



INFLAMMATORY DRY EYE:

INTERSECTIONS WITH SYSTEMIC DISEASES

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BAUSCH + LOMB

DRY EYE DISEASE

Dry eye disease (DED) is a common and often underrecognized condition that affects millions of adults in the United States.¹

Patients may describe ocular discomfort, fatigue, or fluctuating vision that can interfere with reading, driving, or digital device use.² From a clinical standpoint, DED is often encountered as a symptom-driven complaint rather than a clearly defined diagnosis, particularly outside of eyecare settings. DED symptoms reflect the underlying loss of tear film homeostasis that defines the disease.³ The tear film is essential for optical quality and protection of the corneal and conjunctival surfaces. When tear film stability declines, hyperosmolarity triggers epithelial stress and activates inflammatory pathways that contribute to a self-perpetuating cycle of tissue damage and symptoms.⁴

DED can substantially affect quality of life, productivity, and emotional well-being.^{5,6} For individuals already living with systemic illness, chronic ocular symptoms may add further burden. Although many factors contribute to DED, systemic inflammation is an important and often overlooked driver. Autoimmune and endocrine disorders can disrupt tear production, alter ocular surface physiology, and increase inflammatory activity.^{7,8} Because many patients first report symptoms to general practitioners, rheumatologists, dermatologists, or other providers outside of eyecare, awareness of these associations is particularly relevant for non-eyecare providers (ECPs).

DED IN THE CONTEXT OF SYSTEMIC AND AUTOIMMUNE INFLAMMATORY DISEASE

DED is frequently part of a broader inflammatory picture rather than an isolated ocular condition and often occurs in individuals with systemic inflammatory or autoimmune disorders. Conditions such as Sjögren syndrome, rheumatoid arthritis, systemic lupus erythematosus, thyroid dysfunction, and diabetes are associated with a higher likelihood of tear film instability and/or ocular surface inflammation.^{7,8-10} These conditions may affect the lacrimal functional unit, the integrated system of glands, ocular surface tissues, eyelids, and neural pathways responsible for maintaining the tear film. Disruption in any part of this system can result in DED.¹¹

Systemic inflammation may further intensify DED by altering glandular secretion, affecting tear composition, and increasing epithelial susceptibility to stress. These changes contribute to hyperosmolarity and immune activation on the ocular surface.¹¹ Patients with autoimmune disease often report more persistent dryness, burning, photophobia, or fluctuating vision and are more likely to exhibit chronic ocular surface inflammation.¹¹ Evidence from studies in adults with type 2 diabetes mellitus also demonstrates reduced tear stability and secretion and increased ocular surface symptoms compared with nondiabetic individuals.¹²

In practice, patients may report ocular symptoms during visits focused on systemic disease management. For those who receive ongoing management in primary care, rheumatology, endocrinology, or dermatology settings, such environments can play an important role in early recognition of DED.⁹ Identifying DED symptoms in these patients and addressing them early may help reduce disease burden and support long-term ocular surface health.

INFLAMMATION AS A KEY DRIVER OF DED

Inflammation plays a central role in the development and progression of DED.

Understanding the inflammatory basis of DED helps explain why symptoms may persist despite treatment with lubricating drops. Tear film instability and desiccating stress activates innate immune responses on the ocular surface, including cytokines, matrix metalloproteinases, and chemokines. This can lead to an adaptive immune response and the migration of activated T cells to the ocular surface, resulting in further release of inflammatory cytokines (Figure 1).^{4,11,13} When these processes persist, a self-perpetuating inflammatory cycle can develop.

Increased expression of intercellular adhesion molecule 1 (ICAM-1) on the corneal and conjunctival

epithelium is a recognized feature of inflammatory DED and may be particularly prominent in autoimmune-associated disease.¹⁴ T cells express lymphocyte function-associated antigen 1 (LFA-1) on their surface. Interaction between LFA-1 and ICAM-1 facilitates T-cell adhesion, migration, and activation, representing an upstream driver of ocular surface inflammation.¹⁵ From a treatment perspective, this interaction represents an important point of intervention in the inflammatory cascade.

