MIEBO® (perfluorohexyloctane ophthalmic solution):

A Deep Dive Into **Clinical Data**

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Miebo® (perfluorohexyloctane ophthalmic solution)

INDICATION

MIEBO® (perfluorohexyloctane ophthalmic solution) is indicated for the treatment of the signs and symptoms of dry eye disease.

IMPORTANT SAFETY INFORMATION

- MIEBO should not be administered while wearing contact lenses. Contact lenses should be removed before use and for at least 30 minutes after administration of MIEBO
- Instruct patients to instill one drop of MIEBO into each eye four times daily

Please see additional Important Safety Information throughout and accompanying full Prescribing Information for MIEBO on pages 14 and 15.

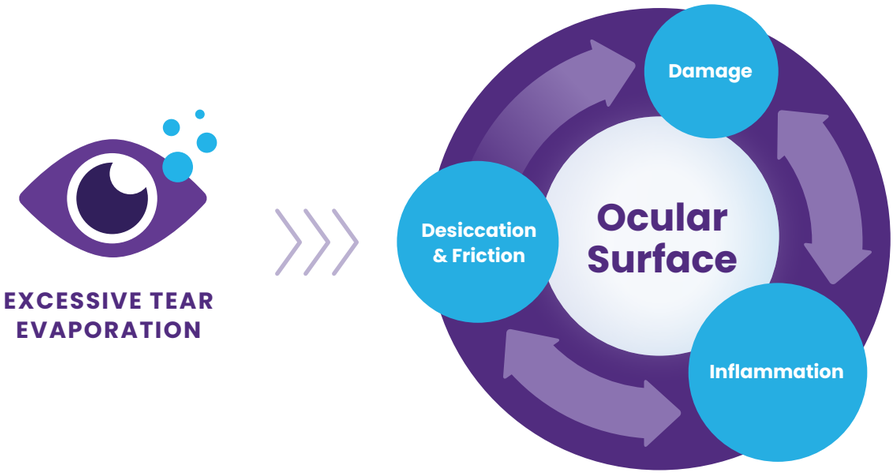
BAUSCH + LOMB

As a prevalent, multifaceted condition, dry eye disease (DED) can involve many diagnostic and management challenges. Despite the availability of varied treatment approaches, patient frustration and non-adherence continue.[1,2,3] Delayed efficacy and bothersome side effects are commonly reported with some current treatments and contribute to the high rates. But in recent years, the treatment landscape has changed.

The majority of DED is characterized by excess tear evaporation, leading to tear film instability and subsequent ocular discomfort.[4] DED is also one of the most common reasons patients seek professional eyecare services.[5] Patients with DED may experience a spectrum of symptoms, including ocular dryness, visual disturbance, excess tearing, and burning/stinging.[6]

While dry eye predominantly affects older individuals, the prevalence is rising across all adult age groups, which can be attributed to ubiquitous use of digital devices and screens.[7,8] DED can significantly impact a patient's quality of life and impose substantial economic burden, with annual productivity loss in the US estimated to exceed $11,000 per patient with DED.[9,10]

FIGURE 1. Excess tear evaporation leads to a vicious cycle of inflammation on the ocular surface resulting in signs and symptoms of dry eye disease (DED).[17,21,22]



DED Classification & Pathophysiology

DED is generally categorized based on the primary underlying mechanism of loss of tear film homeostasis. The two main classifications are aqueous deficient, characterized by insufficient tear production, and evaporative, defined by excessive tear evaporation.[11] While more than half of DED cases involve a combination of both processes,[12,13] recent studies have found that purely aqueous-deficient dry eye represents only about 10% of cases, whereas excessive evaporation contributes to DED in up to 94% of individuals.[4,14,15]

The pathogenesis of DED is complex and multifactorial, involving age-related changes (eg, those mediated by hormone shifts), topical and systemic medications, environmental stressors, lifestyle factors (eg, digital screen use and contact lens wear), nutritional deficiencies (such as a lack of omega-3 fatty acids in the diet), infectious agents, ocular surface trauma, and autoimmune diseases (eg, Sjögren syndrome).[7,16]

While more than half of DED cases involve a combination of both processes,[12,13] recent studies have found that purely aqueous-deficient dry eye represents only about 10% of cases, whereas excessive evaporation contributes to DED in up to 94% of individuals.[4,14,15]

