remission without any exudation in the macula at 4 months follow-up. The authors concluded that dexamethasone 0.7 mg intravitreal implant appeared to be a safe and effective method in the treatment of ME in patients with IRVAN syndrome and could possibly be a treatment option for other cases of inflammatory induced ME.

Saatci et al (2013) reported the effectiveness of Ozurdex in a patient with retinitis pigmentosa (RP) and bilateral cystoid ME unresponsive to topical carbonic anhydrase inhibitors. A 36-year old man with bilateral cystoid ME associated with RP that was unresponsive to topical carbonic anhydrase inhibitors underwent bilateral 0.7-mg Ozurdex 2 weeks apart. Spectral domain optical coherence tomography revealed resolution of ME 1 week following each injection in both eyes and his VA improved. However, ME recurred 2 months later in OS (left eye) and 3 months later in OD (right eye). Second implant was considered for both eyes. No implant-related complication was experienced during the follow-up of 7 months. The authors concluded that inflammatory process seems to play a role in RP. Intravitreal dexamethasone implant may offer retina specialists a therapeutic option especially in cases unresponsive to other treatment regimens in eyes with RP-related ME.

Srour et al (2013) evaluated the anatomical and functional outcomes of Ozurdex in patients with ME secondary to RP. A total of 3 patients (4 eyes), aged 24 to 46 years, presented with refractory ME secondary to RP were included in this study. Ozurdex was administered to treat ME. The anatomical (CMT) and functional (BCVA) outcomes as well as adverse events were recorded. All patients completed 6 months follow-up. After Ozurdex therapy, all patients showed regression of ME. At baseline, mean CMT was 443 ± 185 μm (range of 213 to 619 μm); ME improved to 234 ± 68 μm (range of 142 to 307 μm) at 1 month, to 332 ± 177 μm (range of 139 to 513 μm) at 3 months, and to 305 ± 124 μm (range of 144 to 447 μm) at 6 months. Recurrent ME was recorded in 2 patients (both patients at 3 months from Ozurdex therapy). Re-treatment with intravitreal Ozurdex was performed in 2 patients. Mean BCVA improved form 20/160 (range of 20/50 to 20/200) (baseline) to 20/100 (range of 20/40 to 20/125) at 1 month, to approximately 20/125 (range of 20/100 to 20/200) at 3 months, and to approximately 20/125 (range of 20/100 to 20/160) at 6 months. No serious ocular and systemic adverse events were observed during the study period. The authors concluded that Ozurdex provided anatomic and functional improvements and may represent a valuable treatment option for patients with ME secondary to RP. These preliminary findings need to be validated by well-designed studies.

According to the prescribing information, Ozurdex is contraindicated in patients with active or suspected ocular or peri-ocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and
fungal diseases. Furthermore, Ozurdex is also contraindicated in individuals with advanced glaucoma.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

67027
67028

HCPCS codes covered if selection criteria are met:

J7312

ICD-9 codes covered if selection criteria are met:

362.07  Diabetic macular edema [for patients who are phakic or pseudophakic]
362.35  Central retinal vein occlusion
362.36  Venous tributary (branch) occlusion
362.83  Retinal edema [not covered if secondary to idiopathic retinal vasculitis, aneurysms, neuroretinitis (IRVAN) syndrome, or retinitis pigmentosa]
363.00 - 363.08  Focal chorioretinitis and focal retinochoroiditis
363.10 - 363.15  Disseminated chorioretinitis and focal retinochoroiditis
363.20 - 363.22  Other and unspecified forms of chorioretinitis and retinochoroiditis

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):

360.00 - 360.9  Disorders of the globe
362.12  Exudative retinopathy [Coats' disease]
365.10 - 365.13  Open-angle glaucoma
365.20 - 365.23  Primary angle-closure glaucoma
365.31  Corticosteroid-induced glaucoma [Glaucomatous stage]
365.52  Pseudoexfoliation glaucoma
365.62 - Glaucoma associated with other ocular disorders
365.65

365.73 Severe stage glaucoma [Advanced stage]

373.00 - Inflammation of eyelids
373.9

376.00 Acute inflammation of orbit, unspecified
376.01 Orbital cellulitis
376.10 Chronic inflammation of orbit, unspecified

The above policy is based on the following references:


22. National Horizon Scanning Centre (NHSC). Dexamethasone intravitreal implant (Posurdex) for macular oedema secondary to central or branch retinal vein occlusion. Horizon Scanning Technology Briefing. Birmingham, UK: National Horizon Scanning Centre (NHSC); 2009.


