Medical Coverage Policy | Intravitreal and Punctum Corticosteroid Implants

EFFECTIVE DATE:10|01|2015
POLICY LAST UPDATED: 05|18|2021

OVERVIEW
An intravitreal implant is a drug delivery system, injected or surgically implanted in the vitreous of the eye, for sustained release of drug to the posterior and intermediate segments of the eye. Intravitreal corticosteroid implants are being investigated for a variety of inflammatory eye conditions.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Prior authorization review is not required.

POLICY STATEMENT
Medicare Advantage Plans and Commercial Products
A fluocinolone acetonide intravitreal implant 0.59 mg (Retisert®) may be considered medically necessary for the treatment of:

- Chronic non-infectious intermediate, posterior, or panuveitis.

A fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien®) may be considered medically necessary 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.

A dexamethasone intravitreal implant 0.7 mg (Ozurdex™) may be considered medically necessary for the treatment of:

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

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 not covered for Medicare Advantage Plans and not medically necessary for Commercial Products 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 patients with noninfectious intermediate uveitis or posterior uveitis and cataract undergoing cataract surgery

A fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq®) is considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products for the treatment of chronic noninfectious posterior uveitis affecting the posterior segment of the eye

Medicare Advantage Plans
All other uses of a corticosteroid intravitreal implant are considered not covered as the evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Commercial Products
All other uses of a corticosteroid intravitreal implant are considered not medically necessary as the evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Evidence of Coverage or Subscriber Agreement for applicable physician administered injectable drug benefits/coverage.

BACKGROUND

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. Three intravitreal corticosteroid implants, ie, fluocinolone acetonide 0.59 mg (Retisert), 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 patients receiving implants developed cataracts and required cataract surgery. Further, most also developed glaucoma, with 75% of patients 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 patients 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, patients 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 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, Yutiq) at both 6 and 12 months. However, serious limitations of these findings include inconsistency in the magnitude of the benefit at 12 months (odds ratio 67.09; 95% confidence interval 8.81-511.06 in published RCT and odds ratio 3.04; 95% confidence interval 1.52, 6.08 in the unpublished RCT) and, with more imputed recurrences in the sham groups than the treatment groups, we also can't 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). Due to these inconsistencies and serious methodological limitations the evidence is insufficient to determine that the technology results in an 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 patients 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 that the technology results in an improvement in the net health outcome.

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 patients 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 patients 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 that the technology results in an improvement in the net health outcome.
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 patients 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 patients 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 patients vs. 1 letter in phakic patients). A major limitation of these implants is that nearly 80% of all phakic patients will develop cataracts and will require cataract surgery. Further, intraocular pressure was elevated in 34% of patients who received this implant compared with 10% of controls. The evidence is sufficient to determine that the technology results in a meaningful an 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 patients 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 patients 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 an 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 an 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 that the technology results in an improvement in the net health outcome.

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 patients 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 patients with refractory or intolerant birdshot retinopathy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cystoid macular edema who receive an intravitreal dexamethasone implant (0.7 mg), the evidence includes 1 observation-controlled RCT (n=14), 3 comparative observational studies and numerous case series. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The RCT found improved mean visual acuity and eye anatomy outcomes with intravitreal dexamethasone compared to the control eyes, but these differences were not sustained at 6 months. The comparative observational studies included 269 patients (range, 60 to 135) and also lacked responder analysis of the proportion of patients with a 15-or-more letter improvement. One case series evaluated the proportion of patients with a 3-line improvement in best-corrected visual acuity; although 88% of patients achieved this outcome at 2 months, the proportion with improvement was not sustained at 6 months (27.8%). Additional blinded, multicenter RCTs are needed that compare intravitreal dexamethasone to another established treatment. The trials should be adequately powered for measuring proportion of patients in whom vision had improved by 15 letters or more. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 patients with idiopathic macular telangiectasia type 1. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with postoperative chronic macular edema (pseudophakic cystoid macular edema, Irvine-Gass syndrome) who receive an intravitreal dexamethasone implant (0.7 mg), the evidence 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. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. 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 proportion of patients in whom vision had improved by 15 letters or more. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 that the technology results in an improvement in the net health outcome.

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 patients with proliferative retinopathy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 patients with radiation retinopathy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 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 patients in India. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Compared with oral corticosteroids, intravitreal dexamethasone 0.7 mg had similar benefits and avoided 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 an improvement in the net health outcome.

CODING

Medicare Advantage Plans and Commercial Products

The following code(s) are covered when filed with an approved diagnosis noted below:

J7311 Fluocinolone acetonide, intravitreal implant
J7312 Injection, dexamethasone, intravitreal implant, 0.1 mg
J7313 Injection, fluocinolone acetonide, intravitreal implant, 0.01 mg

J7314 Injection, fluocinolone acetonide, intravitreal implant (Yutiq), 0.01 mg
68841 Insertion of drug-eluting implant, including punctal dilation when performed, into lacrimal canaliculus, each (New code effective 1/01/2022)

Medically necessary ICD-10 diagnosis
D18.09
E08.37
E09.37
E10.37
E11.37
E13.37
H20.10-H20.13
H30.90-H30.93
H34.8110-H34.8192
H34.8310-H34.8392
H35.020-H35.23
H35.071-H35.079
H35.30-H35.3294
H35.711-H35.719
H35.81

RELATED POLICIES
Suprachoroidal Delivery of Pharmacologic Agents

PUBLISHED
Provider Update, July 2022
Provider Update, June 2021
Provider Update, September 2020
Provider Update, August 2019
Provider Update, October 2018

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