Downstream cytokines such as interleukin-17, interferon-gamma, and tumor necrosis factor-alpha contribute to epithelial injury and goblet cell loss.⁴ These inflammatory changes correlate with symptom severity and reinforce the role of inflammation as a therapeutic target in DED.¹¹

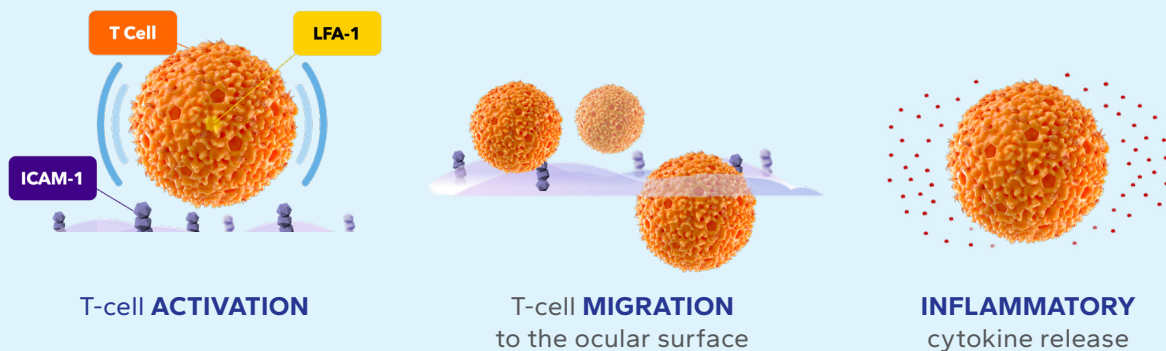


Figure 1. T-Cell-Mediated Inflammation is Central to DED Pathogenesis and Progression^{11,14,15}
DED, dry eye disease; ICAM-1, intercellular adhesion molecule 1; LFA-1, lymphocyte function-associated antigen 1

RECOGNIZING DED IN NON-EYECARE SETTINGS

DED can be challenging to diagnose, as symptoms are often nonspecific and may be described as dryness, burning, watering, fluctuating vision, ocular fatigue, grittiness, redness, or light sensitivity.^{4,16} Because these symptoms overlap with other common complaints, focused questioning is often required. From a practical standpoint, brief screening questions or validated symptom questionnaires can be incorporated into routine visits and aid identification of DED in primary care and specialty medical settings.¹⁷

“Dry eye disease is rarely just a lubrication problem. In many patients, especially those with systemic inflammatory disease, what we are really seeing is an inflammatory condition of the ocular surface that will not resolve without addressing that underlying inflammation.”

-Dr. Bloomenstein

Several DED risk factors are worth keeping in mind, including older age, female sex, autoimmune

“Dry eye is driven by inflammation. For many years, it was thought to be just a problem of aging and lack of lubrication, but that is absolutely not all that is going on.”

-Dr. McDonald

disease, thyroid dysfunction, diabetes, dermatologic inflammation, high digital device use, and polypharmacy.^{8,18} Ocular symptoms in patients with autoimmune or endocrine disease may also reflect underlying systemic inflammatory activity.^{7,10,12} Coordination of care with an ECP can support timely DED diagnosis and management, when appropriate.

When symptoms persist despite topical lubricants, environmental modifications, or basic education, initiation of prescription therapy may be warranted. Referral to an optometrist or ophthalmologist is recommended if symptoms remain unresponsive to treatment or if ocular surface damage is suspected.¹⁷ Importantly, data from the Bausch + Lomb 2025 State of Dry Eye Survey indicate strong patient openness to prescription therapy for the treatment of DED, with many individuals reporting they would consider a prescription option if recommended.¹⁹

CLINICAL CONSIDERATIONS FOR HEALTHCARE PROVIDERS

Recognition of an inflammatory component can help guide DED treatment decisions. Several prescription therapies with anti-inflammatory activity are FDA approved for the treatment of DED. These include short (≤2-week) courses of the corticosteroid loteprednol etabonate 0.25%, cyclosporine A in several ophthalmic formulations, and lifitegrast ophthalmic solution 5%, marketed as Xiidra.²⁰ These therapies address inflammatory pathways that contribute to symptom persistence and ocular surface damage.^{4,11}

INDICATION

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

IMPORTANT SAFETY INFORMATION

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.

In patients whose DED presentation suggests ongoing inflammatory activity, including those with autoimmune disease, Xiidra (lifitegrast ophthalmic solution) 5% may be appropriate.¹⁵ Effective use requires patient education regarding dosing, potential adverse effects such as instillation-site irritation, blurred vision, or dysgeusia, and realistic expectations for onset of improvement. Many patients report symptom changes between 2 and 12 weeks with consistent use.²¹

“When patients report fluctuating vision, burning, foreign body sensation, or red eyes that worsen during the day or with computer use, these are strong signs of inflammatory dry eye. Starting Xiidra and then referring for follow-up with an ECP is doing the patient a great favor.”

