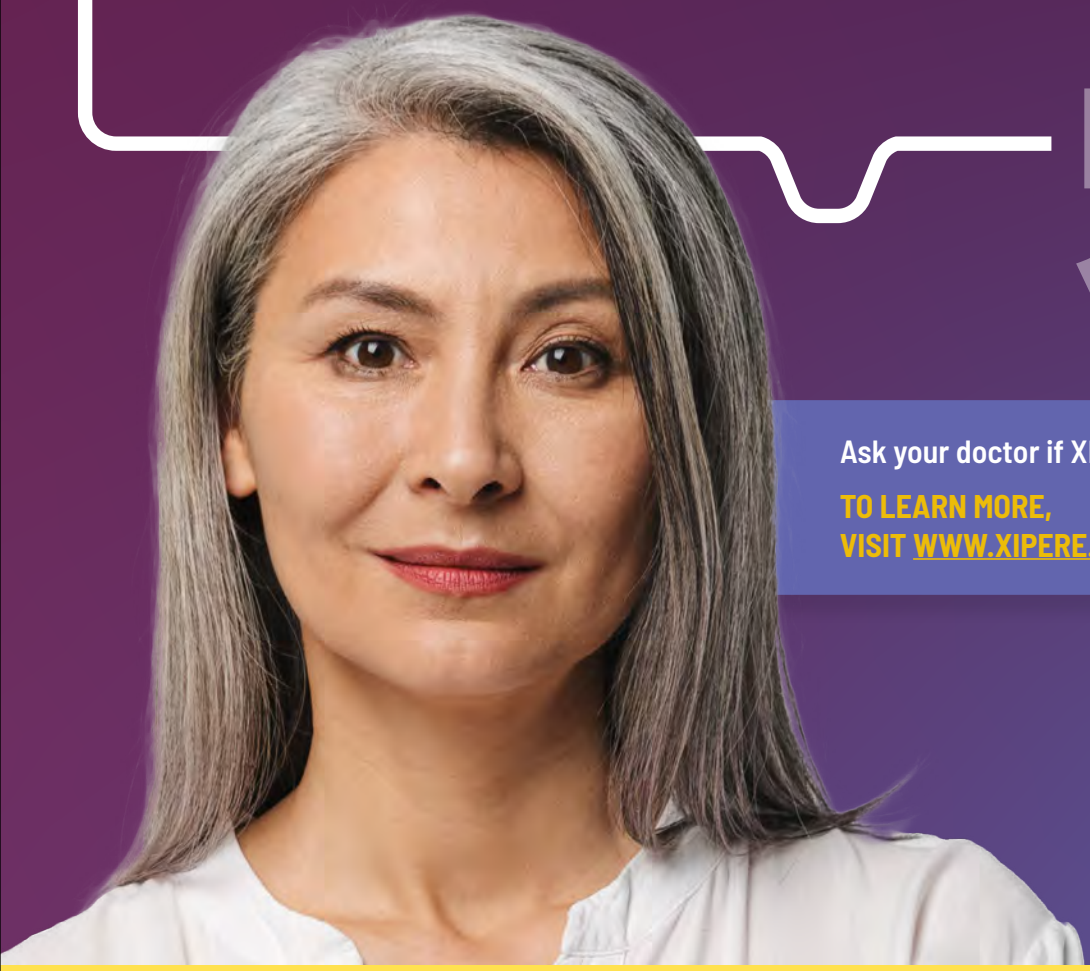
UNDERSTANDING YOUR XIPERE® TREATMENT

How you can fight back against uveitic macular edema



Marie, Age 51
Not an actual patient.

Ask your doctor if XIPERE® is right for you.

TO LEARN MORE,
VISIT WWW.XIPERE.COM/PATIENT

Indication

XIPERE® (triamcinolone acetonide injectable suspension) is a corticosteroid used to treat macular edema associated with an eye disease called uveitis.

Important Safety Information

- Your eye doctor will monitor you for elevated eye pressure following treatment and manage it with medication or surgery if required.

Please see additional Important Safety Information and accompanying full Prescribing Information.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

WHAT TO KNOW ABOUT UVEITIC MACULAR EDEMA

What is uveitic macular edema?

Uveitic macular edema is a complication of acute or chronic uveitis, or the inflammation of the uveal tract, and is the leading cause of visual impairment in cases with uveitis. Patients with this condition have an accumulation of fluid in the retinal layers or the subretinal space.

