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Lifitegrast: a novel drug for patients with dry eye disease

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***Abstract*:** The objective of this article is to review the pharmacology, efficacy, and safety of lifitegrast and determine its role relative to other agents in the management of dry eye disease. A PubMed search (1946 to December 2018) using the terms *lifitegrast* and *SAR 1118* was conducted to identify relevant articles. *In vitro* or *in vivo* evaluations of lifitegrast published in the English language were eligible for inclusion. Phase II and III trials were selected for review of efficacy and safety. Four randomized controlled trials evaluated the efficacy and safety of lifitegrast 0.5% ophthalmic solution for 12 weeks, and 1 additional trial assessed safety for 1 year. In a majority of the trials, lifitegrast caused statistically significant improvements in inferior corneal fluorescein staining scores and eye dryness scores. The most common adverse effects were eye irritation, dysgeusia, and reduced visual acuity, and most were mild to moderate in severity. Lifitegrast has a novel mechanism of action and is safe and effective for the treatment of dry eye disease. At this time, lifitegrast may be considered as an option for patients who have an inadequate response to artificial tears.

Keywords: clinical pharmacology, drug development and approval, literature evaluation, ophthalmology

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Introduction

Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by loss of homeostasis of the tear film.[1] It affects nearly 7% of adults in the United States, and the prevalence is expected to increase as the population ages.[2] DED costs approximately US$3.8 billion annually in health care expenditures and is associated with significant losses in productivity.[3] It is more common among women, perhaps due to risk factors such as low androgen levels and high estrogen levels.[1] Other potential risk factors include contact lens use, nutritional deficiencies, ophthalmic surgery, various diseases (e.g. diabetes mellitus, Parkinson disease), and numerous medications (e.g. anticholinergics, antidepressants, antihistamines, antihypertensives, anxiolytics, isotretinoin).

The pathophysiology of DED involves tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities.[1] Two main subtypes have been identified: evaporative dry eye, which is caused by extreme evaporation from the tear film with a normally functioning lacrimal gland, and aqueous deficient dry eye, which is caused by reduced tear secretion from a dysfunctional lacrimal gland. Regardless of the etiology, the symptoms of DED typically involve ocular discomfort and visual disturbances. As a result, patients may have difficulty performing daily activities and are also at increased risk for depression and anxiety.[1,4] Unfortunately, signs of DED from objective ocular tests may not correlate with symptoms, which complicates diagnosis and evaluation of the disease.[1]

Patients with DED are typically treated with lifestyle modifications, tear supplementation, and pharmacologic interventions based on disease characteristics.[5] Lifestyle changes include ensuring adequate fluid intake, minimizing alcohol use,

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getting adequate sleep, using humidifiers, and avoiding air conditioning and forced air heating.[5,6] Artificial tears are often used for symptomatic relief.[5] Topical cyclosporine, a nonglucocorticoid immunomodulatory agent, has been a mainstay of therapy since its approval by the U.S. Food and Drug Administration (FDA) in 2003.[7,8] Lifitegrast, a lymphocyte function-associated antigen-1 (LFA-1) antagonist, became the second drug approved for DED in July 2016 and offers a novel mechanism of action.[9,10] This article will provide a review of the available literature on lifitegrast to help clinicians determine its place in therapy.

Data selection

A PubMed search (1946 to December 2018) using the terms lifitegrast and SAR 1118 (the original molecular designation for lifitegrast) was conducted to identify relevant articles. Articles were eligible for inclusion if they were *in vitro* or *in vivo* evaluations of lifitegrast published in the English language. Phase II and III trials of the drug for DED were selected for evaluation of efficacy and safety. The prescribing information was accessed from the manufacturer's Website.