Evaporative DED often stems from eyelid-related conditions, with meibomian gland dysfunction (MGD) being the leading cause.[17] MGD is defined by chronic meibomian gland abnormalities, which contribute to altered quantity and quality of secreted meibum. MGD compromises the tear film's lipid layer, leading to accelerated tear evaporation and ocular surface destabilization.[18]

Digital device use and contact lens wear are other significant contributors to evaporative DED. Prolonged use of digital screens can lead to reduced blink rates, which in turn causes tear film instability through reduced meibum output, thus exacerbating tear evaporation.[19] Patients may experience this not only as dryness and irritation, but often as fluctuating vision, which can be very bothersome. In a survey of 461 dry eye sufferers, about two-thirds reported cutting back on daily activities, most often screen time, to relieve symptoms.[20]

Regardless of the underlying etiology, the resulting diminished tear volume and quality initiate a self-perpetuating cycle of desiccation stress and increased friction on the ocular surface, leading to increased tear film osmolarity, chronic inflammation, and progressive ocular tissue damage (**Figure 1**).[17,21,22]

Diagnosing & Managing DED

The multifaceted nature of DED and its symptomatic overlap with other ocular surface disorders, such as blepharitis, conjunctivitis, and ocular allergy, demand a comprehensive diagnostic process.[7]

The American Academy of Ophthalmology (AAO) Dry Eye Syndrome Preferred Practice Pattern (Dry Eye PPP) and the seminal Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II report recommend an iterative approach, beginning with triaging questions to screen for DED and evaluate ocular history.[23,3] Medical eye evaluations with regular follow-ups are also recommended to exclude other causes of ocular irritation.[3]

MIEBO is the only FDA-approved prescription eye drop designed to directly target tear evaporation in DED.

Minimally invasive tests, such as tear osmolarity, matrix metalloproteinase-9 (MMP-9), digital meibomian gland expression, ocular surface staining, and tear breakup time, can help to confirm the diagnosis. Further classification of subtype and severity can be determined through meibography, lipid interferometry, and tear volume assessment.[23,3] This approach enables clinicians to distinguish between DED subtypes and conditions with similar symptoms, facilitating the development of tailored, effective treatment plans for each patient.

The management of DED poses a significant challenge due to its multifactorial etiology, which can directly impact treatment strategies.[22,24] In general, early intervention is recommended for optimal patient outcomes, despite the complexities of diagnosis and management.[24,25] Current treatment options for tear insufficiency include over-the-counter (OTC) tear replacement drops, immunomodulators, punctual occlusion procedures, and tear stimulation therapies.[26]

For lid abnormalities, including MGD, treatments encompass lid hygiene, ocular lubricants, warm compresses, in-office procedures for meibomian gland obstruction, high quality nutritional supplements bandage contact lenses, and management of corneal exposure. Underlying inflammatory causes can be addressed with immunomodulators such as cyclosporine and lifitegrast, and anti-inflammatory agents such as corticosteroids. Additional options to alleviate DED symptoms include amniotic membrane therapy, surgery, dietary modifications, and environmental changes.

Given that most DED cases involve evaporative mechanisms, a therapy designed to directly inhibit excess tear evaporation presents substantial therapeutic potential in the management of this disease.[4,14,15,17] In 2023, such an option became available with the introduction of MIEBO (perfluorohexyloctane ophthalmic solution).

MIEBO

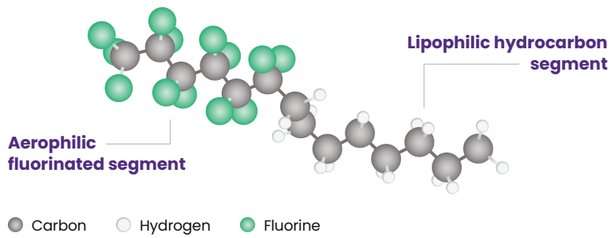
MIEBO is the only FDA-approved prescription eye drop designed to directly target tear evaporation in DED. This innovative, water-free formulation is indicated for treating both the signs and symptoms of DED, with a recommended dosage of one drop four times daily.

