Clinical Policy: Corticosteroids for Ophthalmic Injection (Iluvien, Ozurdex, Retisert, Xipere, Yutiq)

Reference Number: CP.PHAR.385
Effective Date: 09.01.18
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

The following are corticosteroids for ophthalmic injection requiring prior authorization: dexamethasone intravitreal implant (Ozurdex®), fluocinolone acetonide intravitreal implant (Iluvien®, Retisert®, Yutiq™), and triamcinolone acetonide suprachoroidal injection (Xipere™).

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.

Xipere is indicated for the treatment of macular edema associated with uveitis.

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 corticosteroids for ophthalmic injection 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 corticosteroid injections, if available;
   b. Intravitreal anti-vascular endothelial growth factor (VEGF) agents;
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 intravitreal corticosteroid injections, if available, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
6. Failure of one of the following (a or b), unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendix B*):
   a. Systemic corticosteroid;
   b. Non-biologic immunosuppressive therapy;
7. 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 both of the following (a and b), unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*):
   a. Intravitreal corticosteroid injections, if available;
   b. Intravitreal anti-VEGF agents;
6. Dose does not exceed 1 implant per eye.

Approval duration: 3 months (one implant per eye)

D. Macular Edema with Uveitis (must meet all)**:**
1. Diagnosis of macular edema associated with non-infectious uveitis;
2. Request is for Xipere;
3. Prescribed by or in consultation with an ophthalmologist;
4. Age ≥ 18 years;
5. Inadequate response to Triesence® intravitreal injection, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 4 mg (1 vial) per eye every 12 weeks.

Approval duration: 6 months (two injections per eye)

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. Member meets one of the following (a, b, c, d, or e):
   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;
   e. At least 12 weeks have passed since last treatment with Xipere;
4. Dose does not exceed (a or b):
   a. Ozurdex, Iluvien, Retisert, Yutiq: 1 implant per eye;
   b. Xipere: 4 mg (1 vial) per eye.

Approval duration: 3 months (one implant or injection per eye)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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	Dose Limit/ 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
intravitreal corticosteroids: Triesence (triamcinolone)	**All Indications** 4 mg injected intravitreally per affected eye	4 mg/eye

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.
  - Xipere: ocular or periocular infections.
  - 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, Xipere: 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.
- The POINT trial by Thorne et al. found no significant difference between intravitreal triamcinolone acetonide injection and intravitreal dexamethasone implant in terms of safety and efficacy for the treatment of uveitic macular edema.

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
Triamcinolone (Xipere)	Macular edema associated with uveitis	4 mg (0.1 mL) administered as a suprachoroidal injection	One injection per eye every 12 weeks

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
Triamcinolone (Xipere)	Injectable suspension in a single-dose vial: 40 mg/mL

VII. References

1. Iluvien Prescribing Information. Alpharetta, GA: Alimera Sciences, Inc.; November 2016. Available at: www.iluvien.com. Accessed March 30, 2022.
2. Ozurdex Prescribing Information. Irvine, CA: Allergan, Inc.; October 2020. Available at: www.ozurdex.com. Accessed March 30, 2022.

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13. Sen HN, Albin TA, Burkholder BM, et al. Section 9: Uveitis and ocular inflammation. In: American Academy of Ophthalmology 2020-2021 Basic and Clinical Science Course. American Academy of Ophthalmology; 2020.
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15. Yeh S, Khurana RN, Shah M, et al. Efficacy and safety of suprachoroidal CLS-TA for macular edema secondary to noninfectious uveitis: Phase 3 randomized trial. Opthalmology. 2020; 127(7): 948-955.
16. Thorne JE, Sugar EA, Holbrook JT, et al. Periocular triamcinolone vs. intravitreal triamcinolone vs. intravitreal dexamethasone implant for the treatment of uveitic macular edema: the PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) trial. Ophthalmology. 2019; 126(2): 283-295.

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
J7313	Injection, fluocinolone acetonide intravitreal implant, 0.19 mg (Iluvien,)
J7314	Injection, fluocinolone acetonide intravitreal implant, 0.18 mg (Yutiq)
C9092	Injection, triamcinolone acetonide, suprachoroidal (Xipere), 1 mg

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 HCPCS 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	
3Q 2020 annual review: added HIM line of business, removed HIM-Medical Benefit; removed required step through of intravitreal steroid injections from all indications due to lack of commercial availability (Triesence 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 to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	03.17.21	08.21
Ad hoc: for non-infectious posterior uveitis, revised trial criterion from requiring both of the following to requiring one of the following per specialist feedback and guidelines supporting use of all steroids (topical, local [including intravitreal implants], and systemic) as first line; RT4: added Xipere to policy with corresponding criteria for uveitic macular edema and changed policy name from "corticosteroid intravitreal implants" to "corticosteroids for ophthalmic injection"; added step through of intravitreal steroid injections back to all indications as Triesence is now available.	12.16.21	02.22
Added legacy WellCare line of business (WCG.CP.PHAR.385 to be retired).	01.26.22	05.22
3Q 2022 annual review: no significant changes; updated HCPCS code for Xipere; references reviewed and updated.	03.30.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.22.22	

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.