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**Lifitegrast ophthalmic solution 5% for the treatment of the signs and symptoms of dry eye disease: a review of clinical trials and real-world evidence**

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## **Abstract**

**Introduction:** Dry eye disease (DED) is a multifactorial symptomatic disease characterized by a loss of tear film and/or ocular surface homeostasis. Lifitegrast ophthalmic solution 5% is a lymphocyte function-associated antigen-1 antagonist used to treat the signs and symptoms of DED.

**Areas covered:** This article examines the lifitegrast mechanism of action, pharmacology and formulation, efficacy, safety, and real-world evidence for treatment of DED, based on a comprehensive review of the literature.

**Expert opinion:** Inflammation is a well-recognized contributor to DED pathogenesis. Persistent challenges to the ocular surface over time can trigger or perpetuate inflammatory responses that further exacerbate the clinical signs and symptoms of DED. Lifitegrast has demonstrated efficacy in reducing both signs and symptoms of DED in controlled clinical trials and in real-world clinical settings. The mechanism that directly inhibits inflammatory processes allows for a rapid response, with improvements in ~2 weeks for some symptom outcomes. Given the heterogeneity of DED and the diversity of initiating factors, optimizing disease management may require targeting multiple, patient-specific pathogenic mechanisms of DED. Educating general practitioners and patients about the disease state, the role of inflammation, and availability of anti-inflammatory treatments such as lifitegrast may further improve DED outcomes and overall quality of life.

**Keywords:** anti-inflammatory agents, eye diseases, ocular surface disease, ophthalmic solutions, therapeutics

## Article highlights

- Inflammation is implicated in the development and progression of dry eye disease (DED), and lifitegrast ophthalmic solution 5% is indicated for treatment of both the signs and symptoms of DED
- Across both clinical trials and real-world studies, lifitegrast has demonstrated improvements in signs and symptoms in patients with DED, with some improvements noted as early as 2 weeks after treatment initiation
- Lifitegrast was considered safe and well tolerated across five clinical trials, and adverse events reported to a federal pharmacovigilance database were generally consistent with those observed in the clinical development program
- Tear inflammatory biomarkers and advanced imaging may enhance identification of DED mechanisms and severity, enabling treatment monitoring and more personalized, effective management of DED
- Anti-inflammatory therapies such as lifitegrast may be considered for treatment of DED when inflammatory mechanisms are suspected, and for possible prevention of worsening or progression of DED, which is driven by inflammatory processes over time

## **1. Introduction**

Dry eye disease (DED) is a multifactorial symptomatic disease characterized by a disruption of the tear film and/or loss of ocular surface homeostasis [1]. Etiological drivers of DED include tear film component deficiencies, eyelid anomalies, ocular surface abnormalities, and systemic diseases, which reflect the etiological diversity of DED [2]. Inflammatory processes directly or indirectly contribute to, and often perpetuate, many DED subtypes, including those driven by ocular surface abnormalities [2,3].

DED imposes a substantial burden and can negatively affect health-related quality of life (HR-QoL), work productivity, and daily living activities [4,5]. A reduction in physical and mental HR-QoL has been observed in individuals with DED, independent of other chronic comorbid disorders [4]. Burdens of highly symptomatic DED have exceeded those associated with other eye diseases (eg, retinal detachment, glaucoma) and chronic disorders (eg, migraine, rheumatoid arthritis) and have been comparable to angina [4,6]. In people with moderate-to-severe DED, the degree of interference with daily living activities, including general day-to-day activities, working, avocations, and relationships, has been strongly associated with the severity of ocular discomfort [5]. Moreover, the increasing use of digital devices and associated rise in digital eye strain, as well as the growing financial burden of DED, have continued to contribute to the overall impact of the disease [7,8].

## **2. Overview of the market**

First-line treatments for DED aim to stabilize the tear film and include lifestyle and behavioral modifications, tear film supplements, and avoidance of environmental factors that may exacerbate the symptoms. Warm compresses and lid massage may be used to improve lipid layer

thickness and Meibomian gland function [9]. Treatment of DED also is important to optimize outcomes associated with cataract and refractive surgery [10]. For all patients, diagnostic tests can help identify the underlying driver of DED and support suitable treatment selection that targets the specific disease mechanism involved [2].

In cases of DED where inflammation is an underlying etiological driver, anti-inflammatory therapies can be effective to reduce the signs and symptoms of DED [9]. Anti-inflammatory treatment options include corticosteroids (eg, loteprednol etabonate 0.25%) for short-term use [11], calcineurin inhibitors (eg, cyclosporin A [cyclosporine], tacrolimus) [12-15], a lymphocyte function-associated antigen-1 (LFA-1) antagonist (lifitegrast) [16-18], tumor necrosis factor (TNF) inhibitors (eg, licaninlimab) [19], and antioxidants (eg, visomitin) [20]. In this review, we summarize the current evidence on lifitegrast ophthalmic solution 5%, including its mechanism of action; pharmacological profile; and its efficacy, safety, and real-world evidence in the management of DED.

### **3. Methods**

PubMed was searched through January 2026, using the following search terms: “lifitegrast” OR “SAR 1118”. Searches were limited to English-language articles. To identify additional relevant publications, reference lists of selected articles were reviewed. Articles (including preclinical research, randomized and observational clinical trials, real-world studies, and review articles) relevant to the mechanism of action, pharmacological profile, and the efficacy, safety and tolerability of lifitegrast in the treatment of patients with DED were selected for inclusion in this review. Because this article is based on previously conducted studies, ethical approval was not required.

#### 4. Mechanisms of ocular surface inflammation

Ocular surface stress triggers an inflammatory/immune response, characterized by the release of proinflammatory cytokines (eg, interleukin [IL]-1, IL-6, TNF-alpha [TNF- $\alpha$ ]), matrix metalloproteinases, and chemokines [21]. Antigen-presenting cells (APCs), such as resident dendritic cells, become activated, migrate to the regional lymph nodes, and facilitate T-cell activation and recruitment to the ocular surface, thereby amplifying the inflammatory cascade. This heightened immune response contributes to epithelial damage and tear film dysfunction (**Figure 1**) [21]. Leukocyte adhesion and trafficking play a central role in this process, mediated in part by LFA-1, a  $\beta 2$  integrin expressed on the surface of leukocytes and dendritic cells that regulates cell–cell and cell–extracellular matrix interactions [21,22]. Intercellular adhesion molecule-1 (ICAM-1) is the primary ligand for LFA-1 and is expressed on the surface of leukocytes, endothelial cells, keratinocytes, and epithelial cells [21]. LFA-1/ICAM-1 interactions may play a key role in the cell-mediated immune response and inflammatory pathways involved in DED, the activation and differentiation of naive T-cells, and migration of effector T-cells to the ocular surface. These LFA-1/ICAM-1 interactions also sustain T-cell activation and the release of proinflammatory cytokines and facilitate recruitment of additional LFA-1–expressing T-cells, thereby perpetuating ocular surface inflammation [21].

#### 5. Introduction to the drug

Lifitegrast ophthalmic solution 5% (Xiidra, Bausch & Lomb) is a first-in-class LFA-1 antagonist indicated for the treatment of both the signs and symptoms of DED [23]. Lifitegrast blocks the interaction of LFA-1 with ICAM-1, thereby reducing T-cell–mediated inflammation (**Figure 2**) [24]. In cell culture experiments, lifitegrast inhibited T-cell adhesion (Jurkat T-cells) to ICAM-1

(half-maximal inhibitory concentration, ~3 nM), and in activated peripheral blood mononuclear cells, lifitegrast decreased the production of proinflammatory cytokines, such as interferon (IFN)- $\gamma$ , IL-1 $\alpha$ , IL-1 $\beta$ , and TNF- $\alpha$  [25]. In a mouse model of DED, topical lifitegrast decreased T-cell proliferation, reduced the number of IFN- $\gamma$ -secreting CD4<sup>+</sup> T-cells, and suppressed chemokine receptor expression from CD4<sup>+</sup> T-cells isolated from regional (draining) lymph nodes [26]. In a model of diabetic retinopathy, lifitegrast attenuated retinal inflammatory processes, including leukocyte adherence (leukostasis) [27].

Additional preclinical evidence further supports the central role of the LFA-1/ICAM-1 pathway in ocular inflammation. In a mouse model of corneal inflammation, lifitegrast reduced neutrophil recruitment and inflammation; furthermore, control of the expression (CD18<sup>-/-</sup> knockout) or physiological function (anti-CD11a) of LFA-1 subunits produced similar results, highlighting the essential role of LFA-1 in corneal inflammation [28]. Preliminary findings (from a conference abstract) also suggest that lifitegrast may interact with the catalytic site of caspase-1. In human corneal epithelial cells exposed to hyperosmolar stress, lifitegrast decreased the expression of IL-1 $\beta$ , IL-6, and IL-8 to similar levels achieved with a known caspase-1 inhibitor (Z-YVAD-FMK) [29]. In a canine model of DED (idiopathic keratoconjunctivitis sicca), lifitegrast treatment was associated with rapid improvements in clinical signs, with increased tear production noted after 2 weeks of treatment [25].

The ability of lifitegrast to inhibit T-cell activation and block the physiological function of activated T-cells through disruption of LFA-1/ICAM-1 interactions distinguishes lifitegrast from other T-cell immunomodulators. By antagonizing LFA-1, lifitegrast interferes with multiple steps in the inflammatory cascade, including activation of naive T-cells in the regional lymph nodes by APCs, migration of effector T-cells to the ocular surface, sustained activation of

effector T-cells, and downstream proinflammatory cytokine release (**Figure 2; Supplementary video**) [21]. This effect of lifitegrast on both naive and activated T-cells provides a mechanism for rapid disruption of ocular surface inflammation. In contrast, the calcineurin inhibitors cyclosporine and tacrolimus act intracellularly in T-cells to inhibit calcineurin phosphatase activity, preventing activation of nuclear translocation of nuclear factor of activated T-cells (NFAT), thereby reducing transcription of early activation cytokines (eg, IL-2) and ultimately suppressing T-cell activation [15,30]. However, these agents do not directly interfere with cell surface adhesion pathways or T-cell trafficking. In contrast, lifitegrast inhibits LFA-1/ICAM-1 interaction at the cell surface, offering an early mechanism to disrupt T-cell recruitment and activation, which may enable a more rapid reduction of inflammatory processes associated with DED, as compared with calcineurin inhibitors [21,31].