Mechanism of action

Lifitegrast is an LFA-1 antagonist.[9] LFA-1 is a heterodimeric integrin composed of α_L and β_2 subunits that is ubiquitously expressed on large granular lymphocytes, B lymphocytes, and T lymphocytes.[9,11] Lifitegrast binds to LFA-1 and inhibits it from interacting with its ligand, intercellular adhesion molecule 1 (ICAM-1), an immunoglobulin superfamily cellular adhesion molecule. ICAM-1 is expressed by endothelial cells when inflammation or an infection is present but may be overexpressed in corneal and conjunctival tissues in individuals with DED. By competitively binding to the intracellular domain of the α_L subunit, lifitegrast prevents the adhesion, activation, migration, and proliferation of lymphocytes, which ultimately lead to cytokine secretion (e.g. interferon gamma, interleukin 4), cell destruction, and self-amplification of the inflammatory immune response that further aggravates symptoms of DED.[9,12–14]

Pharmacodynamics

Lifitegrast is soluble in a phosphate-buffered saline at concentrations up to and exceeding 200 mg/ml, which allows up to a 10% (100 mg/ml) preparation that has an osmolality relatively equal to that of human tears (300 mOsm/L).[15] This is preferred to reduce the likelihood of local irritation. In a study that evaluated the conjunctiva in mice, lifitegrast compared to vehicle demonstrated a statistically significant reduction in the expression of inflammatory mediators, including interferon gamma and chemokine ligand 9.[12] In this same study, lifitegrast increased the number of conjunctival goblet cells and goblet cell area by 39% and 22%, respectively ($p < 0.05$ for both), resulting in a therapeutic improvement within 5 days. In an *in vivo* study of dogs with keratoconjuctivitis, a 1% solution of lifitegrast administered 3 times a day significantly increased tear production at the end of 12 weeks (Schirmer tear test, 3.4 to 5.8 mm; $p < 0.025$).[16] In a separate *in vitro* study, lifitegrast exhibited a preferred negative result in the Ames test and low affinity for cytochrome P450 CYP3A4 and CYP2C9 enzymes ($IC_{50} > 20$ μM and $IC_{50} = 3.0$ μM, respectively) and the human Ether-à-go-go-Related Gene (hERG, $IC_{50} > 20$ μM).[17]

Pharmacokinetics

In a phase I study, time to maximum concentration (t_{max}) of lifitegrast in plasma was detected as early as 5 min after ocular instillation, indicating that the drug is readily absorbed.[18] In an animal study, t_{max} in all ocular tissue samples was determined to be 15–60 min.[19] In humans, lifitegrast 5% administered three times a day resulted in a maximum concentration (C_{max}) of <5 nM.[18] Systemic exposure of lifitegrast is presumed to be minimal due to serum levels being below the lower limit of quantification (BLQ: <0.5 ng/ml) within 1–4 h of dosing. The maximum concentration (C_{max}) in rabbits was 17.4 ng/ml.[19] Drug accumulation in tears was not evident in adults following administration of concentrations ranging from 0.1% to 5% over 27 days.[18] In a phase-III trial of lifitegrast 5% administered twice daily, 38 patients had plasma trough concentrations that were BLQ, whereas nine patients had concentrations ranging from 0.5 to 3.74 ng/ml.[9] Regarding distribution, lifitegrast 5% administered twice daily for a total of nine doses in rabbits produced C_{max} levels ranging from 5190 to 14,200 ng/g in target anterior segment tissues, which consist of the conjunctiva, cornea, and anterior sclera.[19] In humans, the C_{max} ranged from levels BLQ to 8.1 ng/ml in the vitreous humor, a nontarget posterior tissue.[20] In nontarget posterior tissues in rabbits, including the

vitreous humor, optic nerve, and retina, the C_{max} ranged from levels BLQ to 36.1 ng/ml.[19] Excreta analyzed following intravenous administration with radiolabelled drug in dogs showed that approximately 90% was excreted unchanged within the first 48 h, indicating that lifitegrast is only slightly metabolized *in vivo*. Plasma half-life ($t_{1/2}$) in humans is assumed to be short based on a $t_{1/2}$ of 0.85 h detected in rabbits. Given the lack of a distinct elimination phase, the $t_{1/2}$ in most ocular tissues remains unknown, except for in the conjunctiva and sclera in rabbits in which lifitegrast has a $t_{1/2}$ equal to 2.02 and 1.97 h, respectively.[18,19]

Efficacy

The efficacy of lifitegrast was assessed in four randomized controlled trials of 12 weeks in duration. The first phase II study explored three different concentrations of the drug, and subsequently, the phase III studies evaluated the 5% solution.[21–24] A standardized, validated instrument for assessing outcomes in trials of patients with DED has not been established. However, the FDA defines clinically meaningful outcomes for drug approval as demonstration of statistically significant improvement in $\geqslant$1 objective endpoint (sign) and $\geqslant$1 subjective endpoint (symptom). In all studies of lifitegrast, signs of DED were assessed with the inferior fluorescein corneal staining score (ICSS), which was determined by investigators using a scale that ranges from 0 to 4 (0 = no staining, 1 = few/rare punctate lesions, 2 = discrete and countable lesions, 3 = lesions too numerous to count but no coalescent, and 4 = coalescent). Symptoms of DED were assessed with the eye dryness score (EDS), which was rated by patients using a visual analogue scale (VAS) that ranges from 0 (no discomfort) to 100 (maximal discomfort).

