

**Company**

Bausch + Lomb

**Drug or Device Name**

XIPERE®

**Category**

Medical Technology

**Compound/Technical Name**

triamcinolone acetonide injectable suspension

**Trade Name**

XIPERE®

**Date of Approval**

10/22/2021

**Therapeutic Categories**

Ophthalmology

**Indications**

XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use is a corticosteroid indicated for the treatment of macular edema associated with uveitis.

**Background**

Uveitis, or eye inflammation, may not sound serious, but if untreated, it can cause irreversible damage to vital eye tissue. Progression of the disease can lead to significant complications such as glaucoma, cataracts, optic nerve damage, retinal detachment, and vision loss. Although it is widely understood that macular edema, or the build-up of fluid in the macula, is the leading cause of vision loss for those with uveitis, there have been no approved therapies indicated for this condition until recently. In October of 2021, XIPERE® (triamcinolone acetonide injectable suspension) became the first therapy approved for the treatment of macular edema associated with uveitis. It is also the first and only therapy approved utilizing the eye's suprachoroidal space for drug delivery. The administration of XIPERE® via the suprachoroidal space is potentially revolutionary. Treatment for retinal and back of eye diseases has traditionally relied on administration methods that include topical, systemic, sub tenon, and intravitreal therapies, which can achieve low bioavailability, limited penetration to diseased tissue, or unnecessarily expose healthy, non-targeted parts of the eye. To address these shortcomings, researchers have been looking for alternative localized delivery methods that target diseased tissues and minimize off-target side effects. Imagine the back of the human eye as an orange; the fruit represents the vitreous, the fruit's outer membrane represents the retina, and the peel represents the outer scleral (the white part of the eye). In an intravitreal injection, therapies are injected into the center of the fruit (the vitreous) and then dispersed throughout, diffusing into tissues where there may not be disease. What if there was an innovative way to target medication directly to the diseased tissues, or in the example of an orange, right in between the orange peel and the fruit's outer membrane? In the eye, this space is known as the suprachoroidal space, located between the sclera and the choroid tissues. XIPERE® is delivered to this space utilizing a novel injection device, the SCS Microinjector®, to precisely target medication circumferentially to the suprachoroidal space where it then spreads directly to the back of the eye and the central retina, the location of macular edema.

**Development**

In October 2019, Bausch + Lomb, acquired the exclusive license for the commercialization and development of XIPERE® in the United States and Canada. Clearside Biomedical, Inc. developed XIPERE® using its patented, proprietary SCS Microinjector® and oversaw the drug development process through FDA approval. The clinical program for XIPERE® included the pivotal Phase 3 trial (PEACHTREE), a Phase 3, multi-center, non-interventional extension study (MAGNOLIA), and an open-label safety trial (AZALEA). FDA approval was based on results from a randomized, controlled, double-masked Phase 3 clinical trial (PEACHTREE trial) of XIPERE® in which 160 patients with macular edema associated with noninfectious uveitis were randomized to receive XIPERE® or a control injection at baseline and at 12 weeks. XIPERE® is the first and only uveitic macular edema treatment to demonstrate clinical efficacy with a BCVA (Best Corrected Visual Acuity) primary endpoint. The data demonstrated that patients with noninfectious uveitis in the XIPERE® study arm experienced clinically and statistically significant improvement in vision relative to the control arm, demonstrating the efficacy of suprachoroidal injection of XIPERE® for the treatment of macular edema associated with uveitis. No serious adverse events (AEs) considered by the investigators related to treatment were reported.