### **5.1 Pharmacology and formulation**

Lifitegrast (investigational name SAR 1118) is a tetrahydroisoquinoline analog selected for topical ophthalmic delivery due to its strong in vitro potency against its biological target and favorable physiochemical properties [24]. In particular, high aqueous solubility of lifitegrast supports effective distribution across the tear film and local exposure at the ocular surface, while resulting in minimal absorption and rapid systemic clearance following topical administration [24]. The sterile, preservative-free, single-use, ophthalmic formulation consists of lifitegrast at a concentration of 50 mg/mL, which remains soluble at physiological pH levels and is isotonic with human tears [23,24]. It is supplied as a clear, colorless to slightly colored solution with a physiological pH of 7.0–8.0 and an osmolality of 200–330 mOsm/kg, supporting ocular comfort during instillation [23]. These characteristics, along with selection of excipients, help maintain

drug stability and minimize degradation, supporting the overall safety and efficacy of the product.

In a rat model, lifitegrast exposure to ocular tissues was rapid, with maximum exposure detected at 0.5 hours after administration of  $^{14}\text{C}$ -radiolabeled lifitegrast ophthalmic solution 6.5% [27]. Lifitegrast concentrations were highest at the bulbar conjunctiva, palpebral conjunctiva, cornea, and iris ciliary body, although measurable lifitegrast levels were detected in all ocular tissues examined. Systemic exposure was relatively low, with plasma concentrations of lifitegrast more than 100 times lower than those observed in the conjunctival tissues [27]. Consistent with these results, lifitegrast concentrations were found to be highest in the anterior ocular segment tissues after twice-daily (BID) ocular instillation of lifitegrast ophthalmic solution 5% for 5 days in rabbits[32].

## **6. Clinical studies**

In a study conducted in healthy volunteers, lifitegrast administered BID for 10 days achieved therapeutic ocular concentrations ( $>1\ \mu\text{M}$  [ $\sim 600\ \text{ng/mL}$ ]) [33]. Low plasma levels of lifitegrast were detected within 5 minutes of instillation; however, lifitegrast was rapidly cleared from the systemic circulation, with plasma concentrations falling below the limit of detection within 1 to 4 hours of administration. There was no evidence of lifitegrast accumulation in tears or plasma with BID dosing [33]. Clinically, the onset of action of lifitegrast in patients with DED is relatively rapid [34]. A phase 2 study evaluated three different lifitegrast concentrations (0.1%, 1.0%, and 5.0%) in patients with DED using a controlled adverse environment over 84 days and demonstrated that lifitegrast improved DED signs and symptoms compared with placebo across all three doses, with evidence of improvement within 14 days of treatment [34].

### **6.1. Pivotal trials (OPUS-1, OPUS-2, and OPUS-3)**

The OPUS clinical trials consisted of three 12-week, phase 3, multicenter, randomized, placebo-controlled clinical trials (OPUS-1, OPUS-2, OPUS-3) conducted in adult patients with DED in the United States (**Table 1**) [16-18]. The OPUS trials consisted of 2-week screening and 12-week treatment periods. Patients received placebo (vehicle) BID (morning and evening) during the 2-week screening period; patients were then randomized 1:1 to receive lifitegrast or placebo BID during the 12-week treatment period [16-18].

In OPUS-1, which enrolled 588 adult patients, the primary sign endpoint was mean change in inferior corneal fluorescein staining (CFS) score from baseline to day 84, which was significantly reduced (improved) in the lifitegrast group compared with the placebo group ( $p = 0.0007$ ). Additionally, a greater proportion of patients treated with lifitegrast achieved a  $\geq 1$ -point reduction in inferior CFS score than those receiving placebo (22.2% vs 13.9%;  $p = 0.010$ ) [16]. Although mean change in the visual-related function subscale of the Ocular Surface Disease Index (VR-OSDI) from baseline to day 84 (one of the coprimary declared symptom endpoints) was not different between the lifitegrast and placebo groups ( $p = 0.7894$ ), significant improvements with lifitegrast versus placebo were observed in key secondary symptom endpoints, including eye dryness ( $p = 0.0291$ ) and ocular discomfort ( $p = 0.0273$ ), as measured on a visual analog scale (VAS). Lifitegrast (vs placebo) was also associated with improvements in total CFS ( $p = 0.0148$ ), superior CFS ( $p = 0.0392$ ), nasal conjunctival lissamine green staining (CLGS;  $p = 0.0039$ ), and total CLGS ( $p = 0.0086$ ) scores, with improvements in nasal and total CLGS detected as early as day 14 ( $p = 0.0032$  and  $p = 0.0149$ , respectively) [16].

In OPUS-2 ( $n = 718$ ), the coprimary symptom endpoint of change in eye dryness score (VAS) was met, with significantly greater reduction from baseline to day 84 in the lifitegrast

group than the placebo group (-35.30 vs -22.75; treatment effect, 12.61; 95% CI, 8.51–16.70;  $p < 0.0001$ ) [17]. Improvements in eye dryness scores with lifitegrast were observed as early as day 14 (treatment effect, 6.67; 95% CI, 3.05–10.30; nominal  $p = 0.0003$ ), and improvements in ocular discomfort scale (treatment effect, 0.34; 95% CI, 0.15–0.53; nominal  $p = 0.0005$ ) and eye discomfort (treatment effect, 9.77; 95% CI, 5.27–14.28; nominal  $p < 0.0001$ ) scores were noted at day 84. In contrast to OPUS-1, the coprimary sign endpoint of change in inferior CFS score between lifitegrast and placebo groups was not met (treatment effect, 0.03; 95% CI, -0.10–0.17;  $p = 0.6186$ ).

Although neither OPUS-1 nor OPUS-2 achieved both sign and symptom coprimary endpoints simultaneously, several factors may explain the differences in results between trials. The correlation between the signs and symptoms of DED is known to be relatively low, both cross-sectionally and longitudinally [35,36], likely due to the multifactorial nature of DED, measurement variability (eg, subjective scoring of ocular staining), and the potential influence of concomitant ocular comorbidities [2]. OPUS-1 and OPUS-2 had similar study designs; however, there was heterogeneity between patient populations, in part due to differences in patient selection [17]. Patients enrolled in OPUS-2 had moderate-to-severe symptoms of DED (recent artificial tear use [prior 30 days], eye dryness score [VAS]  $\geq 40$ ) and were screened in a natural environment [17]. In contrast, OPUS-1 utilized a controlled adverse environment to enrich the study population, resulting in patients who had dynamic ocular signs; however, no minimal eye dryness (VAS) symptom threshold was required at screening [16,17]. Taken together, the differences in patient selection and baseline characteristics contributed to the discordance between signs and symptoms of DED across the two studies. These observations subsequently

informed the study design of OPUS-3, which examined symptom improvement in patients with a moderate-to-severe eye dryness score (VAS), a criterion similar to that for OPUS-2 [18].

In OPUS-3 (n = 711) [18], the primary symptom endpoint of mean change in eye dryness score (VAS) from baseline to day 84 was significantly reduced in the lifitegrast group as compared with the placebo group (treatment effect, 7.16; 95% CI, 3.04–11.28;  $p = 0.0007$ ), consistent with findings from OPUS-2. Eye dryness scores significantly improved in the lifitegrast group at day 14, the first postbaseline assessment (treatment effect, 7.85; 95% CI, 4.33–11.37;  $p < 0.0001$ ), as well as at day 42 (treatment effect, 9.32; 95% CI, 5.44–13.20;  $p < 0.0001$ ). Ocular discomfort scores decreased over time in both treatment groups, with no between-group differences at days 14, 42, and 84. The lifitegrast group experienced greater improvements in DED symptoms of itching (treatment effect [SE], 4.17 [1.940]; nominal  $p = 0.0318$ ), foreign body sensation (4.43 [2.172]; nominal  $p = 0.0418$ ), and eye discomfort (5.86 [2.071]; nominal  $p = 0.0048$ ) at day 42 compared with placebo. In a post hoc, pooled analysis of data from OPUS-2 and OPUS-3 trials, patients treated with lifitegrast had greater odds of experiencing clinically meaningful improvements (vs placebo) in inferior corneal staining score ( $\geq 1$ -point improvement; odds ratio [OR], 1.29; nominal  $p = 0.02$ ), total corneal staining score ( $\geq 3$ -point improvement; OR, 1.40; nominal  $p = 0.01$ ), eye dryness score ( $\geq 30\%$  improvement; OR, 2.10; nominal  $p < 0.001$ ), and global VAS score ( $\geq 30\%$  improvement; OR, 1.67; nominal  $p < 0.001$ ) [37]. Overall, the OPUS clinical trials demonstrated significant improvements in corneal staining and eye dryness with lifitegrast treatment in patients with varying levels of DED severity.

## **6.2 Safety profile**

The safety profile of lifitegrast was characterized in a pooled analysis of five randomized controlled trials of lifitegrast that comprised one phase 2 trial, three phase 3 trials (OPUS-1, OPUS-2, OPUS-3), and a long-term (1-year) safety trial (SONATA [38]) [39]. Among 2464 patients with DED (lifitegrast, n = 1287; placebo, n = 1177), the most common ocular treatment-emergent adverse events (AEs) in the lifitegrast and placebo groups, respectively, were instillation site irritation (15.2% and 2.8%), instillation site reaction (12.3% and 2.3%), and instillation site pain (9.8% and 2.1%). Dysgeusia was the most common nonocular AE reported by 14.5% of patients who received lifitegrast and 0.3% who received placebo. Dysgeusia was generally transient, although the specific duration was not tracked. Six of the 1287 patients (0.5%) who received lifitegrast discontinued due to dysgeusia. Overall, the number of discontinuations due to AEs was relatively low among patients who received lifitegrast (7.0%) or placebo (2.6%).

