

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

Reference Number: CP.PHAR.385

Effective Date: 05.29.18

Last Review Date: 08.19

Line of Business: Commercial, Medicaid, HIM-Medical Benefit

[Coding Implications](#)[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.*

It is the policy of health plans affiliated with Centene Corporation® 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 both of the following (a and b) unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*):
  - a. Intravitreal steroid injections;
  - b. Intravitreal anti-VEGF agents;

6. Dose does not exceed 1 implant per eye.

**Approval duration: 4 weeks (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  $\geq$  18 years;
  - b. For Retisert: Age  $\geq$  12 years;
5. Failure of all of the following (a, b, and c) unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*):
  - a. Intravitreal steroid injections;
  - b. Systemic corticosteroid;
  - c. Non-biologic immunosuppressive therapy;
6. Dose does not exceed 1 implant per eye.

**Approval duration: 4 weeks (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  $\geq$  18 years;
5. Failure of both of the following (a and b) unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*):
  - a. Intravitreal steroid injections;
  - b. Intravitreal anti-VEGF agents;
6. Dose does not exceed 1 implant per eye.

**Approval duration: 4 weeks (one implant per eye)**

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

**II. Continued Therapy**

**A. All Indications in Section I (must meet all):**

1. Currently receiving medication via Centene benefit 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 6 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: 4 weeks (one implant per eye)**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

**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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit 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

*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                                                       | Dose Limit/<br>Maximum Dose      |
|--------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|----------------------------------|
| Anti-VEGF agents (e.g., bevacizumab, Lucentis <sup>®</sup> , Eylea <sup>®</sup> )                                                          | <b>Macular Edema</b><br>Refer to prescribing information             | Refer to prescribing information |
| Intravitreal steroid injections (e.g., triamcinolone [Triesence <sup>®</sup> , Trivaris <sup>™</sup> ], dexamethasone, fluocinolone, etc.) | <b>Macular Edema and Uveitis</b><br>Refer to prescribing information | Refer to prescribing information |
| Systemic corticosteroids (e.g., prednisone)                                                                                                | <b>Uveitis</b><br>prednisone 5 – 60 mg/day PO in 1 – 4 divided doses | Varies                           |
| azathioprine (Azasan <sup>®</sup> , Imuran <sup>®</sup> )                                                                                  | <b>Uveitis</b><br>1.5 – 2 mg/kg/day PO                               | 2.5 mg/kg/day                    |

| Drug Name                                                        | Dosing Regimen                                                           | Dose Limit/<br>Maximum Dose |
|------------------------------------------------------------------|--------------------------------------------------------------------------|-----------------------------|
| chlorambucil<br>(Leukeran <sup>®</sup> )                         | <b>Uveitis</b><br>0.2 mg/kg PO QD, then taper to 0.1 mg/kg PO QD or less | 0.2 mg/kg/day               |
| cyclophosphamide<br>(Cytoxan <sup>®</sup> )                      | <b>Uveitis</b><br>1 – 2 mg/kg/day PO                                     | N/A                         |
| cyclosporine<br>(Sandimmune <sup>®</sup> , Neoral <sup>®</sup> ) | <b>Uveitis</b><br>2.5 – 5 mg/kg/day PO in divided doses                  | 5 mg/kg/day                 |
| methotrexate<br>(Rheumatrex <sup>®</sup> )                       | <b>Uveitis</b><br>7.5 – 20 mg/week PO                                    | 30 mg/week                  |
| mycophenolate mofetil<br>(Cellcept <sup>®</sup> )                | <b>Uveitis</b><br>500 – 1,000 mg PO BID                                  | 3 g/day                     |
| tacrolimus (Prograf <sup>®</sup> )                               | <b>Uveitis</b>                                                           | N/A                         |

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

#### *Appendix C: Contraindications / Boxed Warnings*

- Contraindication(s):
  - Iluvien, Ozurdex, Retisert, Yutiq are contraindicated in 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 are contraindicated in patients with glaucoma with cup to disc ratios of greater than 0.8.
  - Ozurdex is contraindicated in patients with posterior lens capsules that is torn or ruptured because of the risk of migration into the anterior chamber.
- 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  $\mu$ m in the bevacizumab group and 187  $\mu$ m 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 $\pm$ 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.
- Ozurdex: The main rationale behind the 6-month restriction is safety. The onset of improvement in BCVA with Ozurdex occurs in the first 2 months after implantation, with a further duration of action of 1 to 3 months. However, one of the main clinically significant adverse effects of corticosteroid implants is increased intraocular pressure (IOP). During the clinical trials, the mean IOP measurement in the study subjects showed that it increased by an average of 4 mmHg at Month 1.5 and returned to baseline by Month 6. This data pattern was replicated for each cycle of 6 months. Given that this was an average increase, while about 28% of the subjects showed IOP elevation of  $\geq$  10 mmHg from baseline, 15% showed of  $\geq$  30 mmHg from baseline, and 3% of subjects required surgical procedures for management of elevated IOP, there is a significant safety concern for repeated implantation of Ozurdex more frequently than 6 months. This is supported by the clinical trial design which also limited successive treatments with Ozurdex to at least 6 months apart. Other safety concerns for more frequent implantation of Ozurdex are cataracts and conjunctival hemorrhage.

## 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 6 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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11. Pommier S, Meyer F, Guigou S, et al. Long-term real-life efficacy and safety of repeated Ozurdex injections and factors associated with macular edema resolution after retinal vein occlusion: The REMIDO 2 Study. *Ophthalmologica*. 2016;236(4):186-192.

## Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description                                                                |
|-------------|----------------------------------------------------------------------------|
| J7311       | Injection, fluocinolone acetonide intravitreal implant, 0.59 mg (Retisert) |
| J7312       | Injection, dexamethasone intravitreal implant, 0.1 mg                      |

| HCPSC Codes | Description                                                                |
|-------------|----------------------------------------------------------------------------|
| J7313       | Injection, fluocinolone acetonide intravitreal implant, 0.19 mg (Iluvien,) |
| J7314       | Injection, fluocinolone acetonide intravitreal implant, 0.18 mg (Yutiq)    |

| Reviews, Revisions, and Approvals                                                                                                                                                       | Date     | P&T Approval Date |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-------------------|
| Policy created                                                                                                                                                                          | 05.29.18 | 08.18             |
| 3Q 2019 annual review: added description, initial and continuation criteria, administration, and HCPSC codes for Yutiq; consolidated contraindications; references reviewed and updated | 05.20.19 | 08.19             |
| Updated JCODE for Yutiq from J7313 to J7314 (effective 10/1/19)                                                                                                                         | 08.22.19 |                   |

### **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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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