Perfluorohexyloctane, the sole ingredient in MIEBO, is a semifluorinated alkane with an amphiphilic structure consisting of both a lipophilic and aerophilic segment.[27] The lipophilic segment inserts into the lipid layer while the aerophilic segment orients toward the air, thus forming a monolayer at the tear film's air-liquid interface.* As expected, this unique structure allows MIEBO to reduce tear evaporation. Furthermore, in vitro gravimetric studies demonstrated that a single drop of MIEBO inhibits saline evaporation 4× more effectively than human meibum lipids from a healthy volunteer.[27†]

Although many of the therapeutic properties of perfluorohexyloctane are dependent on its unique chemical structure, its low surface tension also plays a large role.[28] This characteristic allows MIEBO to spread rapidly and evenly across the ocular surface. This spreading ability and the formation of a monolayer can help diminish the shear forces exerted by the eyelid during blinking, alleviating a common source of irritation in DED.[29,30] The low surface tension also facilitates the formation of smaller drops, which can prevent spillover following topical instillation.[29,30]

In addition to promising therapeutic effects, MIEBO demonstrated extended surface residence time on the ocular surface. In a rabbit pharmacokinetic study, MIEBO was detectable in tears for at least 6 hours and in meibomian glands for up to 24 hours after repeated dosing.[31] Upon application of MIEBO, these properties can collectively contribute to the formation of a long-lasting, protective barrier on the ocular surface and help reduce friction and evaporation while promoting tear film stability and epithelial healing.

FIGURE 2. Model of perfluorohexyloctane molecule[27]



*The exact mechanism of action of MIEBO is unknown
†The clinical significance of these in vitro data has not been established

Overview of the MIEBO Clinical Development Program

MIEBO's unique therapeutic approach is distinguished by a proven efficacy and safety profile as consistently demonstrated across three US phase 3 trials: GOBI (NCT04139798), MOJAVE (NCT04567329), and KALAHARI (NCT04140227). These rigorous studies provided robust data supporting MIEBO's potential as an intervention for DED management.

GOBI and MOJAVE were randomized, double-masked, 8-week, saline-controlled studies evaluating the safety and efficacy of MIEBO in patients with DED and clinical signs of MGD.

These are the only studies known to specifically target this patient population, which aligns with MIEBO's distinctive mechanism of action.[32,33] In these two studies, 1217 patients (GOBI: N=597; MOJAVE: N=620) were randomized 1:1 to receive MIEBO or hypotonic saline (0.6%) four times daily.

The primary efficacy endpoints in GOBI and MOJAVE were changes from baseline in total corneal fluorescein staining (tCFS) and visual analog scale (VAS) eye dryness score at day 57. Key secondary endpoints included central corneal fluorescein staining (cCFS) at day 57, and total fluorescein staining (tCFS) and eye dryness at day 15. Notably, hypotonic saline, a common component of artificial tears, served as an "active" control because MIEBO is a one-ingredient formulation with no vehicle.[32]

The KALAHARI trial, an open-label extension of GOBI, was designed to examine the long-term efficacy and safety of MIEBO over 52 weeks.[34] The study included 208 patients from GOBI, with 97 patients continuing MIEBO treatment and 111 transitioning from saline to MIEBO. Key safety assessments were ocular and non-ocular adverse events. Efficacy endpoints included changes from the GOBI study baseline in tCFS and VAS eye dryness score. Results from the KALAHARI study attest to the efficacy of MIEBO through as long as 60 weeks of usage.

Across all three trials, patient baseline demographics and clinical characteristics were comparable between treatment groups (**Table 1**), and 100% of participants had clinical signs of MGD with a score ≥3. The consistency in patient profiles facilitated the pooling of GOBI and MOJAVE trial results, allowing for a robust and comprehensive analysis of MIEBO's efficacy.

TABLE 1. Baseline clinical characteristics in GOBI, MOJAVE, and KALAHARI[32-34]