What are the symptoms?

Disturbance in contrast sensitivity

Your ability to distinguish between finer and finer increments of light versus dark

Difficulty reading

Metamorphopsia

Seeing straight lines as curved lines

Micropsia

Objects appearing smaller than they actually are

Positive relative scotoma

An area of vision loss presents itself as a black spot

How is it treated?

If it is not due to an infection, steroids likely will be used first and then other drugs may be used depending upon the response of the patient.

What happens if it goes untreated?

If macular edema continues for more than six months, cysts may form. Fibrosis and scarring from both edema and underlying uveitis may also occur. If that happens, the patient's visual outcome is usually poor.

DID YOU KNOW?

When a patient with uveitis experiences a decrease in vision, uveitic macular edema is the most frequent cause.

Important Safety Information (CONT)

- See your eye doctor right away if your eyes become red, sensitive to light or painful, or if you notice changes in vision.

Please see additional Important Safety Information and accompanying full Prescribing Information.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

WHAT IS XIPERE®?

A corticosteroid indicated for the treatment of macular edema associated with uveitis

How it works

A first-of-its-kind targeted therapy, XIPERE is delivered through a space in the eye that has the potential to reach the back of your eye—which is where your macular edema associated with uveitis is happening.

This area is called the suprachoroidal space. XIPERE is designed specifically to target this area, which surrounds the entire back part of your eye.

After your first XIPERE® injection

Your doctor will tailor a treatment regimen specific to your condition.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

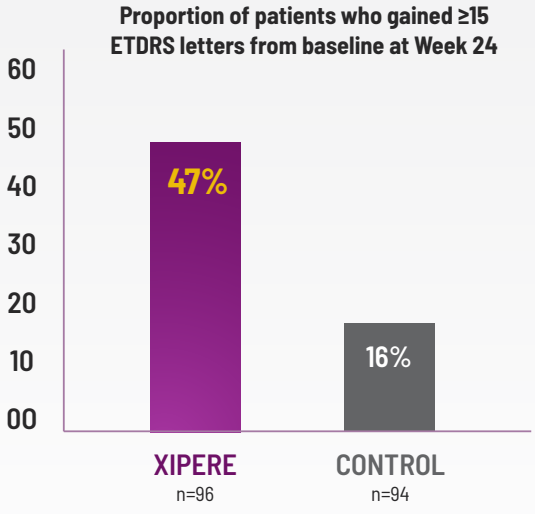
WHY XIPERE®?

In the treatment of uveitic macular edema, XIPERE® has been shown in clinical trials to provide a significant improvement in best corrected visual acuity (BCVA)

47%

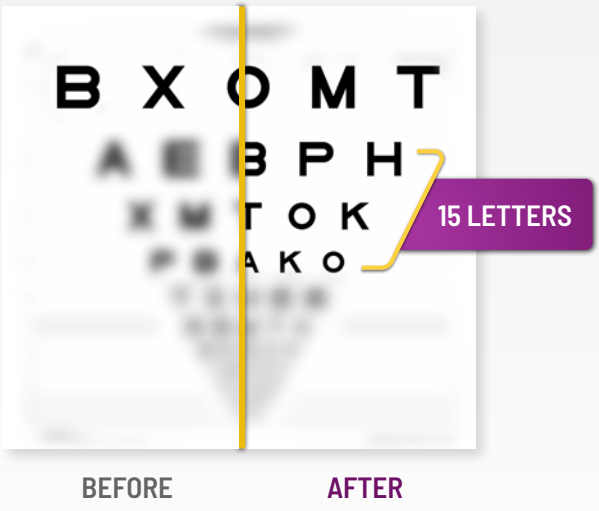
Of patients in a clinical trial for XIPERE achieved the improvement in BCVA (best corrected visual acuity) of ≥15 letters vs 16% of patients who were given a treatment that contained no medication.*

*XIPERE, n=96; Control, n=64.



15 LETTERS GAINED

In clinical studies, XIPERE provided a significant improvement in BCVA of ≥ 15 letters at 6 months from start of treatment in the group of patients on XIPERE versus the no medication group.



WHAT'S BCVA?

You've heard of 20/20 vision, that's a reading of BCVA. If you have your vision corrected with glasses or contacts, it's the best you can see on the eye chart.

XIPERE® was well tolerated by patients in clinical trials

The safety of XIPERE was assessed across 3 studies that lasted as long as 48 weeks.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

PREPARING FOR TREATMENT WITH XIPERE®

Check out this playlist to help you relax before your appointment on the ride over.