The phase II trial for lifitegrast compared 0.1%, 1.0%, and 5.0% ophthalmic solutions with placebo.[21] It included 230 participants who were 18 years of age or older, had established DED in both eyes, used or desired to use artificial tears within the previous 6 months, presented with conjunctival redness, and met specific criteria on various ocular tests (ICSS $\geqslant$2 in any eye, Schirmer test $>$1 and $<$10 in any eye, and best-corrected visual acuity $>$0.7). Patients in all groups were instructed to instill 1 drop of ophthalmic solution into both eyes every morning and evening for 84 days. Use of artificial tears or other ophthalmic medications was prohibited. The primary objective efficacy endpoint (sign) was ICSS at day 84. A statistically significant improvement in the mean change in ICSS was noted for the 1% and 5% solutions compared to placebo (results for the 5% solution and placebo are shown in Table 1); however, the improvement was not significant for the 0.1% solution. The secondary objective endpoints (signs) were the Schirmer test, conjunctival staining score, tear film break-up time, and blink rate. A statistically significant increase in tear production occurred only in the lifitegrast 5% group compared to placebo over the 84 days. There were no statistically significant improvements with lifitegrast in the conjunctival staining score, tear film break-up time, or blink rate. The secondary subjective endpoints (symptoms) were the ocular surface disease index (OSDI), ocular discomfort score (ODS), and VAS. The OSDI is a validated patient questionnaire that assesses 12 items regarding visual-related function, triggers, and symptoms. The OSDI score significantly improved within 14 days of treatment with each dose of lifitegrast compared to placebo. The ODS ranges from 0 (no discomfort) to 4 (severe discomfort). Improvements in ODS were observed in all groups, but the results were only statistically significant for lifitegrast 5% compared to placebo in a per-protocol analysis. The VAS was used to score blurred vision, burning/stinging, eye dryness, foreign body sensation, itching, pain, and photophobia. Improvements were noted for burning/stinging, eye dryness (results for the 5% solution and placebo are shown in Table 1), and photophobia, but the results were only statistically significant for lifitegrast 5.0% compared to placebo for burning/stinging. The researchers concluded that lifitegrast improved signs and symptoms of DED when used for 84 days. Because dose-dependent improvements across many assessments were observed in this phase II trial, the 5% solution was pursued in phase III trials.

The OPUS trials were randomized, double-blind, placebo-controlled, phase III studies that led to the approval of lifitegrast.[22–24] All were conducted at multiple centers in the United States. Participants were randomized 1:1 to receive topically administered lifitegrast 5.0% or placebo twice daily. Studies consisted of three periods: screening (day 14 to day 0), treatment (days 0–84), and follow-up (day 85 or 86). Eligible participants included adults $\geqslant$18 years who had minimal signs (i.e. ICSS and Schirmer test score) and symptoms (i.e. EDS and ODS) of DED at

Table 1. Efficacy of lifitegrast 5% solution in clinical trials.[9,21–24]

	Phase II		OPUS-1		OPUS-2		OPUS-3	
	Lifitegrast (*N* = 58)	Placebo (*N* = 58)	Lifitegrast (*N* = 293)	Placebo (*N* = 295)	Lifitegrast (*N* = 358)	Placebo (*N* = 360)	Lifitegrast (*N* = 355)	Placebo (*N* = 356)
Inferior corneal fluorescein staining score (sign)*								
Mean score at baseline (SD)	1.77 (0.515)	1.65 (0.513)	1.84 (0.597)	1.81 (0.599)	2.39 (0.763)	2.40 (0.722)	2.46 (0.681)	2.46 (0.746)
Mean change at day 84 (SD)	0.04 (0.745)	0.38 (0.785)‡	−0.07 (0.868)	0.17 (0.819)‡	−0.73 (0.926)	−0.71 (0.943)	−0.80 (0.939)	−0.63 (0.911)‡
Eye dryness score (symptom)$								
Mean score at baseline (SD)	51.6 (24.69)	51.8 (23.55)	40.2 (28.64)	41.6 (29.69)	69.7 (16.95)	69.2 (16.76)	68.3 (16.88)	69.0 (17.08)
Mean change at day 84 (SD)	−14.4 (25.36)	−7.2 (25.29)	−15.2 (31.48)	−11.2 (28.78)‡	−35.3 (28.40)	−22.8 (28.60)‡	−37.7 (28.91)	−30.5 (28.03)‡