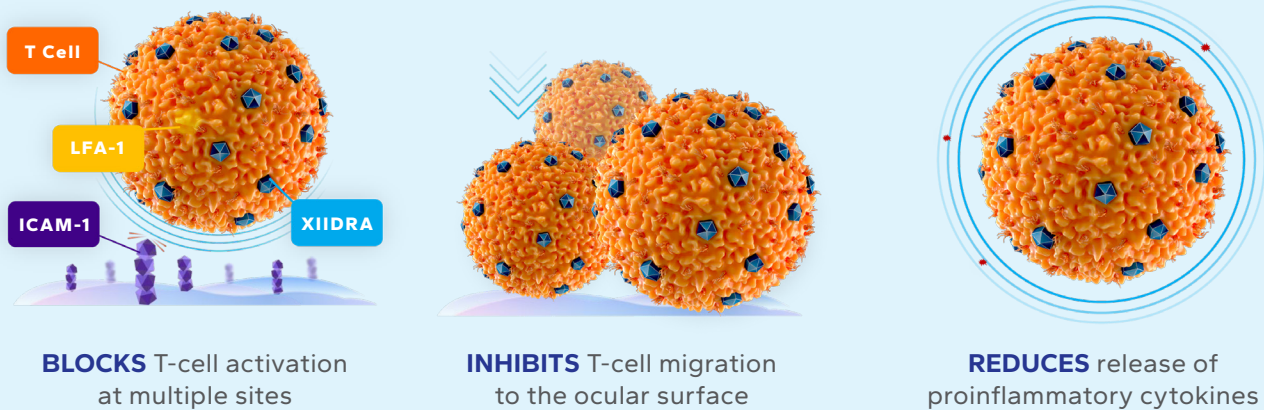
-Dr. McDonald

“Prove to me you don’t have dry eye disease, because so many patients do. In my practice, we assume there is an inflammatory component unless we can clearly rule it out.”

-Dr. Bloomenstein

XIIDRA: A TARGETED ANTI-INFLAMMATORY TREATMENT FOR DED

Lifitegrast was developed to address a specific immunologic interaction involved in ocular surface inflammation and inhibits binding between LFA-1 on T cells and ICAM-1 on the ocular surface, endothelial cells of lymphatic tissues and dendritic cells. By preventing these interactions, Xiidra reduces T-cell adhesion, migration, and activation and limits downstream inflammatory signaling (**Figure 2**).^{15,22}



The exact mechanism of action of Xiidra in DED is not known.

Figure 2. Xiidra Reduces Inflammation by Targeting T Cells^{15,20,22}

DED, dry eye disease; ICAM-1, intercellular adhesion molecule 1; LFA-1, lymphocyte function-associated antigen 1

IMPORTANT SAFETY INFORMATION (CONT'D)

In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

In clinical studies, this mechanism was associated with improvements in both symptoms and signs of DED that were meaningful to patients.^{21,23,25} Participants in the OPUS-1, OPUS-2, and OPUS-3 studies reported meaningful improvements in eye dryness, with some individuals experiencing benefits as early as 2 weeks and continued improvement through 12 weeks (Figure 3).^{21,23-24} Improvements in inferior corneal fluorescein staining, a key DED sign associated with

desiccation stress and loss of epithelial cell integrity were observed at 12 weeks in two out of the three studies,¹⁷ further supporting beneficial effects of Xiidra (lifitegrast ophthalmic solution) 5% on the ocular surface.^{21,23}

Long-term safety data from the 1-year SONATA study show that Xiidra was generally well tolerated. Most adverse events were mild and transient, and no serious ocular treatment-emergent events were reported.²⁵