Have someone drive you to and from the office for your treatment as you may not be able to drive after.

Your eye doctor will use anesthesia applied to the eyelid and surface of the eye to help manage pain or discomfort.

To find out if XIPERE® is right for you, talk to your doctor.

Important Safety Information (CONT)

- XIPERE® is not appropriate for use in patients with eye infections. It should be used with caution in patients with a history of herpes simplex in the eye.

Please see additional Important Safety Information and accompanying full Prescribing Information.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

AFTER TREATMENT WITH XIPERE®

This is a **first-of-its-kind targeted therapy** which is delivered through a space in the eye that has the potential to reach the back of the eye—where your macular edema associated with uveitis is happening.

After your XIPERE® injection, your eye doctor will monitor you for elevated eye pressure following treatment and manage it with medication or surgery if required.

See your eye doctor right away if your eyes become red, sensitive to light or painful, or if you notice changes in vision.

If being treated with XIPERE for extended periods of time, you will be monitored for problems with the body's hormonal system, which controls the ability to respond to stress.

In clinical studies, the most common eye-related side effects were increased eye pressure and eye pain. Other side effects included cataract, floaters or flashes of light, injection site pain, burst blood vessels, reduced or blurred vision, dry eye, light sensitivity, redness, infection, swelling, watery eyes, eye or eyelid irritation, bumps on the eyelid, itchy eyes, and drooping eyelid.

The most common non-eye-related side effect was headache.

Let your doctor know if you are pregnant or plan to become pregnant as corticosteroids should be used during pregnancy or nursing only if the potential benefit justifies the potential risk to the fetus or nursing infant.

IN A SMALL SUBSET OF PATIENTS*,

50%

MAINTAINED AN AVERAGE OF ABOUT 12 LETTERS OF BCVA FOR NINE MONTHS

*Study included 28 patients who received XIPERE

Important Safety Information (CONT)

- XIPERE® is not appropriate for use in patients with a known allergy to triamcinolone acetonide or any other components of this product.

Please see additional Important Safety Information and accompanying full Prescribing Information.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

Bausch + Lomb is committed to providing savings and reimbursement support for XIPERE®

XIPERE Savings Program

You may be eligible* to **pay as little as a $0 copay** with the XIPERE Savings Program.
Visit **xipere.copaysavingsprogram.com** to find out if you qualify.

Reimbursement support

1. After your doctor determines that XIPERE® is right for you, their office staff will work with a **FOCUS ON ACCESS™ (FOA) Representative** to complete a Patient Information and Enrollment form for you. Your doctor will ask you to sign the patient authorization section of the form.

2. Within 24 hours, an FOA representative will contact your insurance company to determine your health insurance benefits and coverage for XIPERE. They will also determine if you may be eligible to pay as little as a $0 copay through the XIPERE Savings Program.

3. Then, a FOA representative will call you to explain your insurance coverage and discuss cost support options with you such as the XIPERE Savings program.

4. Once that is completed, you can then schedule your first XIPERE treatment.

5. After that, you can continue to utilize FOA for support as needed, in case your insurance changes.

Visit www.xipere.com/patient for more information

on the FOA program or call 1-866-272-8838 Monday – Friday, 9:00 AM to 5:00 PM ET

*Terms, Conditions and Limitations Apply. Your doctor can refer you to the Focus on Access program to determine your eligibility for patient assistance. Insurance plans and coverage are subject to change. Bausch + Lomb does not guarantee coverage or reimbursement for the product.

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

Some days my macular edema may still hold me back, but I can feel good knowing that, together, we are

FIGHTING BACK WITH XIPERE®

Indication

XIPERE® (triamcinolone acetonide injectable suspension) is a corticosteroid used to treat macular edema associated with an eye disease called uveitis.

Important Safety Information

- Your eye doctor will monitor you for elevated eye pressure following treatment and manage it with medication or surgery if required.
- See your eye doctor right away if your eyes become red, sensitive to light or painful, or if you notice changes in vision.
- XIPERE is not appropriate for use in patients with eye infections. It should be used with caution in patients with a history of herpes simplex in the eye.
- XIPERE is not appropriate for use in patients with a known allergy to triamcinolone acetonide or any other components of this product.
- Use of corticosteroids such as XIPERE may produce cataracts, increased eye pressure and glaucoma, and may increase the likelihood of eye infections.
- Patients being treated with XIPERE for extended periods of time will be monitored for problems with the body's hormonal system, which controls the ability to respond to stress.
- In clinical studies, the most common eye-related side effects were increased eye pressure and eye pain. Other side effects included cataract, floaters or flashes of light, injection site pain, burst blood vessels, reduced or blurred vision, dry eye, light sensitivity, redness, infection, swelling, watery eyes, eye or eyelid irritation, bumps on the eyelid, itchy eyes, and drooping eyelid.

