NEW DRUG APPROVAL

Brand Name	Xipere™
Generic Name	triamcinolone acetonide
Drug Manufacturer	Clearside Biomedical, Inc.

New Drug Approval

FDA Approval Date: October 22, 2021
Review Designation: Standard
Review Type: Type 3 - New Dosage Form; NDA: 211950
Access Restrictions: None

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Macular edema is the build-up of fluid in the macula, an area in the center of the retina. The retina is the light-sensitive tissue at the back of the eye and the macula is the part of the retina responsible for sharp, straight-ahead vision. Fluid buildup causes the macula to swell and thicken, which distorts vision. The primary symptom of macular edema is blurry or wavy vision near or in the center of your field of vision. Colors might also appear washed out or faded. Most people with macular edema will have symptoms that range from slightly blurry vision to noticeable vision loss.
Reported rates of uveitic ME ranging from 20% to 70%, depending on the ancillary tests used (fundus examination, fluorescein angiography, optical coherence tomography). Macular edema might develop due to uveitis itself or occur as an adverse effect of drugs taken for different diseases. It is more frequently observed in adults than in children, in chronic uveitis, and in intermediate uveitis. Males with ankylosing spondylitis are more prone to develop ME than females. Three patterns of uveitic ME are observed, either isolated or in combination: cystoid ME, the most frequently encountered pattern seen in up to 80% of cases, diffuse ME and serous retinal detachment.

Efficacy

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.

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

Patients 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	

* 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. BCVA mean change from baseline at different visits is shown in Figure 1. Central subfield retinal thickness (CST) mean change from baseline at different visits is shown in Figure 2.

Figure 1: Mean Change from Baseline in BCVA

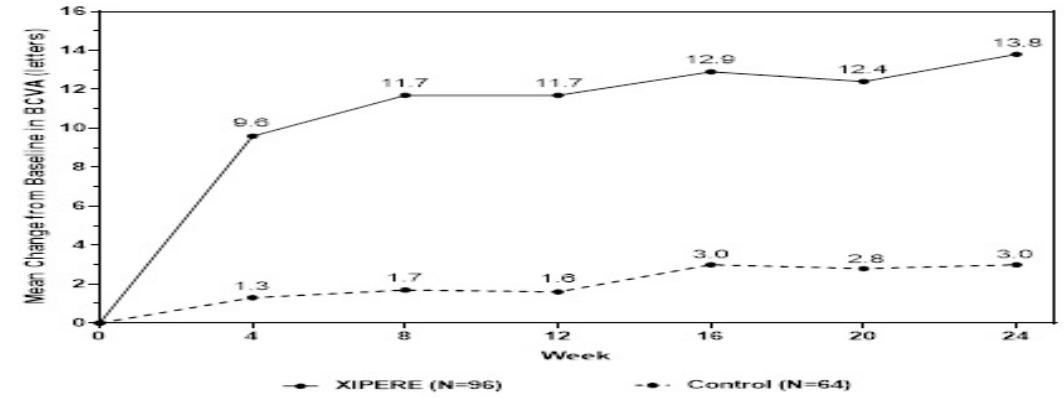
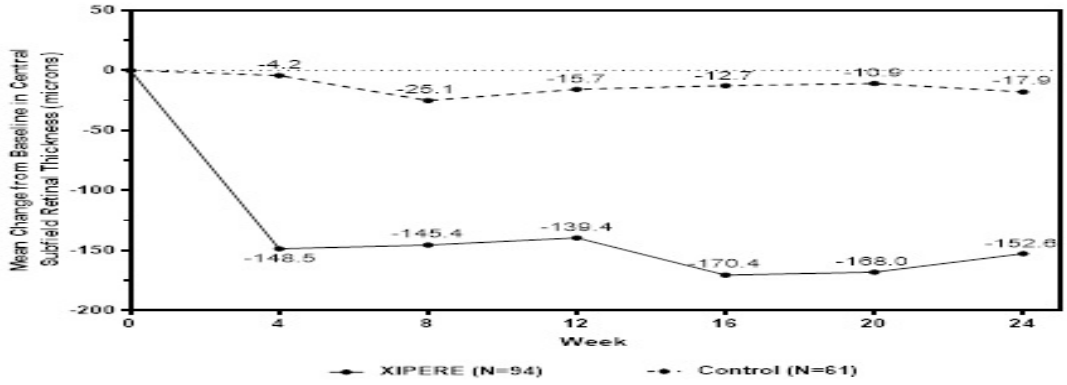


Figure 2: Mean Change from Baseline in CST



Safety

ADVERSE EVENTS

In controlled studies, 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 ocular (study eye) adverse reactions occurring in ≥ 2% of patients and non-ocular adverse reactions occurring in ≥ 5% of patients are shown in below screenshot.

Adverse Reaction	XIPERE™ (N = 96) n (%)	Control (N = 64) n (%)
Ocular		
Increased intraocular pressure, non-acute [a, b]	13 (14%)	9 (14%)
Eye pain, non-acute [b]	11 (12%)	0
Cataract [c]	7 (7%)	4 (6%)
Increased intraocular pressure, acute [a, d]	6 (6%)	0
Vitreous detachment	5 (5%)	1 (2%)
Injection site pain	4 (4%)	2 (3%)
Conjunctival haemorrhage	4 (4%)	2 (3%)
Visual acuity reduced	4 (4%)	1 (2%)
Dry eye	3 (3%)	1 (2%)
Eye pain, acute [d]	3 (3%)	0
Photophobia	3 (3%)	0
Vitreous floaters	3 (3%)	0
Uveitis	2 (2%)	7 (11%)
Conjunctival hyperaemia	2 (2%)	2 (3%)
Punctate keratitis	2 (2%)	1 (2%)
Conjunctival oedema	2 (2%)	0
Meibomianitis	2 (2%)	0
Anterior capsule contraction	2 (2%)	0
Chalazion	2 (2%)	0
Eye irritation	2 (2%)	0
Eye pruritus	2 (2%)	0
Eyelid ptosis	2 (2%)	0
Photopsia	2 (2%)	0
Vision blurred	2 (2%)	0
Non-ocular		
Headache	5 (5%)	2 (3%)

[a] Includes intraocular pressure increased and ocular hypertension

WARNINGS & PRECAUTIONS

Potential Corticosteroid-Related Effects 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.
Alterations in Endocrine Function Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia can occur following administration of a corticosteroid. Monitor patients for these conditions with chronic use.

CONTRAINDICATIONS

- Ocular or periocular infections.
- Hypersensitivity to triamcinolone or any component of this product.

Clinical Pharmacology

MECHANISMS OF ACTION

Triamcinolone acetonide is a synthetic glucocorticoid (glucocorticoids are often referred to as corticosteroids) with immunosuppressive and anti-inflammatory activity. The primary mechanism of action for triamcinolone acetonide is as a corticosteroid hormone receptor agonist.

Dose & Administration

ADULTS

The recommended dosage is 4 mg (0.1 mL) administered as a suprachoroidal injection.

PEDIATRICS

N/A

GERIATRICS

N/A

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injectable suspension: triamcinolone acetonide 40 mg/mL in a single-dose vial.