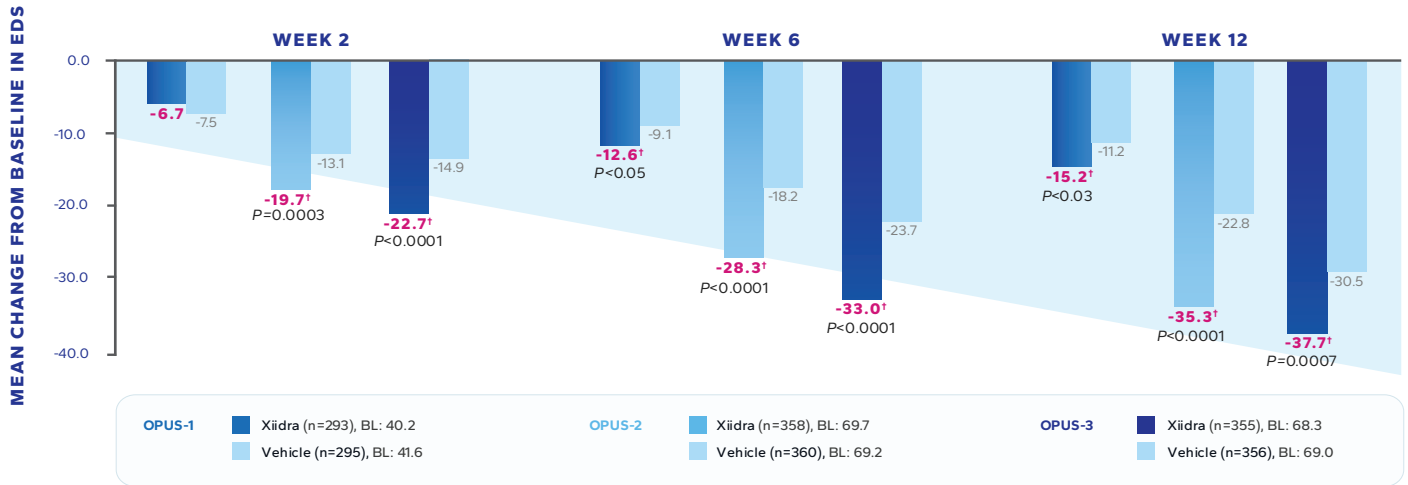


Figure 3. Xiidra Improves Symptoms of Eye Dryness*²⁰⁻²⁴

*Xiidra significantly reduced symptoms of eye dryness at 2 weeks in 2 out of 3 phase 3 clinical studies and at 6 and 12 weeks in all 3 studies. †Statistically significant improvement compared with vehicle. In OPUS-2 and -3, Week 2 was an ad-hoc and a secondary endpoint, respectively. In the phase 2 and OPUS-2 study, Week 6 was a secondary and an ad-hoc endpoint, respectively. In OPUS-2 and -3, Week 12 was the co-primary and primary endpoint, respectively. An earlier, phase 2, double-masked, placebo-controlled trial was conducted, in which Xiidra demonstrated improvements in symptoms (Eye Dryness Score) at 6 and 12 weeks and signs (inferior corneal staining) at 12 weeks. | BL, baseline; EDS, eye dryness score

CONCLUSION

DED is a common, chronic condition with meaningful effects on ocular comfort, visual function, and daily activities. Its association with systemic inflammatory and autoimmune disorders makes it highly relevant to clinicians across multiple specialties.

>50%
Reduction from
baseline in symptoms
by Week 12 in
OPUS-2 and -3^{21,24}



IMPORTANT SAFETY INFORMATION (CONT'D)

Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

KEY TAKEAWAYS

- **DED is a common condition and frequently encountered in clinical practice**

Millions of adults experience symptoms that often present first outside of eyecare settings

- **DED is not just a lubrication problem**

Inflammation is a primary driver of symptoms and disease progression

- **Systemic disease is an important consideration in DED**

Autoimmune and inflammatory conditions are associated with more persistent DED symptoms

- **Some symptoms may suggest inflammation**

Fluctuating vision, burning, redness, and light sensitivity may indicate inflammatory involvement

- **LFA-1/ICAM-1 is a key pathway**

This interaction drives T-Cell-mediated ocular surface inflammation in DED

“When inflammatory DED is suspected, initiating Xiidra and referring patients to an eyecare professional can enable inflammation to be addressed early, when intervention may make the greatest difference.”

-Dr. Bloomenstein

- **Xiidra (lifitegrast ophthalmic solution) 5% targets DED inflammation**

Xiidra was specifically designed to block LFA-1/ICAM-1 specifically for the treatment of DED

- **Providers outside eyecare can play a critical role**

Early recognition, treatment initiation, and coordination with ECPs can help improve outcomes

Greater awareness of these connections may support earlier recognition and more comprehensive, collaborative management across healthcare settings.

Targeted treatment with Xiidra may help interrupt the DED inflammatory cycle and provide early relief with long-term control. Collaboration among primary care, rheumatology, dermatology, endocrinology, and eyecare professionals can help optimize outcomes.