Discontinuations due to the most common AEs occurred in  $\leq 1\%$  of patients who received lifitegrast in each of the 12-week trials and  $< 2\%$  of patients who received lifitegrast in the 1-year trial. Moreover, drop comfort scores in patients who received lifitegrast decreased (improved) during visits (eg, within 3 minutes of instillation) and over the course of the 12-week and 1-year trials, suggesting that discomfort with lifitegrast is mild and transient. Overall, lifitegrast BID was safe and well tolerated across five clinical trials [39].

Lifitegrast (BID) use in contact lens wearers with eye dryness and discomfort was effective and well tolerated in two prospective studies [40,41]. In a 12-week study in symptomatic soft contact lens wearers (n = 40), lifitegrast significantly improved scores of end-of-day dryness (VAS), end-of-day discomfort (VAS), and Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) at 2, 6, and 12 weeks compared with baseline ( $p < 0.01$ ), demonstrating similar

improvements to those characterized in previous clinical trials [40]. Importantly, these symptom improvements were associated with a significant increase in comfortable contact lens wear time, which improved by approximately 3 hours by week 6 and was maintained through week 12 ( $p < 0.01$ ), reflecting patients' ability to tolerate their contact lenses for longer periods without dryness or discomfort. Similarly, in an 8-week study in patients with contact lens discomfort who used silicone hydrogel contact lenses, a significant improvement in contact lens dry eye (CLDEQ-8) scores was reported with lifitegrast use ( $p \leq 0.0001$ ) [41].

These findings are clinically meaningful, as contact lens wear is a common risk factor for ocular surface dryness, increased tear film instability, and heightened ocular inflammatory responses [42,43]. Improvements in end-of-day dryness and discomfort specifically address some of the most burdensome symptoms reported by contact lens users, which can directly influence wearing time, tolerance, and overall satisfaction. The observed reductions in CLDEQ-8 scores further support the use of lifitegrast in reducing contact lens-associated discomfort, a frequent reason for contact lens discontinuation [40,41]. Collectively, these studies suggest that lifitegrast may be a valuable therapeutic option for symptomatic contact lens wearers with eye dryness and discomfort.

## **7. Real-world evidence**

Real-world use of lifitegrast in patients with DED has been evaluated through eyecare provider (ECP) [44-46] and patient [47] surveys, a case series [48], retrospective claims data [49,50], and postmarketing pharmacovigilance database analyses [51,52] (**Table 2**). Survey studies of lifitegrast for DED indicate real-world effectiveness (ie, improvements in both signs and symptoms), with high patient and ECP satisfaction with treatment and improvements in patient

QoL [44-47]. In a cross-sectional survey of ECPs (n = 21) who treated patients with DED with lifitegrast or cyclosporine ophthalmic emulsion 0.05%, 67% of patients were satisfied with either lifitegrast or cyclosporine to stimulate tear production [44]. Satisfaction with treatment effectiveness was reported by 86% of physicians for lifitegrast and 81% for cyclosporine ophthalmic emulsion 0.05% [44]. In a large survey of ECPs (n = 517) that included a chart review (n = 600), the use of other DED-related treatments decreased after initiation of lifitegrast; for example, use of artificial tears declined from 75.5% to 45.2% of patients 6 months after initiation of lifitegrast [45]. Fewer patients reported DED symptoms from before versus 6 months after initiation of lifitegrast treatment (eg, eye dryness [87.5% vs 6.9%], blurred vision [57.7% vs 4.7%], ocular burning/stinging [56.0% vs 3.2%], and foreign body sensation [49.8% vs 1.7%]). Moreover, use of lifitegrast was associated with a reduction in the severity of common clinical signs (eg, corneal staining) and improvements in QoL [45]. In another survey of 12 ECPs who collectively treated an average of 1288 patients annually, approximately one-third (34.2%) of their patients reported near or complete symptom resolution after the first prescription of lifitegrast, and two-thirds (66.7%) of ECPs indicated near or complete resolution of patient symptoms within 1 to 3 months of treatment initiation (**Figure 3**) [46]. Overall, compared with other treatments, ECPs indicated moderate-to-high levels of satisfaction with lifitegrast in the areas of onset of action, effectiveness, ease of administration, and patient comfort. Additionally, ECPs described improvements in activities of daily living, ocular well-being, and general well-being of patients treated with lifitegrast. All providers rated the effectiveness of lifitegrast in patients who wear contact lenses as “somewhat” or “very” effective. Seven providers (58.3%) reported at least one patient with an AE during treatment (burning/stinging [n = 6], blurred vision [n = 5], dysgeusia [n = 3], and discharge [n = 1]); these AEs were mild to moderate in severity

and consistent with the known safety profile of lifitegrast [46]. In a cross-sectional survey of patients with DED (n = 207) who were treated or had been treated with lifitegrast or cyclosporine ophthalmic emulsion 0.05%, 63% of current lifitegrast users and 51% of current cyclosporine users were satisfied with the onset of treatment effect [47]. Satisfaction with management of symptoms was similar between current lifitegrast and cyclosporine users (77% vs 78%), as was ease of use (72% vs 78%). Patient dissatisfaction across items was relatively low, with dissatisfaction related to onset of action reported by 11% of current lifitegrast users and 29% of current cyclosporine users. Reports of burning sensation (“always” or “usually”) were similar between current lifitegrast and cyclosporine users (22% vs 21%), and dysgeusia was reported by more current lifitegrast users than cyclosporine users (29% vs 3%). Fifty percent of current lifitegrast users “rarely” or “never” experienced blurred vision, compared with 63% of current cyclosporine users. The most common reason for switching from lifitegrast or cyclosporine ophthalmic emulsion 0.05% was doctor recommendation, rated as “very important” or “extremely important” by 77% and 79% of users who switched from lifitegrast and cyclosporine, respectively [47]. In a prospective, observational case series of adults with DED (n = 50), treatment with lifitegrast for 12 weeks was associated with improvements in mean Ocular Surface Disease Index (OSDI) score (baseline, 52.2; week 12, 31.2;  $p < 0.001$ ) and tear osmolarity (baseline, 317 mOsm/L; week 12, 293 mOsm/L;  $p < 0.001$ ) [48]. Improvements from baseline to week 12 also were noted in Schirmer test scores (11.7 to 17.4,  $p < 0.001$ ), tear film breakup time (8.1 s to 10.4 s,  $p < 0.001$ ), and lissamine green staining (1.0 to 0.1,  $p < 0.001$ ) [48].

Retrospective database analyses have been conducted to examine real-world treatment patterns for DED that included lifitegrast among other treatments (**Table 2**) [49,50]. In an

analysis of claims from the IBM MarketScan Commercial and Medicare Supplemental Databases (July 1, 2015, to February 28, 2018), adherence to treatment during a 12-month period was relatively low in patients treated with lifitegrast (9.7%) or cyclosporine ophthalmic emulsion 0.05% (5.9%) [49]. Nonpersistence (no refill after supply was exhausted for 90 days [lifitegrast] or 120 days [cyclosporine]) occurred in 6.8% of patients in the lifitegrast group and 7.1% of the cyclosporine ophthalmic emulsion 0.05% group, and fewer patients in the lifitegrast group discontinued treatment within 12 months of initiation compared with the cyclosporine group (64.4% vs 70.8%). Overall, 31.7% of patients in the lifitegrast group and 27.5% of patients in the cyclosporine ophthalmic emulsion 0.05% group remained on treatment 12 months after initiation [49].

In another analysis of claims data from the Symphony Health Integrated Dataverse (July 2019 to June 2021), the median time to treatment discontinuation was similar between users of lifitegrast and cyclosporine ophthalmic solution 0.09% (269 vs 354 days;  $p = 0.825$ ) [50]. Similarly, the proportions of patients using lifitegrast and cyclosporine ophthalmic solution 0.09% who remained on treatment after 1 year from the date of the first treatment claim did not differ significantly between groups (44.0% vs 49.8%;  $p = 0.854$ ) [50].

Adverse events reported to the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) that listed lifitegrast as the primary suspect drug were analyzed in two studies to characterize real-world treatment safety (**Table 2**) [51,52]. In both studies, the most common eye disorders by preferred term with lifitegrast were eye irritation, vision blurred, and eye pain. The most common general disorders and administration site conditions by preferred term were instillation site pain and instillation site reaction. Dysgeusia was the most frequently reported nervous system disorder. In all, the most commonly reported AEs in these

real-world analyses were consistent with the safety profile established in clinical trials [51,52]. Real-world studies complement clinical trial evidence by providing insights into treatment use, effectiveness, tolerability, and patient experience in routine clinical practice, but, as with all observational research, the findings should be interpreted in the context of the individual study designs, including the absence of control groups in some studies, potential selection and recall bias, and variability in data collection methods. It is also worth bearing in mind that database studies may be affected by incomplete or missing information [53]. For the current analysis, two of the provider surveys included relatively small numbers of respondents ( $n = 12$  and  $n = 21$ ), [44,46] reflecting the experiences of a limited number of practices. Nevertheless, considered alongside the findings from larger surveys, claims analyses, and clinical studies, the available real-world evidence provides supportive insights into the use of lifitegrast in routine clinical practice.

## **8. Preoperative treatment of DED in patients undergoing cataract surgery**

Two prospective studies have demonstrated that preoperative treatment of DED with lifitegrast can meaningfully improve refractive planning and patient-reported outcomes in patients undergoing cataract surgery [54,55]. In a multicenter study by Hovanesian et al, 4 weeks of treatment with lifitegrast in patients with DED undergoing cataract surgery resulted in significant improvements in dry eye symptoms ( $p < 0.0004$ ) and reduced variability in preoperative keratometry, leading to enhanced refractive accuracy following intraocular lens (IOL) implantation [54]. Building on these findings, a more recent prospective interventional trial by Yang et al showed that 6 weeks of preoperative treatment with lifitegrast in combination with preservative-free artificial tears significantly improved ocular surface metrics, including OSDI

scores ( $p = 0.03$ ) and corneal staining ( $p = 0.006$ ), and led to clinically meaningful changes in IOL power calculations in 50% of eyes [55]. Importantly, this study also demonstrated superior postoperative refractive accuracy, with a higher proportion of eyes achieving outcomes within  $\pm 0.25$  D of the intended target after ocular surface optimization. Collectively, these studies underscore the critical role of identifying and treating DED, specifically with lifitegrast, prior to cataract surgery to improve biometry reliability, refractive precision, and patient satisfaction.