  The most common non-eye-related side effect was headache.
- Corticosteroids should be used during pregnancy or nursing only if the potential benefit justifies the potential risk to the fetus or nursing infant. Talk to your eye doctor.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

Please see full Prescribing Information enclosed.

BAUSCH + LOMB

XIPERE®
(triamcinolone acetonide injectable suspension) 40 mg/mL

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use XIPERE™ safely and effectively. See full prescribing information for XIPERE™.

XIPERE™ (triamcinolone acetonide injectable suspension), for suprachoroidal use

Initial U.S. Approval: 1957

---------- INDICATIONS AND USAGE ----------

XIPERE™ is a corticosteroid indicated for the treatment of macular edema associated with uveitis. (1)

---------- DOSAGE AND ADMINISTRATION ----------

The recommended dosage is 4 mg (0.1 mL) administered as a suprachoroidal injection. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------

Injectable suspension: triamcinolone acetonide 40 mg/mL in a single-dose vial. (3)

---------- CONTRAINDICATIONS ----------

- Ocular or periocular infections (4.1)
- Hypersensitivity to triamcinolone or any component of this product (4.2)

---------- WARNINGS AND PRECAUTIONS ----------

Potential Corticosteroid-Related Effects: Use of corticosteroids may produce cataracts, increased intraocular pressure, and glaucoma. (5.1)

---------- ADVERSE REACTIONS ----------

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. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Clearside Biomedical, Inc. at 1-866-494-7373 (1-866-4XIPERE) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

XIPERE™ (triamcinolone acetonide injectable suspension) 40 mg/mL is indicated for the treatment of macular edema associated with uveitis.

2 DOSAGE AND ADMINISTRATION

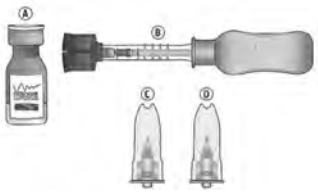
2.1 Dosing Information

For suprachoroidal injection using the SCS Microinjector®. The recommended dose of XIPERE™ is 4 mg (0.1 mL of the 40 mg/mL injectable suspension).

2.2 Preparation for Administration

Suprachoroidal injection is performed under aseptic conditions. The components for administration include:

A. One single-dose glass vial of triamcinolone acetonide injectable suspension 40 mg/mL
B. One SCS Microinjector® syringe with vial adapter attached
C. One 30-G x 900-µm needle
D. One 30-G x 1100-µm needle



Step 1

Figure A

Remove the tray from the carton (see Figure A).
The tray consists of two compartments:
- An open non-sterile compartment that holds the vial
- A sealed compartment that contains a sterile tray

Step 2

Figure B

Examine the tray for damage (see Figure B). Ensure that the sealed compartment cover is intact and that there is no evidence of damage. If damage is present, do not use.

Step 3

Figure C

Remove the vial from the tray (see Figure C). Examine the vial and ensure there is no evidence of damage. Set aside for use in step 6.

Step 4

Figure D

Peel off the compartment cover, exposing the sterile tray (see Figure D).

Step 5

i *ii* *iii*

Figure E

Grasp and hold the long sides of the tray and invert the tray. Squeeze gently to release the sterile tray onto the appropriate sterile preparation surface (see Figure E, *i – iii*).

Step 6

i *ii* *iii* *iv*

Figure F

Vigorously shake the vial for 10 seconds. Inspect the vial for clumping or granular appearance of the sterile contents. If clumping or granular appearance is present, do not use. Remove the protective plastic cap from the vial and clean the top of the vial with an alcohol wipe. Place the vial on a flat surface (see Figure F, *i – iv*). To avoid settling of the suspension, continue to the next steps without delay.

Step 7

Figure G

Remove the syringe with attached vial adapter from the tray (see Figure G). Ensure the vial adapter is secured to the syringe by tightening the connection.