SD: standard deviation.
*Ranked on a scale of 0–4 (0 = none to 4 = confluent).
$Ranked on a 7-item visual analog scale of 0–100 (0 = no discomfort to 100 = maximum discomfort).
‡Value has a $p < 0.05$ compared to lifitegrast.

baseline. Use of topical cyclosporine, artificial tears, or other ophthalmic medications was not permitted. Although each study specified different primary and secondary endpoints, all assessed mean change in ICSS (sign) and mean change in EDS (symptom) from baseline to day 84 (results shown in Table 1).

Some differences in the designs and results among the OPUS trials are noteworthy. First, in the phase II study, a statistically significant benefit in visual-related function on the OSDI, which measures quality-of-life indicators such as reading, driving, and watching television, was found for patients who received lifitegrast.[21] Unfortunately, this benefit was not replicated in OPUS-1 and not evaluated in OPUS-2 or OPUS-3, so such benefits with lifitegrast cannot be expected.[22] Second, differences in eligibility criteria and screening methods resulted in populations with varying degrees of disease severity. In OPUS-1, a minimum EDS was not an inclusion criterion, and disease severity at baseline was mild to moderate.[22] In OPUS-2 and OPUS-3, a minimum EDS of ⩾40 and recent use of artificial tears were added as inclusion criteria and use of a controlled adverse environment as a screening method was removed.[23,24] The combination of these changes led to patients with moderate to severe disease at baseline. Regardless of these differences, lifitegrast significantly improved EDS *versus* placebo in all trials.[22–24] ICSS was only significantly improved in OPUS-1 and OPUS-3, but a clear reason for this finding was not identified.[22,24] Finally, a significant benefit in EDS was observed at day 42 in OPUS-1 and at day 14 in OPUS-2 and OPUS-3.[22–24]

A critical evaluation of the OPUS trials revealed a few additional considerations. The average age was 59 years, and a majority of patients were women, which may reflect the prevalence of DED. In terms of strengths, patients were well matched at baseline, the sample sizes were adequate, and the number of dropouts was small. However, a few limitations were also noted. Due to the specific eligibility requirements in the trials, the results may not be generalizable to a broader population in clinical practice. Because the studies were only 12 weeks in duration, the long-term efficacy and safety of lifitegrast were not determined. Finally, because concomitant use of artificial tears or other ophthalmic medications was not allowed, the efficacy and safety of lifitegrast in combination with such agents were not established.

Safety

The safety of lifitegrast was assessed in the aforementioned trials and in a 1-year, phase III study, the Safety Of a 5.0% coNcentrATion of lifitegrAst

ophthalmic solution (SONATA).[21–26] A pooled analysis of the safety results for all published phase II and III trials has also been published.[27] In addition, some safety data have emerged from postmarketing surveillance.