## **9. Positioning in the current treatment landscape**

DED is a multifactorial symptomatic disease in which inflammation is one of several etiological factors, and the progression of DED is likely driven by inflammatory processes over time, regardless of the initial precipitating factors [2,9]. Intervention with anti-inflammatory therapy in DED is important because inflammation plays a role in driving disease progression, regardless of the initial triggering factors [56]. Once activated, inflammatory pathways become self-perpetuating and can lead to structural damage of the ocular surface, tear film instability, and worsening symptoms. Treating inflammation may help restore ocular surface homeostasis, prevent the escalation of disease severity, and provide symptom relief, thereby improving QoL. This approach parallels strategies used in other chronic diseases, for which management of underlying mechanisms can alter long-term disease outcomes. Therefore, the use of anti-inflammatories for treatment of DED could be considered proactively, at an earlier stage of the disease process, to potentially delay or stop progression.

In addition to etiological factors of DED, there are many lifestyle factors that can influence the ocular surface (eg, nutrition, environment, use of digital devices) [2,9]. Due to the multiple pathogenic drivers of DED, appropriate therapeutic management should consider a

patient's specific signs and symptoms. Some patients may require different types of treatment in combination [9], which might offer improved symptom control beyond what is achieved with a single treatment. To further explore the effects of combined treatments on DED, a clinical study has been planned to investigate the efficacy of treatment with perfluorohexyloctane, a tear stabilizer, and lifitegrast on the signs and symptoms of DED (ClinicalTrials.gov identifier: NCT07128628).

Anti-inflammatory medications such as lifitegrast should be considered in patients with primary inflammatory or immune-mediated systemic conditions, including those that involve inflammation/oxidative stress or cellular damage/disruption of the ocular surface, as well as tear film deficiencies (aqueous, mucin/glycocalyx) [9]. Several systemic inflammatory and T-cell-mediated disorders are commonly associated with dry eye, including collagen vascular diseases such as rheumatoid arthritis and systemic lupus erythematosus [2]. In addition to pharmacological therapy, lifestyle considerations that should be discussed with patients include the avoidance of certain topical or oral medications and environments and activities that precipitate dry eye symptoms, as well as strategies to mitigate the influence of precipitating conditions (eg, use of humidifiers, beta blockers, antihistamines, diuretics, diet, and more frequent breaks from electronic devices) [9,57].

## **10. Regulatory affairs**

Lifitegrast is becoming available in more markets worldwide. There are three product categories, with the first being the original branded lifitegrast ophthalmic solution 5% (Xiidra). The second category is approved generics, which are supported by product-specific bridging or confirmatory data. The third category is unapproved compounded preparations, which are neither regulatorily

nor scientifically interchangeable with the original branded product. In the United States, the first abbreviated new drug application (ANDA) for generic lifitegrast ophthalmic solution 5% was approved on August 4, 2023 (Micro Labs; ANDA 215081), and the FDA found the generic bioequivalent and therapeutically equivalent to Xiidra [58,59]. In China, after the lifitegrast compound patent expired at the end of 2024, the National Medical Products Administration approved a domestically developed lifitegrast ophthalmic solution 5% (Langyueming; Chengdu Kanghong Pharmaceutical Group) as a Category 3 new drug in June 2025 (registration certificate 2025S01943), with approval supported by a Chinese multicenter phase 3 trial in patients with DED [60]. In parallel, some compounding pharmacies and outsourcing facilities in several jurisdictions have begun preparing lifitegrast ophthalmic solutions from bulk active pharmaceutical ingredients without regulatory marketing authorization. The signs, symptoms, safety, and tolerability outcomes described across the OPUS program, SONATA study, real-world studies, and postmarketing pharmacovigilance datasets apply specifically to branded lifitegrast ophthalmic solution 5% (Xiidra) [16-18,38,39,48,51,52]. Although for approved generics, regional confirmatory or bioequivalence data, including the Chinese phase 3 trial for Langyueming, appear directionally consistent with the original branded drug [16-18,60], each product has its own evidence package, and cross-product extrapolation remains inferential rather than reflective of demonstrated equivalence. In contrast, comparable controlled clinical, stability, sterility, and pharmacovigilance data are generally unavailable for compounded preparations, and regulators have repeatedly documented quality concerns for compounded ophthalmic products, including suboptimal potency, sterility failures, and excipient deviations [61,62]. Differences in excipients, pH, osmolality, preservative status, container closure system, sterility assurance, and stability may affect ocular tolerability, surface bioavailability, and clinical performance.

Prescribers should, therefore, use an authorized product, either the original branded drug or, where available, an approved generic within the local regulatory framework, and monitor product-specific changes in instillation comfort, ocular surface findings, response trajectory, and safety profile that may reflect formulation differences among products sharing the same international nonproprietary name.

## **11. Future directions**

Biomarkers of inflammation present in tears, as well as advanced imaging techniques, may be helpful in guiding appropriate treatment of DED [2,63-65]. Cytokines such as IL-6, IL-8, and TNF- $\alpha$ , as well as matrix metalloproteinase-9 (MMP-9), have been associated with DED severity [2,63]. In patients with DED, lifitegrast treatment has been associated with normalization (improvements) of MMP-9 levels [64]. As such, MMP-9 and inflammatory cytokines represent potential biomarkers that could be used to evaluate the effectiveness of anti-inflammatory and other DED treatments, in addition to disease severity.

*In vivo* confocal microscopy (IVCM) allows for direct observation of corneal structures, including the corneal nerve, which are altered in patients with DED [65]. IVCM can detect changes in dendritic cell concentrations associated with inflammation, which potentially could be monitored to evaluate the effectiveness of anti-inflammatory treatments. This technique can also evaluate abnormal changes in Meibomian gland morphology. Tear fluorescein clearance that assesses tear turnover and exchange on the ocular surface could be used to identify patients who have ocular surface inflammation as a product of inadequate tear clearance [65]. In all, advances and improved access to imaging and analytic methods have enhanced identification of disease mechanisms, allowing for more personalized DED treatment.

## **12. Conclusion**

Inflammation is an etiological driver of DED, and lifitegrast, which has a unique anti-inflammatory mechanism and has demonstrated efficacy and safety for the treatment of DED in short- and long-term clinical trials. Importantly, the favorable safety and tolerability profile, as well as measures of efficacy with lifitegrast characterized in real-world studies, were consistent with findings from clinical trials. Lifitegrast is associated with a rapid onset of action (as early as 2 weeks after initiation), and initiation of lifitegrast therapy is associated with a reduction in the use of other topical therapies for DED. In conclusion, the evidence demonstrates that lifitegrast is a key anti-inflammatory option that safely and rapidly improves the signs and symptoms of DED.

## **13. Expert opinion**

DED is a heterogeneous disease, and identifying specific etiological drivers for a patient is essential for effective DED management [1,2]. Although inflammation is a well-recognized underlying factor for the development of many DED subtypes, it might not be a significant factor for the development of others [2,3]. Yet, persistent challenges to the ocular surface over time, regardless of the initiating driver(s), can elicit an inflammatory response, which can further exacerbate the signs and symptoms of DED [3]. Lifitegrast may help prevent the progression of DED and reduce the severity of signs and symptoms over time, even when inflammation is not a direct driver of disease initiation. Preventive use of lifitegrast may, therefore, provide meaningful value to patients with DED, given the burden of DED on QoL [4,5].

Lifitegrast has demonstrated efficacy in reducing both the signs and symptoms of DED in clinical trials and in real-world studies [16-18,45,46]. The mechanism of lifitegrast that directly

inhibits inflammatory processes could lead to a more rapid response, as compared with the mechanism of cyclosporine, which does not affect the function of activated T-cells and is associated with a slower onset of action [12,15,21,24,66]. Given the heterogeneity of DED and the diversity of initiating factors along with diagnostic advances, disease management may be optimized by targeting multiple patient-specific mechanisms of DED. To investigate this hypothesis, a clinical trial of perfluorohexyloctane and lifitegrast in patients with DED was recently initiated. Positive results associated with targeting multiple DED mechanisms could lead to further exploration of other treatments in combination to better address the needs of this heterogeneous patient population.

Although diagnostic methods to characterize the specific mechanisms of DED have advanced, there remain limitations. Diagnostic imaging can be costly and require skilled expertise to operate, limiting its accessibility [65]. Moreover, operator variability (tear fluorescein clearance) and environmental conditions (interferometry, thermography) can influence the quality of results [65]. Inflammatory biomarkers (eg, IL-6, IL8, TNF- $\alpha$ ) can be highly variable, even among healthy individuals [67]. Integrating the use of multiple biomarkers (eg, imaging, multiplex assay) in conjunction with artificial intelligence (eg, hierarchical clustering, random forest, and neural network predictive models [68]) might improve the sensitivity, specificity, and repeatability of diagnostic methods to characterize DED-associated inflammation, as well as other etiological drivers, and ultimately lead to more precise targeted therapy.

Lifitegrast received FDA approval in 2016 for treatment of the signs and symptoms of DED [23]. In a survey of ECPs published in 2025, 21% of their patients with DED used lifitegrast, most often in combination with other DED treatments [46]. Inflammation is an

important driver of DED pathogenesis [56], and there may be patients who would benefit from an anti-inflammatory such as lifitegrast but do not receive it. This highlights the importance of general practitioners, who often are the first clinicians to encounter patients with DED, and ECPs, who understand the heterogenous nature of the disease, availability of diagnostic tools, and the full treatment armamentarium. Improved awareness may support earlier identification of DED, appropriate treatment selection, and prevention of disease progression.

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### **Data availability statement**

Data sharing is not applicable to this article, as no new data were created or analyzed.