Step 8

Figure H

Holding the clear barrel of the syringe, connect the vial adapter to the vial by firmly pushing the spike of the vial adapter straight through the center of the vial septum until it snaps securely into place (see Figure H).

NOTE: Do not introduce additional air into the syringe prior to connecting the vial adapter to the vial.

Step 9

i *ii*

Figure I

Invert the entire assembly so that the vial is directly above the syringe. Slide the white plunger handle all the way back and forth multiple times to fill the entire syringe with drug and remove any remaining air (see Figure I, *i* and *ii*).

NOTE: The syringe should be handled by the clear barrel during filling, connecting and disconnecting procedures. The white plunger handle has a stop to prevent complete removal of the plunger from the syringe.

Step 10

Figure J

While holding the vial adapter and vial, disconnect the syringe by twisting it off of the adapter (see Figure J).

Retain the vial, with the vial adapter connected, in the event re-access is necessary.

Step 11

Figure K

Connect the 900-µm needle to the syringe by twisting onto the syringe (see Figure K). At the discretion of the physician, the longer needle may be used. Ensure a secure connection.

Step 12

Figure L

Hold the syringe barrel with the needle pointing up. Expel air bubbles and excess drug by slowly sliding the white plunger handle so that the plunger tip aligns with the line that marks 0.1 mL on the syringe (see Figure L).

NOTE: Perform the suprachoroidal injection without delay to prevent settling of the drug.

2.3 Administration

The suprachoroidal injection procedure should be carried out under controlled aseptic conditions, which include the use of sterile gloves, a sterile drape, a sterile eyelid speculum (or equivalent), and a sterile cotton swab. Adequate anesthesia and a broad-spectrum microbicide applied to the periocular skin, eyelid, and ocular surface are recommended to be given prior to the suprachoroidal injection.

Step 13

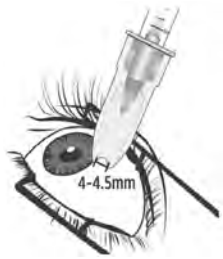
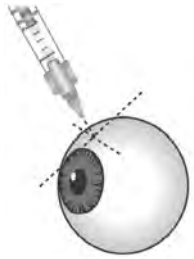


Figure M

Identify the injection site by measuring 4 – 4.5 mm posterior to the limbus using the tip of the needle cap or ophthalmic calipers (see Figure M).

Step 14



Carefully pull off the needle cap to expose the needle. Holding the syringe perpendicular to the ocular surface, insert the needle through the conjunctiva into the sclera (see Figure N).

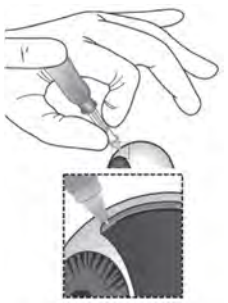
Figure N

Step 15

Once the needle is inserted into the sclera, ensure that the hub of the needle is in firm contact with the conjunctiva, compressing the sclera and creating a dimple on the ocular surface using a light amount of force against the eye. Maintain the dimple and perpendicular positioning throughout the injection procedure (see Figure O).

Figure O

Step 16



While maintaining the dimple on the ocular surface, gently press the white plunger handle so that the plunger moves forward and drug is slowly injected over 5 – 10 seconds. Movement of the plunger will be felt as a loss of resistance and indicates that the needle is in the correct anatomical location for suprachoroidal injection (see Figure P).

If resistance is felt and the plunger does not advance, confirm the hub is in firm contact with the conjunctiva creating a dimple and that the syringe is positioned perpendicular to the ocular surface. Small adjustments in positioning may be necessary.

Figure P

Step 17

Maintain the hub against the eye for 3 – 5 seconds after the drug product has been injected.

Step 18

Remove the needle slowly from the eye while holding a sterile cotton swab next to the needle as it is withdrawn. Immediately cover the injection site with a sterile cotton swab.

Step 19

Hold the swab over the injection site with light pressure for a few seconds and then remove.

If continued resistance is experienced during injection attempts:

- Remove the needle from the eye and examine the eye for any issues. If patient safety is not at risk, the physician may use medical judgment to restart the injection procedure at a new site adjacent to the original injection site.
- If resistance continues and patient safety is not at risk, the physician may use appropriate medical judgment to change to the additional included needle in the sterile tray. Twist to remove the needle and reconnect the syringe to the vial by twisting the syringe onto the vial adapter. Repeat the preparation and injection process as stated in steps 9 – 18 with the additional needle (allowing for any partial dose given with the first needle when completing preparation Step 12).

