Triamcinolone Acetonide (XIPERE) Injection
National Drug Monograph
January 2023
VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA Approval Information

Description/Mechanism of Action

- Triamcinolone acetonide (TCA) suprachoroidal injection is approved for treatment of macular edema associated with uveitis (UME).

Dosage Form(s) Under Review

- Each package contains a microinjector syringe with vial adapter, 900-µm needle, 1100-µm needle, and vial of proprietary preservative-free TCA injectable suspension 40 mg/mL. Each package is single-dose and used only for the treatment of one eye. The dose is 4mg of TCA (0.1mL) administered via suprachoroidal injection. In the PEACHTREE trial, patients received a dose at baseline and at week 12.

- The proprietary SCS Microinjector optimizes suprachoroidal insertion and administration of drug. Minimal training is needed for the retinal specialist and the procedure can be done in the office-setting.

- Advantages of suprachoroidal injection allows for targeted delivery of drug to the posterior segment of the eye and may limit corticosteroid exposure to the anterior segment thereby potentially limiting adverse events such as cataracts and elevated intraocular pressure (IOP) compared to other methods of steroid administration.

Clinical Evidence Summary

Efficacy Considerations

The PEACHTREE trial is a phase 3, 24-week randomized controlled trial comparing suprachoroidal injection of triamcinolone acetonide formulation (CLS-TA) 4mg (n=96) to sham (n=64) in patients with non-infectious uveitis (anterior, intermediate, posterior, or panuveitis) and macular edema due to uveitis (central subfield thickness (CST) of 300 µm or more measured by optical coherence tomography). Study treatments were given at baseline and week 12. Rescue therapy could be administered starting at week 4 per study criteria.

Patients were excluded if they had any active ocular disease or infection in the study eye other than uveitis, IOP greater than 22mmHg or uncontrolled glaucoma. For patients with IOP ≤ 22mmHg, up to two IOP lowering drugs was allowed. Stable doses of oral prednisone up to 20mg/d (or equivalent other steroid) and or systemic immunomodulatory treatments were allowed.

Baseline information includes best-corrected visual acuity (BCVA) Early Treatment Diabetic Retinopathy Study (ETDRS) 54.2 letters, CST 498.7µm, 56% phakic, location of uveitis anterior 26%, intermediate 36%, posterior 22%, panuveitis 32%. Percentage of patients with active uveitis was not shown.

The primary outcome was improvement from baseline of 15 or more ETDRS letters in BCVA at week 24. The secondary outcome was reduction from baseline in CST at week 24.

The improvement in BCVA and CST was greater with CLS-TA than that in sham group (**Table 1**). Improvements were seen as early as week 4 and sustained through week 24. Among those in the CLS-TA group with active uveitis at baseline, two-thirds had resolution of inflammation at week 24.

Table 1: Efficacy Outcomes

	CLS-TA n=96	Control n=64	Comments
BCVA improvement ETDRS letters (% pts): • 15 or more letters • 10 or more letters • 5 or more letters	 47% 60 76	 16% 30 39	• Lack of active control • No data on administering more than 2 doses of CLS-TA. Study drug was not administered in the MAGNOLIA extension trial • IVT or periocular steroids was given in 80.4% rescued **control** patients
Mean ETDRS letter gained	13.8	3.0	
Mean decrease CST (µm)	-153	-18	
ME resolution (CST <300µm) at week 4 (% pts)	53	2	
>/=20% reduction in CST (%pts)	61	21	
Need for rescue therapy (%)	13	72	
Median time to first rescue (days)	89	36	

Abbreviations: BCVA=best-corrected visual acuity; CLS-TA=suprachoroidal triamcinolone; CST=central subfield thickness; ETDRS=Early Treatment Diabetic Retinopathy Study; IVT=intravitreal; ME=macular edema

Patients from sites with high enrollment who did not require rescue therapy in the PEACHTREE trial were included in the MAGNOLIA extension study for an additional 24 weeks (n=28 CLS-TA; n=5 sham). Study drug was not administered during the extension trial. In the CLS-TA group 11 out of 28 (39%) and 3 out of 5 (60%) in the sham group received rescue therapy. In a Kaplan-Meir analysis of the combined MAGNOLIA and PEACHTREE studies, the median time to rescue therapy was 257 days versus 55.5 days for the CLS-TA and sham arms, respectively. In the CLS-TA group completing the study, there was a mean gain of 16.8 letters at the last visit of the PEACHTREE trial and 12.1 letters at 48 weeks; reduction in CST was 178µm and 174µm at the two time points respectively.

