Policy Number	**OTH903.035**
Policy Effective Date	**08/15/2025**

Triamcinolone acetonide

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Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Suprachoroidal injection of triamcinolone acetonide injectable suspension (Xipere®) **may be considered medically necessary** for the treatment of macular edema associated with uveitis when the following criteria are met:

- Individual is 18 years of age or older;
- Individual does not have infectious uveitis;
- Prescriber will not exceed the U.S. Food and Drug Administration (FDA) labeled dose of 4 mg per affected eye.

Suprachoroidal injection of triamcinolone acetonide injectable suspension (Xipere®) **is considered experimental, investigational and/or unproven** for all other non-FDA approved indications.

Policy Guidelines

None.

Description

Background

The structure of the eye is classified under two subheadings: anterior segment and posterior segment. The anterior segment comprises the front one-third of the eye and includes the pupil, cornea, iris, ciliary body, aqueous humor, and lens; the posterior segment comprises the back two-thirds of the eye and includes the vitreous humor, retina, choroid, macula, and optic nerve.

Many ocular diseases are treated with either topical or systemic medications. Topical application has remained the most preferred delivery route due to ease of administration. Topical application is useful in the treatment of disorders affecting the anterior segment of the eye. Due to the recessed location of the posterior segment of the eye, treatment of diseases in this segment can be quite challenging. Current drug delivery techniques to access the posterior segment of the eye include periocular injections, and intravitreal injections and implants. Drug delivery by injection into the suprachoroidal space has also been proposed in the treatment of posterior segment disease. A potential advantage of suprachoroidal injection would be the ability to minimize systemic adverse effects while delivering higher drug levels to local tissues. This proposed benefit assumes that high drug local levels lead to improved outcomes.

Uveitis
Uveitis encompasses various conditions, of infectious and noninfectious etiologies, that are characterized by inflammation of any part of the uveal tract of the eye (iris, ciliary body, choroid). Infectious etiologies include syphilis, toxoplasmosis, cytomegalovirus retinitis, and candidiasis. Noninfectious etiologies include sarcoidosis, Behçet syndrome, and "white dot" syndromes such as multifocal choroiditis or "birdshot" chorioretinopathy. Uveitis may be idiopathic, have a sudden or insidious onset, a duration that is limited (<3 months) or persistent, and a course that may be acute, recurrent, or chronic.

The classification scheme recommended by the Uveitis Study Group and the Standardization of Uveitis Nomenclature Working Group is based on anatomic location. Patients with anterior uveitis typically develop symptoms such as light sensitivity, pain, tearing, and redness of the sclera. In posterior uveitis, which comprises approximately 5% to 38% of all uveitis cases in the United States (U.S.), the primary site of inflammation is the choroid or retina (or both). Patients with intermediate or posterior uveitis typically experience minimal pain, decreased visual acuity, and the presence of floaters (bits of vitreous debris or cells that cast shadows on the retina). Approximately one-third of uveitis patients develop uveitic macular edema, (2) a build-up of fluid in the macula which causes retinal swelling and distorted vision and may lead to permanent vision loss.

Regulatory Status
Xipere was approved by the U.S. Food and Drug Administration (FDA) in October 2021 for the treatment of macular edema associated with uveitis. (3) Xipere is administered using the SCS Microinjector® (Clearside Biomedical, Inc.) as a suprachoroidal injection to provide targeted delivery into the back of the eye. (4) The recommended dose of Xipere is 4 mg (0.1 mL of the 40 mg/mL injectable suspension). In addition to patients with known hypersensitivity to triamcinolone acetonide, Xipere is contraindicated in patients with active or suspected ocular or periocular 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. (1) Suprachoroidal space (SCS) triamcinolone acetonide is the first (and currently the only) agent specifically approved for uveitic macular edema. It is also the first suprachoroidal delivered formulation to receive regulatory approval.

Rationale

This policy is based on the U.S. Food and Drug Administration labeled indication for Xipere® (triamcinolone acetonide injectable suspension).

