Clinical Policy: Corticosteroid Intravitreal Implants (Iluvien, Ozurdex, Retisert, Yutiq)

Reference Number: ERX.SPA.332
Effective Date: 09.01.19
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Dexamethasone (Ozurdex®) and fluocinolone acetonide (Iluvien®, Retisert®, Yutiq™) intravitreal implants contain a corticosteroid.

FDA Approved Indication(s)
Iluvien is indicated 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.

Ozurdex is indicated for the treatment of:
- Macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO)
- Non-infectious uveitis affecting the posterior segment of the eye
- Diabetic macular edema (DME)

Retisert and Yutiq are indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that corticosteroid intravitreal implants are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Macular Edema following BRVO or CRVO (must meet all):
1. Diagnosis of macular edema following BRVO or CRVO;
2. Request is for Ozurdex;
3. Prescribed by or in consultation with an ophthalmologist;
4. Age ≥ 18 years;
5. Failure of intravitreal anti-vascular endothelial growth factor (VEGF) agents, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
6. Dose does not exceed 1 implant per eye.

Approval duration: 3 months (one implant per eye)

B. Non-Infectious Uveitis (must meet all)**:**
1. Diagnosis of non-infectious uveitis affecting the posterior segment of the eye;
2. Request is for Ozurdex, Retisert, or Yutiq;
3. Prescribed by or in consultation with an ophthalmologist;
4. Member meets one of the following (a or b):
   a. For Ozurdex, Yutiq: Age ≥ 18 years;
   b. For Retisert: Age ≥ 12 years;

5. Failure of both of the following (a and b), unless both are contraindicated or clinically significant adverse effects are experienced (*see Appendix B*):
   a. Systemic corticosteroid;
   b. Non-biologic immunosuppressive therapy;
6. Dose does not exceed 1 implant per eye.

Approval duration: 3 months (one implant per eye)

C. Diabetic Macular Edema (must meet all)**:**
1. Diagnosis of DME;
2. Request is for Ozurdex or Iluvien;
3. Prescribed by or in consultation with an ophthalmologist;
4. Age ≥ 18 years;
5. Failure of intravitreal anti-VEGF agents, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
6. Dose does not exceed 1 implant per eye.

Approval duration: 3 months (one implant per eye)

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member meets one of the following (a, b, c, or d):
   a. At least 4 months have passed since last treatment with Ozurdex;
   b. At least 12 months have passed since last treatment with Iluvien;
   c. At least 30 months have passed since last treatment with Retisert;
   d. At least 36 months have passed since last treatment with Yutiq;
4. Dose does not exceed 1 implant per eye.

Approval duration: 3 months (one implant per eye)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BRVO: branch retinal vein occlusion
CRVO: central retinal vein occlusion
DME: diabetic macular edema
FDA: Food and Drug Administration
VEGF: vascular endothelial growth factor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Maximum Dose
anti-VEGF agents (e.g., bevacizumab, Lucentis®, Eylea®)	**Macular Edema** Refer to prescribing information	Refer to prescribing information
systemic corticosteroids (e.g., prednisone)	**Uveitis** prednisone 5 – 60 mg/day PO in 1 – 4 divided doses	Varies
azathioprine (Azasan®, Imuran®)	**Uveitis** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
chlorambucil (Leukeran®)	**Uveitis** 0.2 mg/kg PO QD, then taper to 0.1 mg/kg PO QD or less	0.2 mg/kg/day
cyclophosphamide (Cytoxan®)	**Uveitis** 1 – 2 mg/kg/day PO	N/A
cyclosporine (Sandimmune®, Neoral®)	**Uveitis** 2.5 – 5 mg/kg/day PO in divided doses	5 mg/kg/day
methotrexate (Rheumatrex®)	**Uveitis** 7.5 – 20 mg/week PO	30 mg/week
mycophenolate mofetil (Cellcept®)	**Uveitis** 500 – 1,000 mg PO BID	3 g/day
tacrolimus (Prograf®)	**Uveitis** 0.1 – 0.15 mg/kg/day PO in 2 divided doses given for 12 weeks	N/A