	GOBI		MOJAVE		KALAHARI		
	MIEBO (n=303)	**Saline** (n=294)	**MIEBO** (n=311)	**Saline** (n=309)	**All KALAHARI Patients** (N=208)	**MIEBO** (n=97)	**Saline to MIEBO** (n=111)
Baseline clinical characteristics, mean (SD)							
tCFS	6.7 (1.8)	6.7 (1.9)	7.0 (2.0)	7.1 (2.1)	6.6 (1.7)	6.5 (1.7)	6.6 (1.8)
Total OSDI score	53.9 (17.6)	54.4 (17.0)	55.2 (17.4)	55.8 (17.2)	55.0 (17.8)	54.2 (17.8)	55.7 (18.0)
Schirmer I test, mm	12.0 (8.3)	11.7 (7.6)	12.7 (7.5)	12.8 (7.9)	12.0 (8.1)	11.7 (8.2)	12.2 (8.0)
MGD score	7.4 (3.1)	7.7 (3.2)	7.9 (3.5)	8.1 (3.5)	7.1 (3.1)	6.9 (3.2)	7.3 (3.0)
TFBUT, sec	3.2 (0.8)	3.3 (0.8)	3.2 (0.9)	3.1 (0.9)	3.2 (0.8)	3.1 (0.7)	3.3 (0.9)
VAS dryness score	66.5 (19.1)	66.8 (18.7)	64.7 (19.5)	64.3 (19.8)	67.7 (19.8)	66.9 (20.6)	68.4 (19.1)

MGD score ranges from 0 to 15 (0 to 3 in each of 5 areas). VAS ranges from 0 to 100; 0=no discomfort and 100=maximal discomfort.

MGD, meibomian gland dysfunction; **OSDI**, Ocular Surface Disease Index; **SD**, standard deviation; **tCFS**, total corneal fluorescein staining; **TFBUT**, tear film breakup time; **VAS**, visual analog scale

Efficacy in the MIEBO Clinical Studies

MIEBO demonstrated robust and consistent efficacy in improving both signs and symptoms of DED in the pivotal trials. GOBI and MOJAVE met their primary efficacy endpoints, with MIEBO significantly improving tCFS and VAS dryness score vs saline control at day 57 ($P<0.001$ for each endpoint in each study).[32,33] A pooled analysis of the GOBI and MOJAVE data at day 57 revealed that MIEBO-treated patients achieved a 2-fold improvement in

IMPORTANT SAFETY INFORMATION (CONT'D)

- The safety and efficacy in pediatric patients below the age of 18 have not been established

MIEBO Clinical Trial Data: The Highlights

MIEBO exhibited robust and reproducible results across two phase 3 studies (GOBI and MOJAVE) and one long-term follow-up study (KALAHARI)

The studies included over 1200 patients with DED and clinical signs of MGD

MIEBO QID improved DED signs (tCFS) and symptoms (VAS eye dryness score)

- Significant improvement vs saline control was achieved as early as day 15 and lasted through day 57 in GOBI and MOJAVE
- MIEBO demonstrated consistent efficacy and safety in a 1-year extension study
- MIEBO also significantly improved cCFS at day 57

MIEBO was well tolerated, with low AE rates and no serious ocular AEs

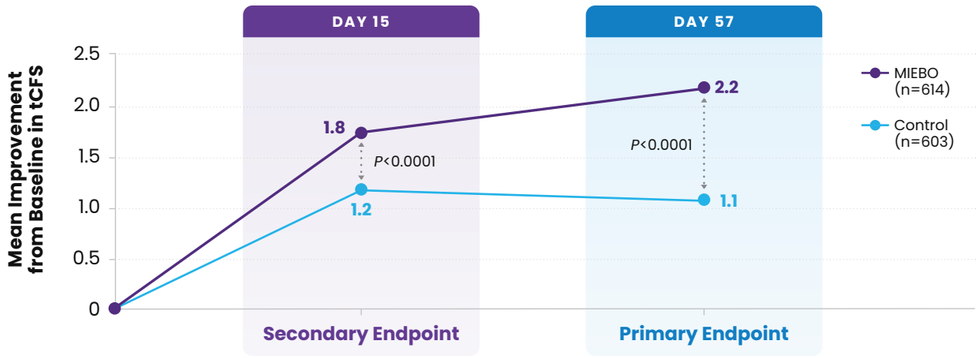
In GOBI and MOJAVE, patients reported that MIEBO is "comfortable" or "very comfortable" with a mean pooled comfort score of 8.0 for MIEBO and 8.4 for saline.* Patients in the KALAHARI study also reported MIEBO drops as "comfortable" with a mean score of 8.4.

*Questionnaire was given on Day 1 of the GOBI and MOJAVE studies. Comfort score ranges from 0 to 10 (0 = not comfortable and 10 = very comfortable). 81% of patients treated with MIEBO reported a score of 7 or higher.