### **AI-based tools and technologies**

The authors declare that no generative AI tools were used in the preparation of this manuscript.

### **Information resources**

The American Academy of Ophthalmology ([aao.org](https://www.aao.org)) provides a list of current and potential future treatments for dry eye (<https://www.aao.org/eye-health/tips-prevention/new-dry-eye-treatments-ocular-surface-disease>), as well as patient resources (<https://www.aao.org/eye-health/tips-prevention-list>). The comprehensive, evidence-based report on management of dry eye from the third Tear Film and Ocular Surface Society Dry Eye Workshop (TFOS DEWS III) is freely available for download from the American Journal of Ophthalmology (<https://www.ajo.com/>). The Dry Eye Foundation ([dryeyefoundation.org](https://dryeyefoundation.org)) and the World Council of Optometry ([dryeye.worldcouncilofoptometry.info](https://dryeye.worldcouncilofoptometry.info)) provide additional information on dry eye for patients and clinicians, respectively.

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ACCEPTED MANUSCRIPT

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## Tables

**Table 1. Summary of efficacy in OPUS clinical trials.**

| Clinical trial                               | OPUS-1 (NCT01421498) [16]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | OPUS-2 (NCT01743729) [17]                                                                                                                                                                                                                                                                                                                                                                                                        | OPUS-3 (NCT02284516) [18]                                                                                                                                                                                                                                                                                                                                                                           |
|----------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Treatment groups*</b>                     | Lifitegrast (n = 293)<br>Placebo (n = 295)                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Lifitegrast (n = 358)<br>Placebo (n = 360)                                                                                                                                                                                                                                                                                                                                                                                       | Lifitegrast (n = 355)<br>Placebo (n = 356)                                                                                                                                                                                                                                                                                                                                                          |
| <b>Primary endpoint findings</b>             | <p><b>Symptom</b></p> <ul style="list-style-type: none"> <li>• Mean change in VR-OSDI from baseline to day 84 was not different between groups (<math>p = 0.7894</math>)</li> </ul> <p><b>Sign</b></p> <ul style="list-style-type: none"> <li>• Mean change in inferior CFS score from baseline to day 84 was significantly reduced (improved) in the lifitegrast group (vs placebo; <math>p = 0.0007</math>)</li> </ul>                                                                                               | <p><b>Symptom</b></p> <ul style="list-style-type: none"> <li>• Mean change in eye dryness score (VAS) from baseline to day 84 was significantly reduced in the lifitegrast group (vs placebo; <math>p &lt; 0.0001</math>)</li> </ul> <p><b>Sign</b></p> <ul style="list-style-type: none"> <li>• Mean change in inferior CFS score from baseline to day 84 was not different between groups (<math>p = 0.6186</math>)</li> </ul> | <p><b>Symptom</b></p> <ul style="list-style-type: none"> <li>• Mean change in eye dryness score (VAS) from baseline to day 84 was significantly reduced (improved) in the lifitegrast group (vs placebo; <math>p = 0.0007</math>)</li> </ul>                                                                                                                                                        |
| <b>Findings for other efficacy endpoints</b> | <ul style="list-style-type: none"> <li>• Improvements with lifitegrast (vs placebo) at day 14 were noted in nasal and total CLGS scores (<math>p = 0.0032</math> and <math>p = 0.0149</math>, respectively)</li> <li>• Total CFS (<math>p = 0.0148</math>), superior CFS (<math>p = 0.0392</math>), nasal CLGS (<math>p = 0.0039</math>), and total CLGS (<math>p = 0.0086</math>) scores improved with lifitegrast (vs placebo) at day 84</li> <li>• Eye dryness (VAS; <math>p = 0.0291</math>) and ocular</li> </ul> | <ul style="list-style-type: none"> <li>• Improvements with lifitegrast (vs placebo) were noted in the eye dryness score at day 14 (nominal <math>p = 0.0003</math>)</li> <li>• Ocular discomfort (nominal <math>p = 0.0005</math>) and eye discomfort (nominal <math>p &lt; 0.0001</math>) scores were improved with lifitegrast (vs placebo) at day 84</li> </ul>                                                               | <ul style="list-style-type: none"> <li>• Improvements with lifitegrast (vs placebo) were noted in eye dryness scores at days 14 (<math>p &lt; 0.0001</math>) and 42 (<math>p &lt; 0.0001</math>) and in itching (nominal <math>p = 0.0318</math>), foreign body sensation (nominal <math>p = 0.0418</math>), and eye discomfort (nominal <math>p = 0.0048</math>) scores at day 42 (VAS)</li> </ul> |

|  |                                                                                              |  |  |
|--|----------------------------------------------------------------------------------------------|--|--|
|  | discomfort ( $p = 0.0273$ )<br>scores improved with<br>lifitegrast (vs placebo) at day<br>84 |  |  |
|--|----------------------------------------------------------------------------------------------|--|--|

\*Enrolled patients.

CFS, corneal fluorescein staining; CLGS, conjunctival lissamine green staining; VAS, visual analog scale; VR-OSDI, visual-related function subscale score of the Ocular Surface Disease Index.

**Table 2. Summary of real-world evidence of lifitegrast in DED.**

| Author                | Year | Study description                                                                                                                                                                                                      | Key findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----------------------|------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Survey studies</b> |      |                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| White et al [44]      | 2020 | Survey of ECP (ophthalmologists, optometrists, corneal specialists; n = 21) satisfaction with lifitegrast or cyclosporine ophthalmic emulsion 0.05% in patients with DED                                               | <ul style="list-style-type: none"> <li>• 67% of ECPs were “satisfied” or “very satisfied” with the ability of lifitegrast or cyclosporine ophthalmic emulsion 0.05% to stimulate tear production in patients with DED</li> <li>• Satisfaction with the effectiveness of lifitegrast and cyclosporine ophthalmic emulsion 0.05% was reported by 86% and 81% of ECPs, respectively</li> </ul>                                                                                                                                                                                                               |
| Hovanesian et al [45] | 2021 | Survey of ECP (ophthalmologists, optometrists; n = 517) treatment practices and chart review of patients (n = 600) with DED who received treatment with lifitegrast                                                    | <ul style="list-style-type: none"> <li>• Use of OTC artificial tears, topical corticosteroids, and any cyclosporine in patients with DED decreased after initiation of lifitegrast</li> <li>• Use of lifitegrast was associated with improvements in symptoms (eg, eye dryness) and signs (eg, corneal staining, Schirmer score, TFBUT), including symptom impacts on QoL</li> </ul>                                                                                                                                                                                                                      |
| Koetting et al [46]   | 2025 | Survey of ECP (ophthalmologists, optometrists; n = 12; mean number of patients with DED treated per ECP, 1288) treatment practices and experience with lifitegrast                                                     | <ul style="list-style-type: none"> <li>• 34.2% of patients, according to their ECPs, self-reported near or complete resolution of DED symptoms after first prescription of lifitegrast; 66.7% of providers reported near or complete resolution of symptoms after 1–3 months</li> <li>• Average ECP satisfaction with onset of action, effectiveness, ease of administration, and patient comfort with lifitegrast (vs other prescription treatment) ranged from moderate to high compared with other prescription eye drops, from 6.2–6.9 on a 10-point Likert scale</li> </ul>                          |
| White et al [47]      | 2020 | Survey of patients with DED who were current users of cyclosporine ophthalmic emulsion 0.05% (n = 98) or lifitegrast (n = 96), or had recently switched from one of these treatments to another DED treatment (n = 13) | <ul style="list-style-type: none"> <li>• Treatment satisfaction, as related to onset of effect, was rated as “somewhat satisfied” or “very satisfied” by 63% of current lifitegrast users and 51% of current cyclosporine ophthalmic emulsion 0.05% users</li> <li>• Satisfaction with management of symptoms was similar between current lifitegrast (77%) and cyclosporine (78%) users</li> <li>• Patient dissatisfaction (“somewhat dissatisfied” or “very dissatisfied”) related to onset of action was reported by 11% of current lifitegrast users and 29% of current cyclosporine users</li> </ul> |

| <b>Case series</b>               |      |                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----------------------------------|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Donnenfeld et al [48]            | 2025 | Prospective, observational case series of patients with DED (n = 50) treated with lifitegrast for 12 weeks                                                                | <ul style="list-style-type: none"> <li>• Lifitegrast treatment was associated with improvements in the following clinical sign/symptom outcomes (mean baseline, week 12): OSDI score (52.2, 31.2; <math>p &lt; 0.001</math>), tear osmolarity (317 mOsm/L, 293 mOsm/L; <math>p &lt; 0.001</math>), Schirmer test (11.7, 17.4; <math>p &lt; 0.001</math>), TFBUT (8.1, 10.4 s; <math>p &lt; 0.001</math>), and lissamine green staining (1.0, 0.1; <math>p &lt; 0.001</math>)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                    |
| <b>Claims data studies</b>       |      |                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| White et al [49]                 | 2019 | Retrospective database analysis of claims records from 9772 patients in the IBM MarketScan Commercial and Medicare Supplemental Databases from July 2015 to February 2018 | <ul style="list-style-type: none"> <li>• Overall adherence to treatment over a 12-month period was higher in patients in the lifitegrast group than in the cyclosporine ophthalmic emulsion 0.05% group (9.7% vs 5.9%)</li> <li>• Nonpersistence occurred in 6.8% and 7.1% of patients in the lifitegrast and cyclosporine groups, respectively</li> <li>• Fewer patients discontinued treatment within 12 months of initiation in the lifitegrast group than in the cyclosporine group (64.4% vs 70.8%)</li> <li>• 9.6% of patients in the lifitegrast group switched to cyclosporine ophthalmic emulsion 0.05%, and 5.0% of patients in the cyclosporine group switched to lifitegrast</li> <li>• 31.7% of patients in the lifitegrast group and 27.5% of patients in the cyclosporine group remained on treatment 12 months after initiation</li> </ul> |
| Karpecki et al [50]              | 2023 | Retrospective database analysis of claims records from 7102 patients in the Symphony Health Integrated Dataverse from July 2019 to June 2021                              | <ul style="list-style-type: none"> <li>• The median time to treatment discontinuation was not different between lifitegrast (269 days; 95% CI, 248–303) and cyclosporine ophthalmic solution 0.09% (354 days; 95% CI, 268–NE; <math>p = 0.825</math>)</li> <li>• When adjusting for patient age, Quan-Charlson Comorbidity Index score, health insurance program, and eye-related comorbidities, the odds of treatment discontinuation were similar between lifitegrast and cyclosporine ophthalmic solution 0.09% (adjusted estimated odds ratio, 0.97; 95% CI, 0.84–1.12; <math>p = 0.718</math>)</li> <li>• Similar proportions of patients on lifitegrast and cyclosporine ophthalmic solution 0.09% remained on treatment after 1 year from the date of the first treatment claim (44.0% vs 49.8%; <math>p = 0.854</math>)</li> </ul>                 |
| <b>Pharmacovigilance studies</b> |      |                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Wu et al [51]                    | 2025 | Analysis of AEs reported to the FAERS system from July 2016 to March 2024 that involved lifitegrast (n = 12,390 reports)                                                  | <ul style="list-style-type: none"> <li>• Eye irritation (n = 2229), vision blurred (n = 2210), and eye pain (n = 919) were the most common eye disorders with lifitegrast</li> <li>• Instillation site pain (n = 1279) and instillation site reaction (n = 1019) were the most common general disorders and administration site conditions, and</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