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HIGHLIGHTS OF PRESCRIBING INFORMATION

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

XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

INDICATIONS AND USAGE

Xiidra (lifitegrast ophthalmic solution) 5% is a lymphocyte function-associated antigen-1 (LFA-1) antagonist indicated for the treatment of the signs and symptoms of dry eye disease (DED). (1)

DOSAGE AND ADMINISTRATION

One drop twice daily in each eye (approximately 12 hours apart). (2)

DOSAGE FORMS AND STRENGTHS

Ophthalmic solution containing lifitegrast 50 mg/mL (5%). (3)

CONTRAINDICATIONS

Hypersensitivity. (4)

ADVERSE REACTIONS

The most common adverse reactions (incidence 5%-25%) following the use of Xiidra were instillation-site irritation, dysgeusia, and decreased visual acuity. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb Incorporated at 1-800-553-5340 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2023

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

2 DOSAGE AND ADMINISTRATION

Instill one drop of Xiidra twice daily (approximately 12 hours apart) into each eye using a single-use container. Discard the single-use container immediately after using in each eye.

Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

3 DOSAGE FORMS AND STRENGTHS

Ophthalmic solution containing lifitegrast 50 mg/mL (5%).

4 CONTRAINDICATIONS

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation [see Adverse Reactions (6.2)].

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Hypersensitivity [see Contraindications (4)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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.

In five clinical trials of DED conducted with lifitegrast ophthalmic solution, 1401 patients received at least one dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had less than or equal to 3 months of treatment exposure. One hundred-seventy patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5%-25% of patients were instillation-site irritation, dysgeusia, and reduced visual acuity.

Other adverse reactions reported in 1%-5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Rare serious cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, allergic conjunctivitis, dyspnea, angioedema, and allergic dermatitis have been reported. Eye swelling and rash have also been reported [see Contraindications (4)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Xiidra use in pregnant women to inform any drug-associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from pre-mating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear [see Clinical Pharmacology (12.3)].

Data

Animal Data

Lifitegrast administered daily by IV injection to rats, from pre-mating through gestation day 17, caused an increase in mean pre-implantation loss and an increased incidence of several minor skeletal anomalies at 30 mg/kg/day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg/kg/day (460-fold the human plasma exposure at the RHOD, based on AUC). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal no observed adverse effect level (NOAEL) was not identified in the rabbit.

8.2 Lactation

Risk Summary

There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low [see Clinical Pharmacology (12.3)]. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

8.4 Pediatric Use

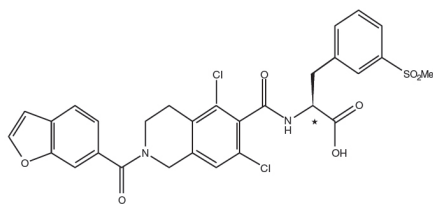
Safety and efficacy in pediatric patients below the age of 17 years have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

11 DESCRIPTION

The chemical name for lifitegrast is (S)-2-(2-(benzofuran-6-carbonyl)-5,7-dichloro-1,2,3,4-tetrahydroisoquinoline-6-carboxamido)-3-(3-(methylsulfonyl)phenyl)propanoic acid. The molecular formula of lifitegrast is C₂₉H₂₄Cl₂N₂O₇S and its molecular weight is 615.5 g/mol. The structural formula of lifitegrast is:



*Chiral center

Lifitegrast is a white to off-white powder, which is soluble in water.

Xiidra (lifitegrast ophthalmic solution) 5% is a lymphocyte function-associated antigen-1 (LFA-1) antagonist supplied as a sterile, clear, colorless to slightly brownish-yellow colored, isotonic solution of lifitegrast with a pH of 7.0-8.0, and an osmolality range of 200-330 mOsmol/kg.

Xiidra contains Active: lifitegrast 50 mg/mL; Inactives: sodium chloride, sodium phosphate dibasic anhydrous, sodium thiosulfate pentahydrate, and water for injection. Sodium hydroxide and/or hydrochloric acid (to adjust pH).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lifitegrast binds to the integrin LFA-1, a cell surface protein found on leukocytes and blocks the interaction of LFA-1 with its cognate ligand intercellular adhesion molecule-1 (ICAM-1). ICAM-1 may be overexpressed in corneal and conjunctival tissues in DED. LFA-1/ICAM-1 interaction can contribute to the formation of an immunological synapse resulting in T-cell activation and migration to target tissues. *In vitro* studies demonstrated that lifitegrast may inhibit T-cell adhesion to ICAM-1 in a human T-cell line and may inhibit secretion of inflammatory cytokines in human peripheral blood mononuclear cells. The exact mechanism of action of lifitegrast in DED is not known.