AE, adverse event; **cCFS**, central corneal fluorescein staining; **DED**, dry eye disease; **MGD**, meibomian gland dysfunction; **QID**, four times a day; **tCFS**, total corneal fluorescein staining; **VAS**, visual analog scale

FIGURE 3. Figure 3. Pooled data from the GOBI and MOJAVE trials of MIEBO vs control showing superior outcomes compared to saline control at day 57 in (**A**) total corneal fluorescein staining (tCFS) and (**B**) visual analog scale (VAS) eye dryness score[32,33,35]

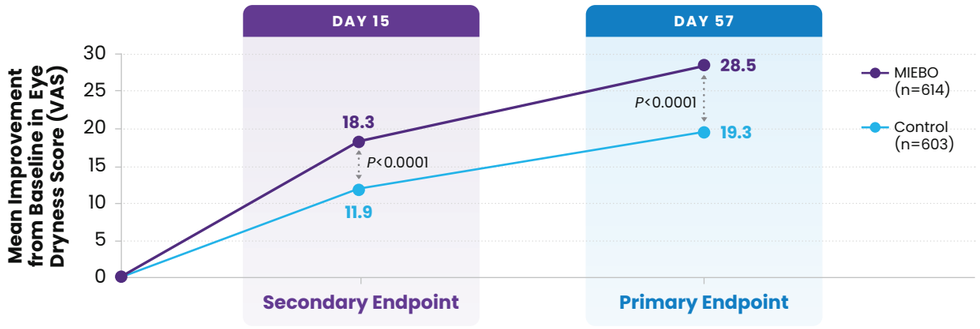
A **Total Corneal Fluorescein Staining** (tCFS)



Mean baseline tCFS=6.9 for MIEBO and saline (control). tCFS grading scale ranges from 0 to 15 (0 to 3 in each of 5 areas).
GOBI: Mean (SD) CFB is −2.0 (2.6) for MIEBO (n=289) vs −1.0 (2.7) for control (n=279; P<0.001) at day 57
MOJAVE: Mean (SD) CFB is -2.3 (2.8) for MIEBO (n=302) vs -1.1 (2.9) for control (n=296; P<0.001) at day 57

MGD, meibomian gland dysfunction; **OSDI**, Ocular Surface Disease Index; **SD**, standard deviation; **tCFS**, total corneal fluorescein staining; **TFBUT**, tear film breakup time; **VAS**, visual analog scale

B **Eye dryness VAS**



Mean baseline eye dryness score=65.6 for MIEBO and 65.5 for saline (control). VAS ranges from 0 to 100; 0=no discomfort and 100=maximal discomfort.
GOBI: Mean (SD) CFB is -27.4 (27.9) for MIEBO (n=289) vs -19.7 (26.7) for control (n=279; P<0.001) at day 57
MOJAVE: Mean (SD) CFB is -29.5 (28.6) for MIEBO (n=302) vs -19.0 (27.2) for control (n=296; P<0.001) at day 57

CFB, change from baseline; **SD**, standard deviation; **tCFS**, total corneal fluorescein staining; **VAS**, visual analog scale

tCFS and a 1.5-fold improvement in VAS eye dryness score from baseline compared to saline control (**Figure 3**).[35]

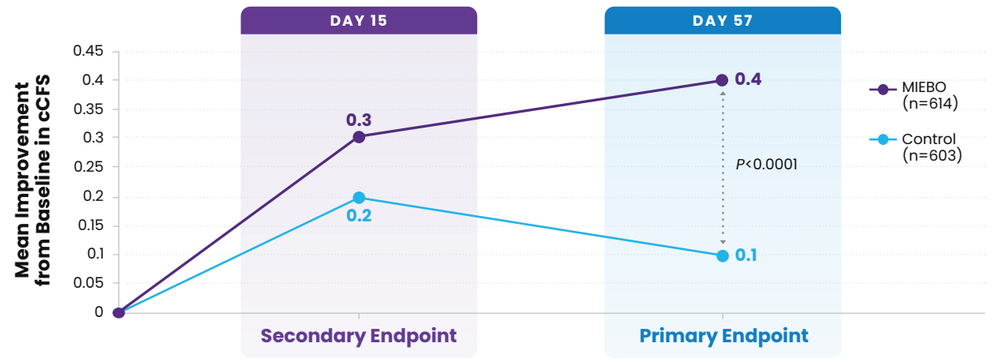
Both GOBI and MOJAVE also met key secondary endpoints, showing significant improvement vs saline control in tCFS and VAS eye dryness scores at day 15 ($P<0.01$) and cCFS at day 57 ($P<0.001$). A pooled analysis shows that patients in the MIEBO group had a 4 fold improvement in cCFS from baseline compared to saline control at day 57 (**Figure 4**).