**Innovation**

Enhanced-depth imaging optical coherence tomography (EDI-OCT) has led to new insights about the suprachoroidal space (SCS). Once considered visible only under pathologic conditions, the suprachoroidal space is now recognized as an administration route that can provide exceptional access and high bioavailability to the posterior segment of the eye for small molecule suspensions. The suprachoroidal space is located between the sclera and the choroid, which expands upon injection, allowing delivery to the posterior structures of the eye. Suprachoroidal administration is an innovative approach for delivering ocular therapies that may facilitate more targeted delivery of therapeutic agents to the retina and choroid. Unlike traditional intraocular administration of therapies, this administration technique via the SCS Microinjector® offers unprecedented access to the back of the eye where sight-threatening disease often occurs and provides targeted delivery to potentially improve efficacy and compartmentalization of medication in an in-office, non-surgical setting. It is designed to provide higher

proportions of absorption relative to intravitreal injection (SOC) and may limit corticosteroid exposure to the anterior segment. Limiting this exposure can reduce the risk of certain adverse events, such as cataracts, intraocular pressure elevation, and exacerbation of glaucoma, which are commonly associated with local corticosteroid delivery techniques. With XIPIRE® as the first and only treatment to utilize the suprachoroidal space for drug delivery, the door is now open for further exploration of this administration route as an alternative in retinal disease management. XIPIRE® may be the first of many therapies approved for suprachoroidal delivery. There are multiple clinical trials utilizing the SCS Microinjector® for suprachoroidal delivery of therapeutic entities for a variety of sight-threatening conditions, including a tyrosine kinase inhibitor for wet AMD, a gene therapy for wet AMD and diabetic retinopathy, and a virus-like drug conjugate for choroidal melanoma, the most common eye tumor in adults. To date there has been a strong positive response to XIPIRE and this novel delivery technique, with more than 800 physicians who have received training to administer XIPIRE via the suprachoroidal space.

#### Pubmed

<https://pubmed.ncbi.nlm.nih.gov/32173113/> <https://pubmed.ncbi.nlm.nih.gov/34406900/> <https://pubmed.ncbi.nlm.nih.gov/33712478/>  
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#### Attachments

- 1656512702Suprachoroidal\_CLS-TA\_for\_non-infectious\_uveitis\_an\_open-label\_safety\_trial\_(AZALEA)\_BJO[1].pdf
- 1656512670Suprachoroidal\_CLS\_TA\_with\_and\_without\_Systemic\_Corticosteroid\_and\_or\_Steroid\_Sparing\_Therapy\_A\_Post\_Hoc\_Analysis\_of\_the\_Phase\_3[1].pdf
- 1656512739Suprachoroidally\_Delivered\_DNA\_Nanoparticles\_Transfect\_Retina\_and\_Retinal\_Pigment\_Epithelium-Choroid\_in\_Rabbits[1].pdf
- 1656512725Suprachoroidal\_Delivery\_of\_Viral\_and\_Nonviral\_Gene\_Therapy\_for\_Retinal\_Diseases[1].pdf
- 1656512714Suprachoroidal\_Delivery\_of\_Small\_Molecules\_Nanoparticles\_Gene\_and\_Cell\_Therapies\_for\_Ocular\_Diseases[1].pdf
- 1656512650Extension\_study\_of\_the\_safety\_and\_efficacy\_of\_CLS-TA\_for\_treatment\_of\_macular\_oedema\_associated\_with\_non-infectious\_uveitis\_(MAG[1]).pdf
- 1656512631Evaluation\_of\_Long-Lasting\_Potential\_of\_Suprachoroidal\_Axitinib\_Suspension[1].pdf
- 1656512590Clinical\_Characterization\_of\_Suprachoroidal\_Injection\_Procedure\_across\_3\_Retinal\_Disorders[1].pdf
- 1656512575Biomechanics\_of\_suprachoroidal\_drug\_delivery\_From\_benchtop\_to\_clinical\_investigation\_in\_ocular\_therapies[1].pdf
- 1656512604CLS-TA\_versus\_rescue\_therapies\_A\_Post\_Hoc\_Analysis\_of\_the\_Phase\_3\_PEACHTREE\_study[1].pdf
- 1656512615Efficacy\_and\_Safety\_of\_Suprachoroidal\_CLS-TA\_for\_Macular\_Edema\_Secondary\_to\_Noninfectious\_Uveitis\_(PEACHTREE)[1].pdf