Immediately following suprachoroidal injection, patients should be monitored for elevation of intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry.

Following suprachoroidal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of eye, photophobia, blurring of vision) without delay *[see Patient Counseling Information (17)]*.

Each XIPERE™ package (microinjector syringe with vial adapter, 900-µm needle, 1100-µm needle, and vial of triamcinolone acetonide injectable suspension 40 mg/mL) is single-dose and should only be used for the treatment of one eye.

After suprachoroidal injection, all drug product and components (used or unused) must be discarded appropriately.

3 DOSAGE FORMS AND STRENGTHS

Injectable suspension: triamcinolone acetonide 40 mg/mL suspension in a single-dose glass vial for use with the supplied SCS Microinjector®.

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

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.

4.2 Hypersensitivity

XIPERE™ is contraindicated in patients with known hypersensitivity to triamcinolone acetonide or any other components of this product.

5 WARNINGS AND PRECAUTIONS

5.1 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.

5.2 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.

Corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Drug induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

XIPERE™ was studied in a multicenter, randomized, sham-controlled, double-masked study in patients with macular edema associated with uveitis. Table 1 summarizes data available from the clinical trial for XIPERE™ treated patients and control patients.

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 Table 1.

Table 1: Ocular Adverse Reactions Reported in ≥ 2% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients

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

Table 1: Ocular Adverse Reactions Reported in ≥ 2% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients *(continued)*

Adverse Reaction	XIPERE™ (N = 96) n (%)	Control (N = 64) n (%)
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
[b] Defined as not occurring on the day of the injection procedure, or occurring on the day of the injection procedure and not resolving the same day
[c] Includes cataract, cataract cortical, and cataract subcapsular
[d] Defined as occurring on the day of the injection procedure and resolving the same day

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with XIPERE™ in pregnant women to inform drug-associated risks. In animal reproductive studies from the published literature, topical ocular administration of corticosteroids has been shown to produce teratogenicity at clinically relevant doses. There is negligible systemic XIPERE™ exposure following suprachoroidal injection *[see Clinical Pharmacology (12.3)]*. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Animal Data

Animal reproduction studies using XIPERE™ have not been conducted. In animal reproductive studies from the published literature, topical ocular administration of corticosteroids to pregnant mice and rabbits during organogenesis has been shown to produce cleft palate, embryofetal death, herniated abdominal viscera, hypoplastic kidneys and craniofacial malformations.

8.2 Lactation

Risk Summary

It is not known whether ocular administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XIPERE™ and any potential adverse effects on the breastfed infant from XIPERE™. There are no data on the effects of XIPERE™ on milk production.

8.4 Pediatric Use

Safety and effectiveness of XIPERE™ in pediatric patients have not been established.

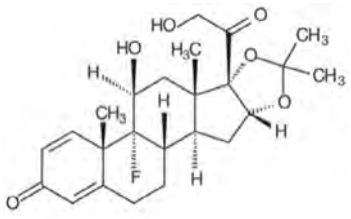
8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients following XIPERE™ administration.

11 DESCRIPTION

XIPERE™ is a sterile, preservative-free, injectable suspension of triamcinolone acetonide, a synthetic corticosteroid for use with the SCS Microinjector®. Each mL of the sterile, aqueous suspension contains 40 mg of triamcinolone acetonide with 0.55% (weight/volume [w/v]) sodium chloride for tonicity, 0.5% (w/v) carboxymethylcellulose sodium, and 0.02% (w/v) polysorbate 80. It also contains potassium chloride, calcium chloride (dihydrate), magnesium chloride (hexahydrate), sodium acetate (trihydrate), sodium citrate (dihydrate), and water for injection. Hydrochloric acid may be used to adjust pH to a target value of 6.5.

The chemical name for triamcinolone acetonide is 9-fluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone. Its chemical structure is:



Molecular weight 434.50; molecular formula $C_{24}H_{31}FO_6$

Triamcinolone acetonide occurs as a white to cream-colored, crystalline powder having not more than a slight odor and is practically insoluble in water and very soluble in alcohol.

XIPERE™ is provided as an injectable suspension in a single-dose glass vial with a rubber stopper and an aluminum seal. The SCS Microinjector® is a piston syringe and a needle approximately 1 mm in length (900-µm and 1100-µm needles are included) for conducting the suprachoroidal injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism 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.