|                  |      |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------------------|------|---------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                  |      |                                                                                                                     | dysgeusia was the most common nervous system disorder (n = 996)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Zhang et al [52] | 2025 | Analysis of AEs reported to the FAERS system from Q3 2016 to Q2 2024 that involved lifitegrast (n = 12,393 reports) | <ul style="list-style-type: none"> <li>• The most common reports of AEs by system organ class were eye disorders (n = 10,935); general disorders and administration site conditions (n = 6649); injury, poisoning, and procedural complications (n = 2444); and nervous system disorders (n = 2361)</li> <li>• Of the eye disorders, the most common reports by preferred term were eye irritation (n = 2245), vision blurred (n = 2237), and eye pain (n = 923)</li> <li>• Of the general disorders and administration site conditions, the most common reports by preferred term were instillation site pain (n = 1280) and instillation site reaction (n = 1019); dysgeusia was described in 1002 reports</li> </ul> |

AE, adverse event; DED, dry eye disease; ECP, eyecare physician; FAERS, US Food and Drug Administration Adverse Event Reporting System; NE, not estimable; OSDI, Ocular Surface Disease Index; OTC, over the counter; QoL, quality of life; TFBUT, tear film breakup time.

## List of Abbreviations

AE, adverse event

ANDA, abbreviated new drug application

APC, antigen-presenting cell

BID, twice-daily

CFS, corneal fluorescein staining

CLDEQ-8, Contact Lens Dry Eye Questionnaire-8

CLGS, conjunctival lissamine green staining

DED, dry eye disease

ECP, eyecare provider

FAERS, US Food and Drug Administration Adverse Event Reporting System

FDA, US Food and Drug Administration

HR-QoL, health-related quality of life

ICAM-1, intercellular adhesion molecule-1

IFN, interferon

IL, interleukin

IOL, intraocular lens

IVCM, *in vivo* confocal microscopy

LFA-1, lymphocyte function-associated antigen-1

MMP-9, matrix metalloproteinase-9

NE, not estimable

NFAT, nuclear factor of activated T-cells

OSDI, Ocular Surface Disease Index

OTC, over the counter

QoL, quality of life

TFBUT, tear film breakup time

TNF- $\alpha$ , tumor necrosis factor-alpha

VAS, visual analog score

VR-OSDI, visual-related function subscale score of the Ocular Surface Disease Index

## TABLE LEGENDS

### Table 1. Summary of efficacy in OPUS clinical trials.

\*Enrolled patients.

CFS, corneal fluorescein staining; CLGS, conjunctival lissamine green staining; VAS, visual analog scale; VR-OSDI, visual-related function subscale score of the Ocular Surface Disease Index.

### Table 2. Summary of real-world evidence of lifitegrast in DED.

AE, adverse event; DED, dry eye disease; ECP, eyecare physician; FAERS, US Food and Drug Administration Adverse Event Reporting System; NE, not estimable; OSDI, Ocular Surface Disease Index; OTC, over the counter; QoL, quality of life; TFBUT, tear film breakup time.

## FIGURE LEGENDS

**Figure 1. The immunoinflammatory pathway of DED.** Ocular surface stress triggers an inflammatory/immune response, characterized by the release of proinflammatory cytokines that activate resident APCs [21]. Activated APCs migrate to regional lymph nodes and facilitate the activation and recruitment of T-cells to the ocular surface, thereby amplifying the inflammatory cascade. APC, antigen-presenting cell; DED, dry eye disease; IFN, interferon; IL, interleukin; TNF- $\alpha$ , tumor necrosis factor-alpha.

**Figure 2. Mechanism of action of lifitegrast and cyclosporin in DED.** Lifitegrast inhibits multiple steps in the inflammatory cascade, and cyclosporin suppresses T-cell activation by APCs via disruption of the molecular process within the T-cell [15,21,30]. APC, antigen-presenting cell; DED, dry eye disease; ICAM-1, intercellular adhesion molecule-1; IL, interleukin; LFA-1, lymphocyte function-associated antigen-1; NFAT, nuclear factor of activated T-cells.

**Figure 3. Time to near or complete symptom resolution with lifitegrast treatment.**

ECP, eyecare provider.

Figure 3 reprinted with permission from Koetting C, et al, Real-world experience with lifitegrast ophthalmic solution in patients with dry eye disease: a provider survey in the USA and Canada. *Ophthalmol Ther*, vol. 14, no. 9, 2109-2124, 2025, Springer Nature [46].

**Supplementary material:** The immunoinflammatory pathway of dry eye disease and lifitegrast mechanism of action animation video.