12.3 Pharmacokinetics

In a subset of DED patients (n = 47) enrolled in a Phase 3 trial, the pre-dose (trough) plasma concentrations of lifitegrast were measured after 180 and 360 days of topical ocular dosing (one drop twice daily) with Xiidra (lifitegrast ophthalmic solution) 5%. A total of nine of the 47 patients (19%) had plasma lifitegrast trough concentrations above 0.5 ng/mL (the lower limit of assay quantitation). Trough plasma concentrations that could be quantitated ranged from 0.55 ng/mL to 3.74 ng/mL.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Animal studies have not been conducted to determine the carcinogenic potential of lifitegrast.

Mutagenesis

Lifitegrast was not mutagenic in the *in vitro* Ames assay. Lifitegrast was not clastogenic in the *in vivo* mouse micronucleus assay. In an *in vitro* chromosomal aberration assay using mammalian cells (Chinese hamster ovary cells), lifitegrast was positive at the highest concentration tested, without metabolic activation.

Impairment of Fertility

Lifitegrast administered at IV doses of up to 30 mg/kg/day (5400-fold the human plasma exposure at the RHOD of lifitegrast ophthalmic solution, 5%) had no effect on fertility and reproductive performance in male and female-treated rats.

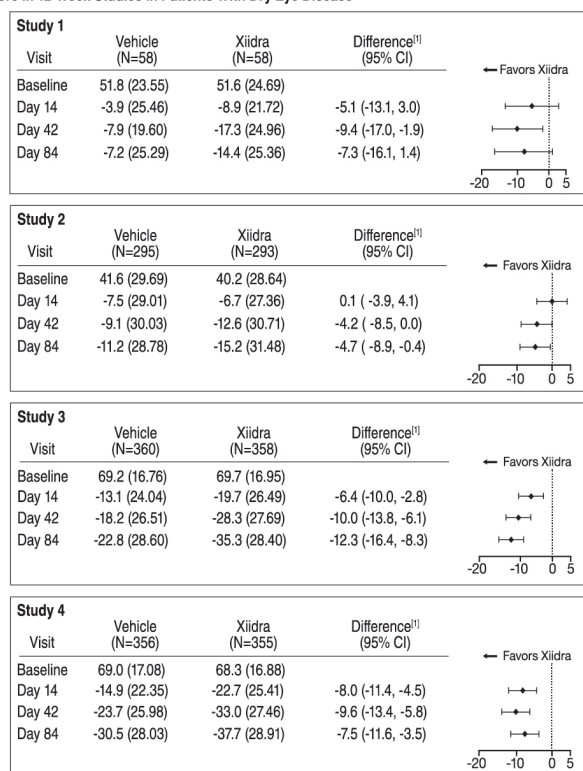
14 CLINICAL STUDIES

The safety and efficacy of lifitegrast for the treatment of DED were assessed in a total of 1181 patients (1067 of which received lifitegrast 5%) in four 12-week, randomized, multi-center, double-masked, vehicle-controlled studies. Patients were randomized to Xiidra or vehicle (placebo) in a 1:1 ratio and dosed twice a day. Use of artificial tears was not allowed during the studies. The mean age was 59 years (range, 19-97 years). The majority of patients were female (76%). Enrollment criteria included minimal signs (i.e., Corneal Fluorescein Staining and non-anesthetized Schirmer Tear Test) and symptoms (i.e., Eye Dryness Score (EDS) and Ocular Discomfort Score) severity scores at baseline.

Effects on Symptoms of Dry Eye Disease

Eye dryness score was rated by patients using a visual analogue scale (0 = no discomfort, 100 = maximal discomfort) at each study visit. The average baseline EDS was between 40 and 70. A larger reduction in EDS favoring Xiidra was observed in all studies at Day 42 and Day 84 (see Figure 1).