12.3 Pharmacokinetics

In animal studies, data demonstrated that suprachoroidal injections resulted in larger amounts in total of triamcinolone acetonide found in the sclera, choroid, retinal pigment epithelial and retina, than with intravitreal injections of triamcinolone acetonide. Lower amounts of triamcinolone acetonide were found in the anterior segment and lens as compared to intravitreal injections of triamcinolone acetonide.

Plasma triamcinolone acetonide concentrations were evaluated in 19 patients with dosing of 4 mg XIPERE™ at Day 0 and Week 12. Plasma triamcinolone acetonide concentrations in all 19 patients were below 100 pg/mL at Week 4, 12, and 24 (concentrations ranged from < 10 pg/mL [LLOQ (lower limit of quantitation) of the assay] to 88.9 pg/mL), with the exception of one patient with a value of 243.4 pg/mL prior to the second dose at Week 12.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No information is available on the carcinogenic potential of triamcinolone acetonide.

Mutagenesis

No information is available on the mutagenic potential of triamcinolone acetonide.

Fertility

No information is available on the effect of triamcinolone acetonide on fertility.

14 CLINICAL STUDIES

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 2).

Table 2: 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

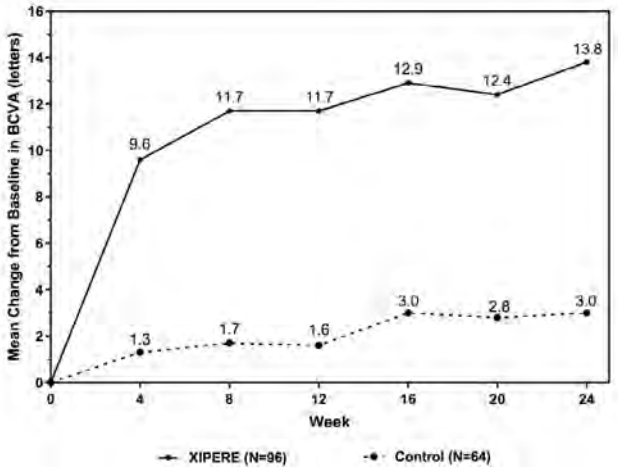
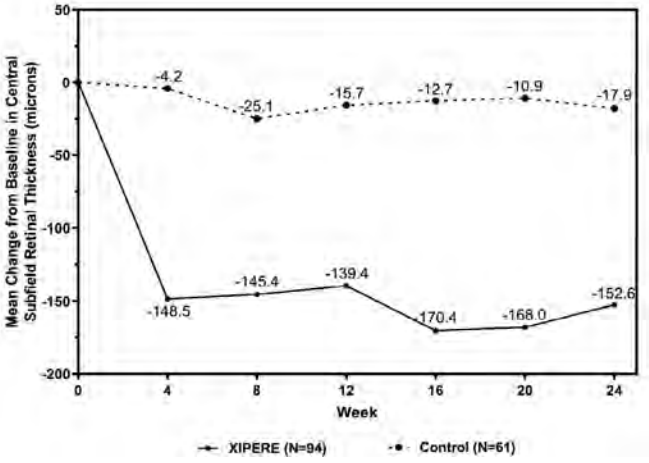


Figure 2: Mean Change from Baseline in CST



16 HOW SUPPLIED/STORAGE AND HANDLING

XIPERE™ is supplied with the following sterile components for administration, sealed in a Tyvek covered tray, and one single-dose glass vial, in a carton with a package insert (NDC 71565-040-01):

- One SCS Microinjector® syringe with vial adapter attached
- One 30-G x 900-µm needle
- One 30-G x 1100-µm needle
- One single-dose vial of triamcinolone acetonide injectable suspension 40 mg/mL (NDC 71565-040-25)

Storage: Store at 15°C to 25°C (59°F to 77°F); do not freeze. The drug vial should be protected from light by storing in the carton. Discard unused portion.

17 PATIENT COUNSELING INFORMATION

Corticosteroid-Related Effects

Advise patients that they may develop elevated intraocular pressure following treatment, which may need to be managed with medication or surgery.

When to Seek Physician Advice

Advise patients that if the eye becomes red, sensitive to light, painful, or develops a change in vision, they should seek immediate care from an ophthalmologist.

Manufactured for:

Clearside Biomedical, Inc.
900 North Point Parkway, Suite 200
Alpharetta, GA 30005

www.clearsidebio.com/patents

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