Safety Considerations

- **Boxed warnings:** None
- **Contraindications:**
  - Ocular or periocular infection
  - Hypersensitivity to triamcinolone or its components
- **Other warnings / precautions**:
  - Use of corticosteroids may produce cataracts, increased intraocular pressure, and glaucoma
  - Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses.
  - Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex. Corticosteroids should not be used in patients with active ocular herpes simplex.
- **Adverse reactions**
  - The most the most common adverse reactions reported by ≥ 10% of patients and at a rate greater than control included elevated intraocular pressure and eye pain. The most common nonocular adverse reaction was headache (5% vs. 3%).

Table 2: Ocular Adverse Events >/= 5% in Either Group

	CLS-TA (%)	Control (%)
Eye pain at time of procedure	12.5	4.7
Eye pain post procedure	6.3	0
Increased IOP	11.5	15.6*
Increased IOP at time of procedure	12.5	4.7

Cataract	7.3	6.3
Vitreous detachment	5.2	1.6
Cystoid macular edema	0	17.2
Uveitis	2.1	10.9

*AEs of elevated IOP in the control arm had undergone rescue therapy with local corticosteroids

- There were no treatment related serious adverse events or deaths
- Discontinuations due to an Adverse Event: 5.2% vs 7.8%

Other Considerations

- Ongoing studies using CLS-TA with or without intravitreal aflibercept in DME and using CLS-TA with intravitreal aflibercept in macular edema following retinal vein occlusion

Other Therapeutic Options

Corticosteroids are the mainstay of treatment in noninfectious UME. Other treatments include systemic corticosteroids and immunomodulatory agents.

The use of topical corticosteroids is reserved for milder forms of UME, usually associated with anterior uveitis. For other cases, periocular or intravitreal corticosteroid injections are used. These include periocular TCA, intravitreal TCA, and dexamethasone implant. Most of the data for periocular or intravitreal TCA and dexamethasone implant are from small retrospective case series, prospective, interventional case series/nonrandomized studies.

More recently, an NIH sponsored study (POINT trial) compared periocular TCA, IVT TCA, and dexamethasone implant in patients with macular edema due to non-infectious anterior, intermediate, posterior, or panuveitis (either active or inactive uveitis was permitted). For the purposes of this review, the POINT trial was used to serve as an indirect comparison to CLS-TA **(Table 3).**

Table 3: Indirect Comparison of CLS-TA and Other Injectable Steroids

	Treatments	Mean ↑BCVA (# letters)	Resolution of ME (wk4)	≥20% ↓ ME	# pts receiving 1/2/3/4 doses	↑IOP (%pts)	IOP↓ meds (%)	Cataracts (%pts)
24-week PEACHTREE trial	CLS-TA	13.8	53%	61%	2 doses per protocol	11.5	7.3	7.3
24-week POINT trial	TCA periocular* TCA IVT DEX IMP	4.1 9.6 9.2	15% 45% 50%	60% 79% 70%	73/36/4/1 79/38/8/3 78/44/3/0	14/20† 26/30† 39/41†	32 43 34	Not reported

Abbreviations: DEX IMP=dexamethasone implant; IOP=intraocular pressure; IVT-intravitreal; ME=macular edema; TCA=triamcinolone
*In the POINT trial, periocular TCA was given either by a periorbital floor or posterior sub Tenon's approach
†In the POINT trial, increased IOP data are shown as ≥ 10mmHg increase in IOP from baseline/IOP ≥ 24 mm Hg

Other ways to administer via the suprachoroidal space

The suprachoroidal space can also be accessed for drug delivery via sclerotomy and insertion of a catheter or canula or by using a standard hypodermic needle. Sclerotomy is performed in an operating room and has risks and potential complications (e.g., hemorrhage, choroidal tear, endophthalmitis). When using a standard hypodermic needle, there is no visualization of the space; therefore, provider skill is required for precise injection. Risks include inadvertent injection into other structures, choroidal hemorrhage, and retinal detachment.

Projected Place in Therapy

- Use should be restricted to retina and uveitis specialists and used for patients with macular edema associated with non-infectious uveitis who have had an inadequate response or clinically significant adverse events to periocular or intravitreal triamcinolone injection or have contraindications.

- Head-to-head trials comparing CLS-TA to other steroids and routes of administration are needed. Based on indirect comparisons, suprachoroidal TCA may result in a lower incidence of increased IOP compared to periorbital/intravitreal TCA or dexamethasone implant. There may be a role for those who are steroid responsive, particularly in those who cannot tolerate an additional increase in IOP (e.g., uncontrolled or difficult to control glaucoma); however, patients with elevated IOP >22mmHg or uncontrolled glaucoma were excluded from the trials, so safety in this population is unknown.

References

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