In the SONATA trial, adults with DED (corneal staining score ⩾2; eye dryness or discomfort score with ⩾40; Schirmer test score ⩾1 and ⩽10 mm) were randomized to receive lifitegrast 5% ophthalmic solution ($n=220$) or placebo ($n=111$) twice daily for 360 days in a double-blind manner.[26] Participants were not allowed to use ophthalmic nonsteroidal anti-inflammatory agents, ophthalmic cyclosporine, or systemic steroids. However, after day 14, use of contact lenses, artificial tears, ophthalmic/nasal antihistamines, ophthalmic loteprednol, and mast cell stabilizers was permitted. The primary outcome was the percentage and severity of treatment-emergent adverse events (TEAEs), and secondary outcomes included various ocular safety measures (corneal fluorescein staining, drop comfort, best-corrected visual acuity, slit-lamp biomicroscopy, and intraocular pressure). For patients in the lifitegrast group, 53.6% experienced ⩾1 ocular TEAE compared to 34.2% in the placebo group. Ocular TEAEs included instillation site irritation (15% in lifitegrast *versus* 4.5% in placebo), instillation site reactions (13.2% *versus* 1.8%), dysgeusia (16.4% *versus* 1.8%), reduced visual acuity (11.4% *versus* 6.3%), and dry eye (1.8% *versus* 5.4%). No serious ocular TEAEs occurred, but 4.1% of patients in the lifitegrast group *versus* 5.4% in the placebo group experienced serious nonocular TEAEs. None of the serious nonocular TEAEs were considered related to the drug, and all resolved except spinal fracture, chronic obstructive pulmonary disease, and a sudden cardiac arrhythmia that resulted in death. Results for secondary outcomes were similar between the lifitegrast and placebo groups. The investigators concluded that lifitegrast 5% was safe and well tolerated for up to 1 year, with a safety profile similar to the 12-week trials.

In 2018, Nichols and colleagues[27] conducted a pooled analysis of five randomized controlled trials to assess the safety and tolerability of lifitegrast 5% administered twice daily. Data were available from a total of 2464 patients ($n=1287$ for lifitegrast; $n=1177$ for placebo). TEAEs that occurred in >5% of patients included instillation site irritation (15.2% in lifitegrast *versus* 2.8% in placebo), instillation site reaction (12.3% *versus* 2.3%), instillation site pain (9.8% *versus* 2.1%), and dysgeusia (14.5% *versus* 0.3%). Overall, TEAEs were mild to moderate in severity and led to discontinuation in 7.0% of patients treated with lifitegrast and 2.6% of those treated with placebo. No serious ocular TEAEs were reported. Serious nonocular TEAEs occurred in 1.6% of patients treated with lifitegrast and 1.4% of those treated with placebo but were not considered related to the drug. In all trials, the mean drop comfort score (a rating by the patient immediately after instillation of the solution) in the placebo group was lower (more comfortable) than in the lifitegrast group. However, among those treated with lifitegrast, the mean score at 3 min after instillation improved from 3.3 at day 0 to 2.0 at day 84 in the 12-week trials, and a similar trend was noted in the SONATA trial. The authors concluded that the lifitegrast 5% was safe and well tolerated for the treatment of DED.

Although the most common adverse events have been highlighted, there are few additional safety issues to consider. Less common adverse reactions (1–5%) include blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.[9] Adverse reactions reported during postmarketing surveillance include anaphylactic reactions, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, eye swelling, and rash. Because lifitegrast has the potential to suppress lymphocytes, two studies evaluated serum lymphocyte concentrations and found minimal changes.[18,27] In addition, none of the trials reported opportunistic infections.[21–26] Finally, no drug interactions have been described in the product labeling or are expected due to the drug's low systemic absorption.[9]

Dosage and administration

Lifitegrast was approved by the FDA for use in DED as a 5% (50 mg/ml) ophthalmic solution instilled as one drop into each eye every 12 h.[9] In phase I and II studies, concentrations ranging from 0.1% to 5.0% administered daily to thrice daily produced dose-dependent effects.[18,20,21] These results led to phase III studies, which assessed 5.0% administered twice daily and found significant improvements over placebo.[22–24,26]

Lifitegrast is supplied in a carton with 12 foil pouches, each containing 5, 0.2 ml, single-use

droppers with sufficient solution for both eyes.[9] Patients should not allow the dropper to contact the eye in order to avoid the possibility of injury or contamination. Contact lenses must be removed prior to administration and may be reinserted after 15 min. The drug is contraindicated in patients with a hypersensitivity to lifitegrast or any of its other ingredients. Lifitegrast has not been well studied in special populations. No data are available on use of the drug in pregnant or lactating women. In rats, intravenous use did not produce teratogenicity at clinically relevant exposures; however, omphalocele has been observed at the lowest dose tested in rabbits. Detection of the drug in breast milk has not been investigated in animal studies, although systemic exposure after ocular administration is low. The safety and efficacy of lifitegrast have not been evaluated in pediatric patients <17 years of age. No differences in safety and efficacy were observed when geriatric patients were compared with younger adults. Use of the drug in patients with renal or hepatic insufficiencies is not addressed in the product labeling.