In the KALAHARI open-label extension trial, tCFS and VAS eye dryness scores continued to show significant reductions from baseline through week 52 (**Figure 5**).[34] Notably, patients in the crossover group—those who switched from saline treatment in GOBI to MIEBO in KALAHARI—demonstrated marked improvements in both tCFS and VAS eye dryness scores within four weeks of initiating MIEBO treatment, with these benefits persisting through week 52.

Safety in the MIEBO Clinical Studies

MIEBO exhibited a favorable safety profile across the pivotal trials and open-label extension study. Most adverse events (AEs) were considered mild or moderate in severity, with blurred vision as the most common ocular AE in the MIEBO group in GOBI (3.0%) and blepharitis (1.6%) in MOJAVE (**Table 2**).[32,33] Ocular AEs occurred in both treatment groups at similar frequencies (in GOBI, 9.6% in the MIEBO group vs 7.5% in the saline group; in MOJAVE, 12.9% in the MIEBO

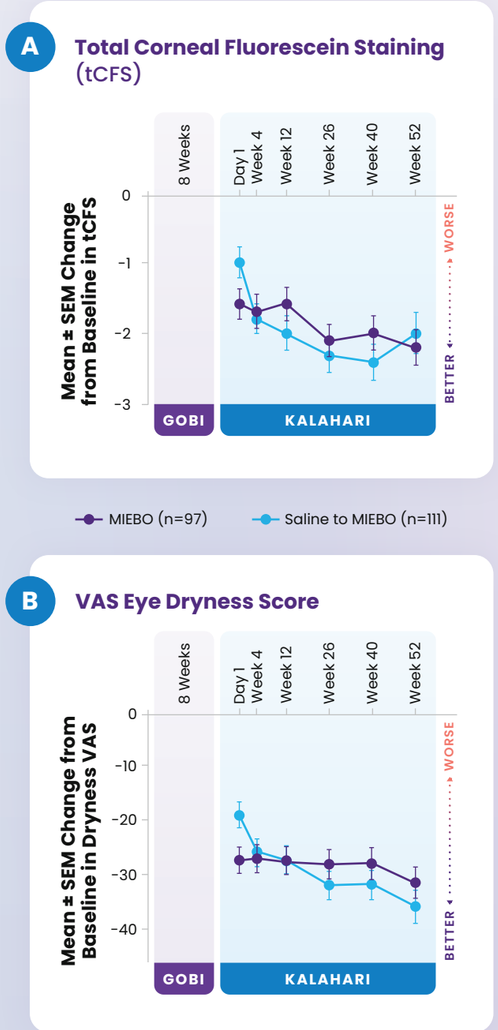
FIGURE 4. Pooled data from the GOBI and MOJAVE trials of MIEBO showing significantly improved cCFS compared to saline control at day 57[32,33]



GOBI: Mean (SD) CFB is -0.4 (0.8) for MIEBO (n=289) vs -0.1 (0.9) for control (n=279; P<0.001) at day 57
MOJAVE: Mean (SD) CFB is -0.4 (0.8) for MIEBO (n=302) vs -0.1 (0.9) for control (n=296; P<0.001) at day 57

cCFS, central corneal fluorescein staining; **CFB**, change from baseline; **SD**, standard deviation

FIGURE 5. In KALAHARI, MIEBO demonstrated sustained improvements from baseline through week 52 in both (**A**) tCFS and (**B**) VAS eye dryness scores[34]



(**A**) Mean (SD) CFB in tCFS is −2.1 (2.5) among the total population (n=208) at week 52. (**B**) Mean (SD) CFB in VAS eye dryness score is -33.7 (28.6) among the total population (n=208) at week 52.

CFB, change from baseline; **SD,** standard deviation; **tCFS**, total corneal fluorescein staining; **VAS**, visual analog scale

group vs 12.3% in the saline group). Instillation site reactions or irritation affected <1% of patients in these studies.