Figure 1: Mean Change (SD) From Baseline and Treatment Difference (Xiidra – Vehicle) in Eye Dryness Score in 12-Week Studies in Patients With Dry Eye Disease

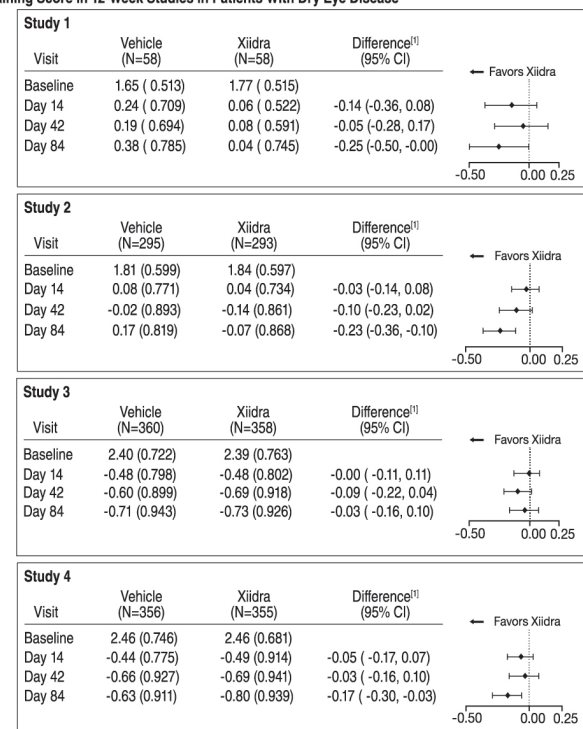


⁽¹⁾ Based on analysis of covariance (ANCOVA) model adjusted for baseline value in Study 1, and ANCOVA model adjusted for baseline value and randomization stratification factors in Studies 2-4. All randomized and treated patients were included in the analysis and missing data were imputed using last-available data. In Study 1, one Xiidra-treated subject who did not have a baseline value was excluded from analysis.

Effects on Signs of Dry Eye Disease

Inferior fluorescein corneal staining score (ICSS) (0 = no staining, 1 = few/rare punctate lesions, 2 = discrete and countable lesions, 3 = lesions too numerous to count but not coalescent, 4 = coalescent) was recorded at each study visit. The average baseline ICSS was approximately 1.8 in Studies 1 and 2, and 2.4 in Studies 3 and 4. At Day 84, a larger reduction in ICSS favoring Xiidra was observed in three of the four studies (see Figure 2).

Figure 2: Mean Change (SD) From Baseline and Treatment Difference (Xiidra – Vehicle) in Inferior Corneal Staining Score in 12-Week Studies in Patients With Dry Eye Disease



⁽¹⁾ Based on ANCOVA model adjusted for baseline value in Study 1, and ANCOVA model adjusted for baseline value and randomization stratification factors in Studies 2-4. All randomized and treated patients were included in the analysis and missing data were imputed using last-available data. In Study 2, one vehicle-treated subject who did not have a study eye designated was excluded from analysis.

16 HOW SUPPLIED/STORAGE AND HANDLING

Xiidra (lifitegrast ophthalmic solution) 5% (50 mg/mL) is supplied in a foil pouch containing 5 low-density polyethylene 0.2 mL single-use containers.

Carton of 60 single-use containers NDC 24208-911-12

Storage:

Store at 20°C to 25°C (68°F to 77°F). Store single-use containers in the original foil pouch.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Handling the Single-use Container

Advise patients not to touch the tip of the single-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

Use With Contact Lenses

Advise patients that contact lenses should be removed prior to administration of Xiidra and can be reinserted 15 minutes after administration [see *Dosage and Administration (2)*].

Administration

Advise patients that the solution from one single-use container is to be used immediately after opening. It can be used to dose both eyes. The single-use container, including any remaining contents should be discarded immediately after administration [see *Dosage and Administration (2)*].

Storage Information

Instruct patients to store single-use containers in the original foil pouch until ready to use [see *How Supplied/Storage and Handling (16)*].

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9800800

PATIENT INFORMATION
XIIDRA® (ZYE-druh)
(lifitegrast ophthalmic solution) 5%
for topical ophthalmic use

What is Xiidra?

Xiidra is a prescription eye drop solution used to treat the signs and symptoms of dry eye disease (DED). It is not known if Xiidra is safe and effective in children under 17 years of age.

Do not use Xiidra:

- If you are allergic to lifitegrast or any of the other ingredients in Xiidra, see **“What are the ingredients in Xiidra?”**

Before you use Xiidra, tell your doctor if you:

- are using any other eye drops
- wear contact lenses
- are pregnant or plan to become pregnant. It is not known if Xiidra will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Xiidra passes into your breast milk. Talk to your doctor about the best way to feed your baby if you use Xiidra.