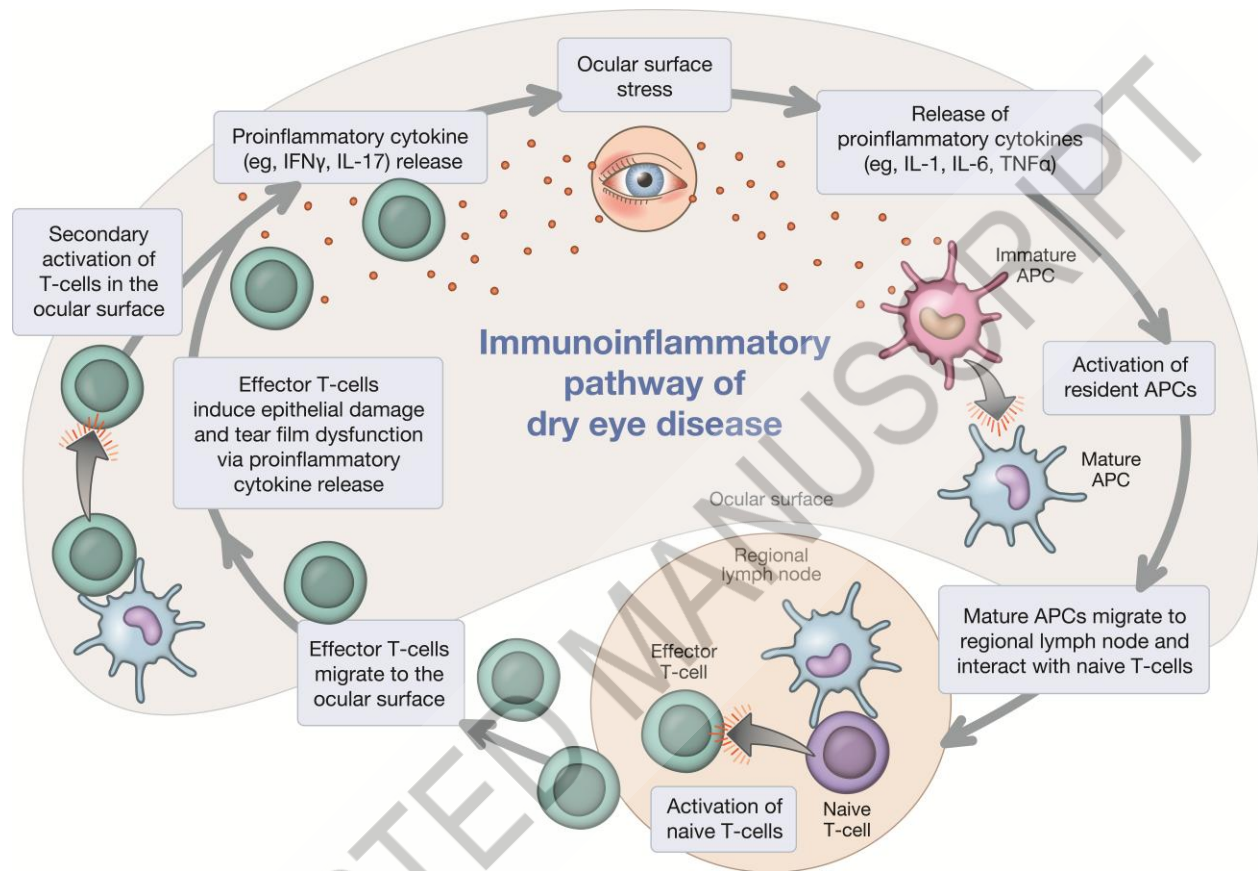


Figure 1

# **Lifitegrast blocks multiple steps in the inflammatory cascade**

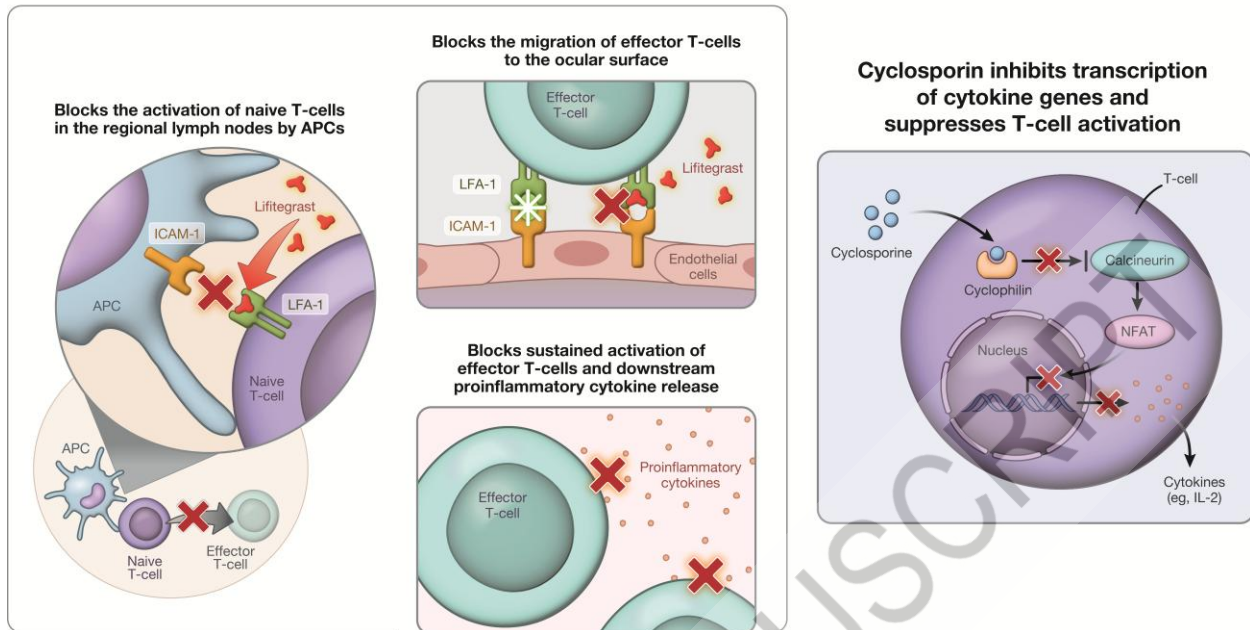


Figure 2

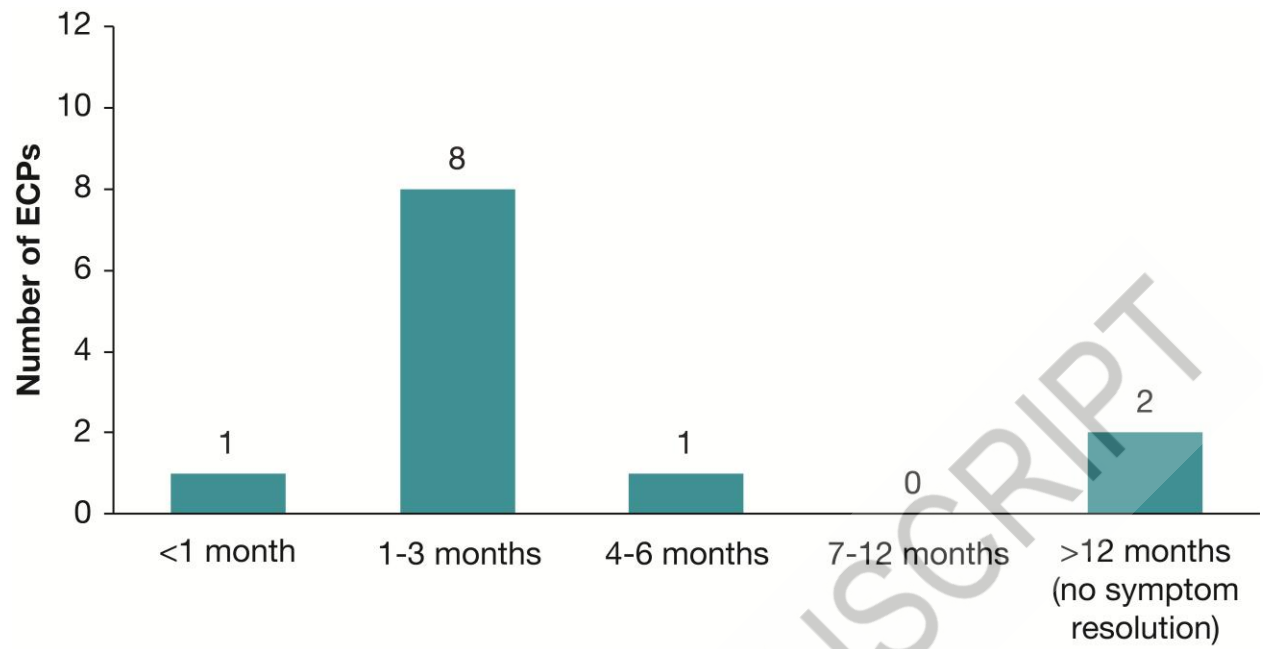


Figure 3

## Video Transcript—Lifitegrast Mechanism of Action

### Scene 1 — Opening: The desert eye

|                  |                                                                                                                         |
|------------------|-------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 1.1</b> | <b>Visual:</b> The camera opens on a desert environment. We pan across the infinite sandy plains. It looks hot and dry. |
| <b>Voiceover</b> | Sufferers of dry eye disease may experience symptoms of discomfort and/or visual disturbances. <sup>1</sup>             |

|                  |                                                                                                                                                                                           |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 1.2</b> | <b>Visual:</b> We continue to pan across the plains and reach a structure in the sand that looks like an eye (e.g. the Eye of the Sahara). Cracks in the sand look like veins in the eye. |
| <b>Voiceover</b> | Dry eye is characterized by a loss of homeostasis of the tear film, resulting in tear film instability, hyperosmolarity, and ocular surface inflammation. <sup>1,2</sup>                  |

|                  |                                                                    |
|------------------|--------------------------------------------------------------------|
| <b>Frame 1.3</b> | <b>Visual:</b> Sand/dust representing stress swirl around the eye. |
| <b>Voiceover</b> | As desiccating and osmotic stress occur to...                      |

|                  |                                                                                                                                                           |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 1.4</b> | <b>Visual:</b> More cracks appear in the sand.                                                                                                            |
| <b>Voiceover</b> | ... the ocular surface, this results in damage triggering immunoinflammatory pathways that play a key role in the pathogenesis of dry eye. <sup>3,4</sup> |

### Scene 2 — Epithelial damage and APC maturation

|                  |                                                                                                                                               |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 2.1</b> | <b>Visual:</b> Crash zoom into the ocular surface, now with more realistic textures of an eye but still maintaining a dry and irritated look. |
| <b>Voiceover</b> | Desiccating and osmotic stress may cause...                                                                                                   |

|                  |                                                                                                                                                                                                                                                                |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 2.2</b> | <b>Visual:</b> Pan down across the epithelial layer and show the damaged epithelial cells producing proinflammatory cytokines proteins (IL-1, IL-6, TNF- $\alpha$ , IFN- $\gamma$ ). In the background, immature antigen-presenting cells (APCs) are visible., |
| <b>Voiceover</b> | ...epithelial cells to produce pro-inflammatory cytokines,...                                                                                                                                                                                                  |

|                  |                                                                                              |
|------------------|----------------------------------------------------------------------------------------------|
| <b>Frame 2.3</b> | <b>Visual:</b> The immature APCs come to the foreground and encounter some of the cytokines. |
| <b>Voiceover</b> | ...triggering antigen-presenting cells,...                                                   |

|                  |                                                                                                |
|------------------|------------------------------------------------------------------------------------------------|
| <b>Frame 2.4</b> | <b>Visual:</b> The APCs change colour and glow to signify that they are now mature and active. |
| <b>Voiceover</b> | ...or APC maturation. <sup>3,4</sup>                                                           |

|                  |                                                            |
|------------------|------------------------------------------------------------|
| <b>Frame 2.5</b> | <b>Visual:</b> The mature APC approaches the lymph vessel. |
| <b>Voiceover</b> | Mature APCs...                                             |

|                  |                                                                                                                                       |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 2.6</b> | <b>Visual:</b> Zoom in to see the APC bind to E-selectin, N-cadherin, and finally VCAM-1 as it rolls across the lymph vessel surface. |
| <b>Voiceover</b> | ...migrate via the afferent arm to the lymph node. <sup>3,4</sup>                                                                     |

|                  |                                                                                       |
|------------------|---------------------------------------------------------------------------------------|
| <b>Frame 2.7</b> | <b>Visual:</b> The APC changes conformation as it intravasates into the lymph vessel. |
| <b>Voiceover</b> | (No voiceover.)                                                                       |

### Scene 3 — T-cell priming in the lymph node

|                  |                                                                       |
|------------------|-----------------------------------------------------------------------|
| <b>Frame 3.1</b> | <b>Visual:</b> Cut to show the mature APC approaching a naïve T cell. |
| <b>Voiceover</b> | Here, they interact with naïve T cells...                             |

|                  |                                                                                                                                                                                                                         |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 3.2</b> | <b>Visual:</b> Zoom in to show the surface interactions. On the APC: ICAM-1, CD80, and MHC. On the T cell: LFA-1 (closed conformation), CD28, and a TCR. MHC is bound to the TCR via an antigen and CD28 binds to CD80. |
| <b>Voiceover</b> | ...through Intercellular Adhesion Molecule-1, ICAM-1,...                                                                                                                                                                |

|                  |                                                                                                                                                  |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 3.3</b> | <b>Visual:</b> LFA-1 and ICAM-1 undergo conformational changes; LFA-1 opens and binds to ICAM-1, which dimerizes. A glow indicates this binding. |
| <b>Voiceover</b> | ...and lymphocyte function-associated antigen-1, LFA-1. This strengthens the T-cell synapses and T-cell activation,...                           |

|                  |                                                                                                                                                                   |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 3.4</b> | <b>Visual:</b> Zoom out to see the whole cells still joined by the synapse. The T cell changes colour to signify that it is now a CD4 <sup>+</sup> T-helper cell. |
| <b>Voiceover</b> | priming them to differentiate into CD4 <sup>+</sup> T- cells. <sup>4</sup>                                                                                        |