Clinical considerations

In 2017, the Tear Film and Ocular Surface Society (TFOS), a nonprofit organization aimed at advancing education and research on topics regarding tear film and the ocular surface, released a newly updated Dry Eye Workshop II (TFOS DEWS II), which consisted of 11 individual reports on various aspects of the disorder.[1] The management and therapy report offered an algorithm comprising four steps.[5] The first two steps involve the most commonly used medications for DED and the final steps involve other approaches, such as oral secretagogues (e.g. pilocarpine, cevimeline), therapeutic contact lenses, and various surgical procedures. However, it is important to note that the steps are not intended to serve as a strict guideline.

In the first step, tear replacement products (i.e. artificial tears) are the only pharmacologic agents.[5] Artificial tears supplement the aqueous component of the tear film and provide temporary relief of burning and eye irritation, which makes them a mainstay in the management of DED. They are available without a prescription and in various formulations such as solutions, ointments, and gels. The typical dose is one to two drops per eye as needed. Tear supplements are composed of lubricants with different types of viscosity agents and vary on the presence or absence of preservatives. Products with high-viscosity agents extend the time of action on the ocular surface but can cause blurry vision and thus may be limited to use at bedtime. Preservative-free products minimize toxicities, which permit more frequent and prolonged use, but are typically higher in cost. In a Cochrane review involving 43 randomized controlled trials, artificial tear products were found to be effective and generally safe, but the overall quality of evidence was low and comparisons between different formulations were unable to be made.[28] Although various other treatments may be added, patients with DED will most likely need to use artificial tears indefinitely.

Pharmacological options in step 2 mainly target the anti-inflammatory component of DED.[5] In the TFOS DEWS II, topical glucocorticoids (e.g. dexamethasone, fluorometholone, lotepredol methylprednisolone, prednisolone) were noted to have positive effects in 11 studies rated as level 1 (well-designed randomized controlled trials) or level 2 (well-designed controlled trials without randomization or well-designed observational studies with a control group) evidence. However, their use is limited to short durations due to potential complications such as cataracts and increased ocular pressure. Topical cyclosporine is a calcineurin inhibitor that decreases ocular surface inflammation and is approved to increase tear production in patients with DED.[7] Six studies that established the benefit of cyclosporine were identified in the TFOS DEWS II; four studies were classified as level 1 evidence and two studies were classified as level 2 evidence.[5] The most common adverse reaction in clinical trials was ocular burning.[7] The dose of cyclosporine emulsion 0.05% is one drop in each eye approximately every 12 h. Currently, it is only available as a brand name product, and the average wholesale price is US$611.16 for 30 days of therapy.[29] Lifitegrast reduces ocular surface inflammation by antagonism of LFA-1 and is indicated for the treatment of signs and symptoms of DED.[9] The TFOS DEWS II rated the phase II and III trials for lifitegrast as level 1 evidence.[5,21–24,26] The most common adverse reactions were instillation site irritation, dysgeusia, and reduced visual acuity.[9] Similar to cyclosporine, lifitegrast is dosed twice daily and costs US$608.40 per month.[9,29] A potential advantage of lifitegrast is that it may work as soon as 2 weeks, which is earlier than may be achieved

with cyclosporine.[1,23,24] The last medications that act with some anti-inflammatory effects for the management of DED are topical and systemic antibiotics (e.g. azithromycin, doxycycline); however, they are typically considered for patients with comorbid conditions such as blepharitis and Meibomian gland dysfunction.[5]

In conclusion, lifitegrast is a safe and effective option for the management of DED. Currently, no active-controlled trials have compared lifitegrast to cyclosporine, and because of the different endpoints used in the placebo-controlled trials, a reliable comparison of efficacy is difficult to make. In addition, no trials have evaluated lifitegrast in combination with cyclosporine, which may be an area for future research that leads to an option for patients who do not respond to a single agent. On the basis of current data, lifitegrast or cyclosporine is a reasonable choice for patients who do not experience adequate relief of symptoms with artificial tears. The approval of lifitegrast provides clinicians with an important new drug with a unique mechanism of action for the management of DED.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Statement

This review did not require an ethical board approval because it did not contain human or animal trials.

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