How should I use Xiidra?

See the complete Instructions for Use at the end of this Patient Information leaflet for detailed instructions about the right way to use Xiidra.

- Use Xiidra as your doctor tells you.
- Use one drop of Xiidra in each eye, two times each day, about 12 hours apart.
- Use Xiidra right away after opening. Throw away the single-use container and any unused solution after you have applied the dose to both eyes. Do not save any unused Xiidra for later.

What are the possible side effects of Xiidra?

The most common side effects of Xiidra include eye irritation, discomfort, or blurred vision when the drops are applied to the eyes, and an unusual taste sensation (dysgeusia).

Seek medical care immediately if you get any symptoms of wheezing, difficulty breathing, or swollen tongue.

These are not all the possible side effects of Xiidra.

Tell your doctor if you have any side effects that bother you. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Xiidra?

- Store Xiidra at room temperature between 68°F to 77°F (20°C to 25°C).
- Store Xiidra in the original foil pouch to protect it from light.
- Do not open the Xiidra foil pouch until you are ready to use the eye drops.
- Return unused single-use containers to their original foil pouch to protect from excessive light exposure.

Keep Xiidra and all medicines out of the reach of children.

General information about the safe and effective use of Xiidra.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or doctor for information about Xiidra that is written for health professionals. Do not use Xiidra for a condition for which it was not prescribed. Do not give Xiidra to other people, even if they have the same symptoms you have. It may harm them.

What are the ingredients in Xiidra?

Active ingredient: lifitegrast

Inactive ingredients: sodium chloride, sodium phosphate dibasic anhydrous, sodium thiosulfate pentahydrate, and water for injection. Sodium hydroxide and/or hydrochloric acid (to adjust pH).

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For more information, go to www.Xiidra.com or call 1-800-553-5340.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: December 2023

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INSTRUCTIONS FOR USE
XIIDRA® [ZYE-druh]
(lifitegrast ophthalmic solution) 5%
for topical ophthalmic use

Read this Instructions for Use before you start using Xiidra and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your doctor about your medical condition or your treatment.

Important Information You Need to Know Before Using Xiidra:

- Xiidra is for use in the eye.
- Wash your hands before each use to make sure you do not infect your eyes while using Xiidra.
- If you wear contact lenses, remove them before using Xiidra.
- Xiidra single-use containers are packaged in a foil pouch. Do not remove from the foil pouch until you are ready to use Xiidra.
- Do not let the tip of the Xiidra single-use container touch your eye or any other surfaces.
- Use one drop of Xiidra in each eye two times each day (one drop in the morning and one drop in the evening, approximately 12 hours apart). Each single-use container of Xiidra will give you enough medicine to treat both of your eyes, one time. There is some extra Xiidra in each single-use container in case you miss getting a drop into your eye. After you have applied the drops, throw away the single-use container and any unused Xiidra. Do not save any unused Xiidra.

Follow Steps 1 to 9 each time you use Xiidra.

Step 1. Take a foil pouch out of the Xiidra box. Open the pouch and remove the strip of single-use containers (see **Figure A**).



Figure A

- Pull off one single-use container from the strip (see **Figure B**).



Figure B

Step 2. Put the remaining strip of single-use containers back in the pouch (see **Figure C**).



Figure C

- Fold the edge to close the pouch (see **Figure D**).



Figure D

Step 3. Hold the Xiidra container upright (see **Figure E**).



Figure E

- Tap the top of the container until all of the solution is in the bottom part of the container (see **Figure F**).



Figure F

Step 4. Open the Xiidra single-use container by twisting off the tab. Make sure that the tip of the single-use container does not touch anything, to avoid contamination (see **Figure G**).



Figure G

Step 5. Tilt your head backwards. If you are not able to tilt your head, lie down.

Step 6. Gently pull your lower eyelid downwards and look up.

Step 7. Place the tip of the Xiidra single-use container close to your eye, but be careful not to touch your eye with it.

Step 8. Gently squeeze the single-use container and let one drop of Xiidra fall into the space between your lower eyelid and your eye. If a drop misses your eye, try again (see **Figure H**).



Figure H

Step 9. Repeat Steps 5 to 8 for your other eye.

There is enough Xiidra in one single-use container for both eyes.

- Once you have applied a drop to both eyes, throw away the opened single-use container with any remaining solution.
- If you use contact lenses, wait for at least 15 minutes before placing them back in your eyes.

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Revised: December 2023

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REF-XDR-0131