Xipere (1)
The efficacy of Xipere was assessed in a 6-month, randomized, multicenter, double-masked, sham-controlled study in patients with macular edema associated with anterior-, intermediate-, posterior-, or pan-uveitis. Patients were treated at baseline and Week 12.

The primary efficacy endpoint was the proportion of patients in whom best corrected visual acuity (BCVA) had improved by ≥ 15 letters from baseline after 24 weeks of follow-up (Table 1).

Table 1: Number of Patients with ≥ 15 Letters Improvement from Baseline at Week 24

Patient Who Gained ≥ 15 Letters from Baseline at Week 24	Xipere (N = 96)	Control (N = 64)
n (%)	45 (47%)	10 (16%)
Estimated Difference (95% CI)	31 % (15%, 46%)	
CMH p-value*	< 0.01	

CI: confidence interval; CMH: Cochran Mantel Haenszel test; N/n: number.
* The p-value was based on a Cochran Mantel Haenszel test for general association between treatment and response with stratification by country.

A statistically significantly greater proportion of patients treated with Xipere achieved a ≥ 15-letter improvement in BCVA than control patients ($p < 0.01$) at Week 24.

Summary of Evidence
The evidence is sufficient to support the use of suprachoroidal injection of triamcinolone acetonide injectable suspension (Xipere®) for the U.S. Food and Drug Administration (FDA) approved indication, which is based on the clinical trial outcomes documented in the published FDA labeling.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	67299, 67516, [Deleted 1/2024: 0465T]
HCPCS Codes	J3299

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. U.S. Food and Drug Administration, Drugs @ FDA. Highlights of Prescribing Information: Xipere. (May 2025). Available at: <https://www.accessdata.fda.gov> (accessed July 7, 2025).

Other:

2. Clearside Biomedical, Inc. About Uveitis and Macular Edema. January 22, 2025. Available at <https://globenewswire.com> (accessed April 25, 2025).
3. Xipere FDA Approval History. Oct 26, 2021. Available at: <https://www.drugs.com> (accessed April 25, 2025).
4. Clearside Biomedical. SCS Microinjector. Available at: <https://www.clearsidebio.com> (accessed April 25, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
08/15/2025	Document updated with literature review. The following changes were made to Coverage: 1) Removed "Suprachoroidal injection of all other pharmacologic agents is considered experimental, investigational and/or unproven for any indication"; and 2) Added "non-FDA approved" to "Suprachoroidal injection of triamcinolone acetonide injectable suspension (Xipere®) is considered experimental, investigational and/or unproven for all other non-FDA approved indications. Added reference 2; other updated and some removed. Title changed from "Suprachoroidal Injection of a Pharmacologic Agent."
04/01/2024	Document updated with literature review. Coverage unchanged. Added references 8 and 9.
3/15/2023	Reviewed. No changes.
9/15/2022	Document updated with literature review. Coverage was completely revised to state: "Suprachoroidal injection of triamcinolone acetonide injectable suspension (Xipere®) may be considered medically necessary for the treatment of macular edema associated with uveitis when the following criteria are met: individual is 18 years of age or older; individual does not have infectious uveitis; and prescriber will not exceed the U.S. Food and Drug Administration (FDA) labeled dose of 4mg per affected eye. Suprachoroidal injection of triamcinolone acetonide injectable suspension

	(Xipere®) is considered experimental, investigational and/or unproven for all other indications. Suprachoroidal injection of all other pharmacologic agents is considered experimental, investigational and/or unproven for any indication." Added references 1-3, 6, 7, and 11.
12/1/2021	Reviewed. No changes.
11/1/2020	Document updated with literature review. The following modification was made to Coverage: Changed "delivery" to "injection". Added/updated references 9-10. Title changed from "Suprachoroidal Delivery of a Pharmacologic Agent".
10/15/2019	Reviewed. No changes.
11/1/2018	Document updated with literature review. Coverage unchanged. Added references 8,13,14.
10/15/2017	Reviewed. No changes.
1/1/2017	New Medical Document. Suprachoroidal delivery of a pharmacologic agent is considered experimental, investigational and/or unproven.