#### Scene 4 — Migration to the ocular surface

|                  |                                                                                                                                                                                                                             |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 4.1</b> | <b>Visual:</b> Follow the T cells as they leave the lymph node via a blood vessel.                                                                                                                                          |
| <b>Voiceover</b> | These cells go on a journey...                                                                                                                                                                                              |
| <b>Frame 4.2</b> | <b>Visual:</b> Follow the T cells as they travel through the blood.                                                                                                                                                         |
| <b>Voiceover</b> | ...through the efferent arm                                                                                                                                                                                                 |
| <b>Frame 4.3</b> | <b>Visual:</b> The T cell sticks to and rolls on the surface of the blood vessel wall.                                                                                                                                      |
| <b>Voiceover</b> | ...eventually forming...                                                                                                                                                                                                    |
| <b>Frame 4.4</b> | <b>Visual:</b> Zoom in to show the conformational change between LFA-1 on the T cell and ICAM-1 on the blood vessel surface. VCAM-1/ $\alpha 4\beta 7$ and E-selectin/PSGL-1 interactions are also shown in the background. |
| <b>Voiceover</b> | ...LFA-1/ICAM-1 interactions with the endothelium,...                                                                                                                                                                       |
| <b>Frame 4.5</b> | <b>Visual:</b> The T cell extravasates through the blood vessel wall.                                                                                                                                                       |
| <b>Voiceover</b> | ...facilitating transmigration to...                                                                                                                                                                                        |
| <b>Frame 4.6</b> | <b>Visual:</b> The T cell appears on the other side of the blood vessel, arriving in the conjunctival stroma.                                                                                                               |
| <b>Voiceover</b> | ...the ocular surface. <sup>4, 5</sup>                                                                                                                                                                                      |

#### Scene 5 — T-cell reactivation at the ocular surface

|                  |                                                                                                                                                                                                                         |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 5.1</b> | <b>Visual:</b> The T cell arrives in the conjunctival stroma and binds to another mature APC. A callout appears showing the LFA-1/ICAM-1 interaction.                                                                   |
| <b>Voiceover</b> | APCs reactivate T cells at the ocular surface,...                                                                                                                                                                       |
| <b>Frame 5.2</b> | <b>Visual:</b> The T cell glows to show it is now active and releases proinflammatory cytokine proteins (IL-1, IL-6, TNF- $\alpha$ , IFN- $\gamma$ ), causing further damage to the already irritated epithelial cells. |
| <b>Voiceover</b> | ...which release proinflammatory cytokines, damaging the epithelium. <sup>3, 4, 5</sup>                                                                                                                                 |
| <b>Frame 5.3</b> | <b>Visual:</b> Follow active T cells as they bind to epithelial cells while continuing to produce cytokines. Callout of the LFA-1/ICAM-1 interaction.                                                                   |

|                  |                                                                                                                                                 |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Voiceover</b> | Activated T cells are retained at the ocular surface, via LFA-1 bound ICAM-1, the expression of which may be increased in dry eye. <sup>4</sup> |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|

## Scene 6 — Lifitegrast mechanism of action

|                  |                                                                                                                    |
|------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Frame 6.1</b> | <b>Visual:</b> Hero shot of lifitegrast in a non-descript environment.                                             |
| <b>Voiceover</b> | Lifitegrast ophthalmic solution 5.0% is indicated for the treatment of signs and symptoms of dry eye. <sup>6</sup> |

|                  |                                                                                                    |
|------------------|----------------------------------------------------------------------------------------------------|
| <b>Frame 6.2</b> | <b>Visual:</b> Lifitegrast binds to LFA-1 on a T-cell surface. CD80/CD28 and MHC/TCR remain bound. |
| <b>Voiceover</b> | It is thought to work by blocking the interaction between LFA-1 and ,...                           |

|                  |                                                                  |
|------------------|------------------------------------------------------------------|
| <b>Frame 6.3</b> | <b>Visual:</b> ICAM-1 is unable to bind to the T cell via LFA-1. |
| <b>Voiceover</b> | ... ICAM-1. <sup>6</sup>                                         |

|                  |                                                                                                                                                                                                                                                                                                   |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 6.4</b> | <b>Visual:</b> The cell-surface interaction shrinks down to a callout in the centre of the screen. A 4-way split screen appears around it, showing the sites of the inflammatory loop that lifitegrast blocks: activation, migration, secondary activation, and proinflammatory cytokine release. |
| <b>Voiceover</b> | This allows it to block several sites of the dry eye immunoinflammatory cycle,...                                                                                                                                                                                                                 |

|                  |                                                                                                                                   |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 6.5</b> | <b>Visual:</b> In the lymph node, the APC fails to bind to the naïve T cell, so the T cell does not transform into a CD4+ T cell. |
| <b>Voiceover</b> | ...inhibiting activation,...                                                                                                      |

|                  |                                                                                             |
|------------------|---------------------------------------------------------------------------------------------|
| <b>Frame 6.6</b> | <b>Visual:</b> The T cell fails to leave the blood vessel and rebounds off the vessel wall. |
| <b>Voiceover</b> | ...preventing migration...                                                                  |

|                  |                                                                                                     |
|------------------|-----------------------------------------------------------------------------------------------------|
| <b>Frame 6.7</b> | <b>Visual:</b> The inactive T cell rebounds off the APC at the ocular surface and remains inactive. |
| <b>Voiceover</b> | ...repressing potentially secondary activation, and...                                              |

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|------------------|------------------------------------------------------------------------------------|
| <b>Frame 6.8</b> | <b>Visual:</b> The T cell rebounds off the epithelial cells at the ocular surface. |
|------------------|------------------------------------------------------------------------------------|

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|------------------|------------------------------------------------------------------------------------|
| <b>Voiceover</b> | ...reducing proinflammatory cytokine release at the ocular surface. <sup>4,6</sup> |
|------------------|------------------------------------------------------------------------------------|

## Scene 7 — Resolution

|                  |                                                                                                                                                                                                                     |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 7.1</b> | <b>Visual:</b> Crash zoom back out of the ocular surface to the eye in the desert. A water droplet (the lifitegrast ophthalmic solution) falls from the sky and spreads over the eye. On-screen disclaimer remains. |
| <b>Voiceover</b> | Lifitegrast ophthalmic solution 5.0% is indicated for the treatment of...                                                                                                                                           |

|                  |                                                                                                              |
|------------------|--------------------------------------------------------------------------------------------------------------|
| <b>Frame 7.2</b> | <b>Visual:</b> The "sand" eye cuts to a realistic eye. On-screen disclaimer remains.                         |
| <b>Voiceover</b> | ...signs and symptoms of dry eye disease and is an LFA-1 antagonist which targets inflammation. <sup>6</sup> |

## Scene 8 — Indication, ISI, and close

|                  |                                                          |
|------------------|----------------------------------------------------------|
| <b>Frame 8.1</b> | <b>Visual:</b> Indication statement displayed on screen. |
| <b>Voiceover</b> | (No voiceover.)                                          |

|                  |                                                                                                                                                   |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Frame 8.2</b> | <b>Visual:</b> Scrolling Important Safety Information (ISI), followed by a "Please see" statement linking to the full US Prescribing Information. |
| <b>Voiceover</b> | (No voiceover.)                                                                                                                                   |

|                  |                                      |
|------------------|--------------------------------------|
| <b>Frame 8.3</b> | <b>Visual:</b> Fade to company logo. |
| <b>Voiceover</b> | (No voiceover.)                      |

## Continuous voiceover (narration only)

### Scene 1 — Opening: The desert eye

Sufferers of dry eye disease may experience symptoms of discomfort and/or visual disturbances.<sup>1</sup> Dry eye is characterized by a loss of homeostasis of the tear film, resulting in tear film instability, hyperosmolarity, and ocular surface inflammation.<sup>1,2</sup> As desiccating and osmotic stress occur to... the ocular surface, this results in damage triggering immunoinflammatory pathways that play a key role in the pathogenesis of dry eye.<sup>3,4</sup>

### Scene 2 — Epithelial damage and APC maturation

Desiccating and osmotic stress may cause... ..epithelial cells to produce pro-inflammatory cytokines,... ..triggering antigen-presenting cells,... ..or APC maturation.<sup>3,4</sup> Mature APCs... ..migrate via the afferent arm to the lymph node.<sup>3,4</sup>

### **Scene 3 — T-cell priming in the lymph node**

Here, they interact with naïve T cells... ..through Intercellular Adhesion Molecule-1, ICAM-1,... ..and lymphocyte function-associated antigen-1, LFA-1. This strengthens the T-cell synapses and T-cell activation,... ..priming them to differentiate into CD4+ T- cells.<sup>4</sup>

### **Scene 4 — Migration to the ocular surface**

These cells go on a journey... ..through the efferent arm... ..eventually forming... ..LFA-1/ICAM-1 interactions with the endothelium,... ..facilitating transmigration to... ..the ocular surface.<sup>4,5</sup>

### **Scene 5 — T-cell reactivation at the ocular surface**

APCs reactivate T cells at the ocular surface,... ..which release proinflammatory cytokines, damaging the epithelium.<sup>3,4,5</sup> Activated T cells are retained at the ocular surface, via LFA-1 bound ICAM-1, the expression of which may be increased in dry eye.<sup>4</sup>

### **Scene 6 — Lifitegrast mechanism of action**

Lifitegrast ophthalmic solution 5.0% is indicated for the treatment of signs and symptoms of dry eye.<sup>6</sup> It is thought to work by blocking the interaction between LFA-1 and ICAM-1.<sup>6</sup> This allows it to block several sites of the dry eye immunoinflammatory cycle,... ..inhibiting activation,... ..preventing migration... ..and repressing potentially secondary activation, and... ..and reducing proinflammatory cytokine release at the ocular surface.<sup>4,6</sup>

### **Scene 7 — Resolution**

Lifitegrast ophthalmic solution 5.0% is indicated for the treatment of... ..signs and symptoms of dry eye disease and is an LFA-1 antagonist which targets inflammation.<sup>6</sup>

### **Scene 8 — Indication, ISI, and close**

*(No voiceover in this scene.)*

### **References**

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