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Iluvien, Ozurdex, Retisert, Yutiq: patients with active or suspected viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in active bacterial, mycobacterial or fungal infections of the eye
  - Iluvien, Ozurdex: patients with glaucoma with cup to disc rations of greater than 0.8
  - Ozurdex: patients with posterior lens capsules that is torn or ruptured because of the risk of migration into the anterior chamber
  - Iluvien, Ozurdex, Yutiq: hypersensitivity
- Boxed warning(s): none reported

Appendix D: General Information
- Based on clinical trials with Retisert:
  - Within 3 years post-implantation, approximately 77% of patients will require intraocular pressure (IOP) lowering medications to control intraocular pressure and 37% of patients will require filtering procedures to control intraocular pressure.
  - Following implantation of Retisert, nearly all patients will experience an immediate and temporary decrease in visual acuity in the implanted eye which lasts for approximately one to four weeks post-operatively.
  - During the 3-year post-implantation period, nearly all phakic eyes are expected to develop cataracts and require cataract surgery.
- In one study, intravitreal bevacizumab (1.25 mg) and the dexamethasone (DEX) (0.7 mg) implant were compared in a randomized, Phase II trial called the BEVORDEX study. 79 Forty-two eyes received intravitreal bevacizumab every 4 weeks, and 46 eyes received an intravitreal DEX (0.7

mg) implant every 16 weeks, with a when necessary (PRN) regimen for 12 months. The primary outcome of the study was to gain ten or more letters in the best-corrected distance visual acuity (BCVA) at 12 months, which was achieved in 40% of the bevacizumab-treated eyes and 41% of the DEX implant-treated group (P=0.99). The mean corneal refractive therapy (CRT) decrease was statistically significant between the groups, and the reduction was 122 µm in the bevacizumab group and 187 µm in the DEX implant group (P=0.015). The mean number of injections over 1 year was 8.6 for the bevacizumab group and 2.7 for the DEX implant group. Finally, in the DEX implant-treated eyes, 11% lost ten or more letters of the BCVA, which was due to cataracts in 4 of 5 cases; none lost ten letters in the bevacizumab-treated eyes.

- The Chart Review of Ozurdex in Macular Edema (CHROME) study evaluated the real-world use, efficacy, and safety of one or more dexamethasone intravitreal implant(s) 0.7 mg (DEX implant) in 120 eyes with macular edema (ME).The mean number of DEX implant injections was 1.7±0.1 in all study eyes; 44.2% of eyes had repeat DEX implant injections (reinjection interval 2.3-4.9 months).
- According to Pommier et al., an average of 2.6 injections of Ozurdex were needed to obtain a 58.6% of patients who gained more than 15 letters, and 51.1% of patients showed macular edema resolution.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Dexamethasone (Ozurdex)	Macular edema, uveitis	Inject the implant containing 0.7 mg dexamethasone intravitreally	One implant injection per eye every 4 months
Fluocinolone (Iluvien)	Diabetic macular edema	Inject the implant containing 0.19 mg fluocinolone intravitreally	One implant injection per eye every 12 months
Fluocinolone (Retisert)	Uveitis	Inject the implant containing 0.59 mg fluocinolone intravitreally	One implant injection per eye every 30 months
Fluocinolone (Yutiq)	Uveitis	Inject the implant containing 0.18 mg fluocinolone intravitreally	One implant injection per eye every 36 months

VI. Product Availability

Drug Name	Availability
Dexamethasone (Ozurdex)	Biodegradable intravitreal implant: 0.7 mg
Fluocinolone (Iluvien)	Non-biodegradable intravitreal implant: 0.19 mg
Fluocinolone (Retisert)	Non-biodegradable intravitreal implant: 0.59 mg
Fluocinolone (Yutiq)	Non-biodegradable intravitreal implant: 0.18 mg

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.20.19	08.19
3Q 2020 annual review: removed required step through of intravitreal steroid injections from all indications due to lack of commercial availability (Triescence is the only intravitreal steroid injection on market, and it is currently on shortage without a known resolution date); references reviewed and updated.	06.22.20	08.20
Revised dosing frequency for Ozurdex from q6 months to q4 months per literature review, guideline recommendations, market analysis, and specialist feedback.	08.19.20	11.20
3Q 2021 annual review: revised approval durations from 4 weeks to 3 months to allow for staggered dosing of bilateral implants; references reviewed and updated.	03.17.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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