In both trials, blurred vision was reported at a slightly higher percentage of patients in the MIEBO group (GOBI: 3.0%; MOJAVE: 1.3%) compared to the saline group (GOBI and MOJAVE: 0.3%). One patient in each group experienced severe eye irritation (MIEBO in GOBI and saline in MOJAVE). No serious ocular AEs were reported, and discontinuation rates due to AEs were low and comparable to saline control. Only 1 out of 614 patients treated with MIEBO discontinued due to an AE. Neither study found clinically meaningful changes in best-corrected visual acuity (BCVA), slit-lamp examination findings, intraocular pressure (IOP), or dilated fundoscopy examination results.

The KALAHARI extension trial corroborated these safety findings. Patients continuing in the extension trial showed low rates of AEs with MIEBO (13.9% experiencing ≥1 ocular AEs), most of which were mild in nature.[34] The most frequent ocular AEs (>2 patients) were non-treatment related vitreous detachment (1.9%), allergic conjunctivitis (1.4%), blurred vision (1.4%), and increased lacrimation (1.4%; **Table 2**). No serious ocular AEs were reported. One severe case of bilateral eyelid irritation that did not lead to study discontinuation occurred, which the investigator considered possibly related to the study medication. Five patients (2.4%) experienced ocular AEs that led to discontinuation (one patient each with blurred vision, chalazion, dry eye, increased lacrimation, and increased IOP). Other safety endpoints (BCVA, biomicroscopy, IOP, fundoscopy) showed no meaningful changes.

TABLE 2. The most common ocular adverse events (AEs) in GOBI, MOJAVE, and KALAHARI[32-34]

	GOBI		MOJAVE		KALAHARI		
	MIEBO (n=303) n (%)	**Saline** (n=294) n (%)	**MIEBO** (n=311) n (%)	**Saline** (n=309) n (%)	**All KALAHARI Patients** (N=208) n (%)	**MIEBO** (n=97) n (%)	**Saline to MIEBO** (n=111) n (%)
Ocular AEs							
No. of patients with at least 1 ocular AE	29 (9.6)	22 (7.5)	40 (12.9)	38 (12.3)	29 (13.9)	16 (16.5)	13 (11.7)
Ocular AEs that occured in >2% of patients in any group							
Allergic conjunctivitis	–	–	–	–	3 (1.4)	2 (2.1)	1 (0.9)
Blepharitis	–	–	5 (1.6)	1 (0.3)	–	–	–
Blurred vision	9 (3.0)	1 (0.3)	4 (1.3)	1 (0.3)	3 (1.4)	0 (0.0)	3 (2.7)
Chalazion	–	–	–	–	2 (1.0)	1 (1.0)	1 (0.9)
Conjunctival hemmorrhage	1 (0.3)	4 (1.4)	–	–	–	–	–
Conjunctival hyperemia	–	–	4 (1.3)	6 (1.9)	–	–	–
Conjunctival papillae	–	–	4 (1.3)	5 (1.6)	–	–	–
Dry eye	–	–	–	–	2 (1.0)	2 (2.1)	0 (0.0)
Eye discharge	3 (1.0)	0 (0.0)	1 (0.3)	4 (1.3)	–	–	–
Eye pain	–	–	1 (0.3)	4 (1.3)	–	–	–
Eye pruritus	–	–	2 (0.6)	3 (1.0)	–	–	–
Hordeolum	–	–	3 (1.0)	2 (0.6)	2 (1.0)	1 (1.0)	1 (0.9)
Increased lacrimation	–	–	–	–	3 (1.4)	3 (3.1)	0 (0.0)
Instillation site pain	3 (1.0)	3 (1.0)	–	–	2 (1.0)	1 (1.0)	1 (0.9)
Ocular hyperemia	–	–	4 (1.3)	1 (0.3)	–	–	–
Punctate keratitis	0 (0.0)	3 (1.0)	–	–	–	–	–
Visual acuity reduction	–	–	3 (1.0)	3 (1.0)	–	–	–
Vitreous detachment	–	–	–	–	4 (1.9)	2 (2.1)	2 (1.8)

Conclusions

MIEBO is a preservative-, water-, pH-, osmolarity-, and steroid-free formulation of perfluorohexyloctane approved to treat the signs and symptoms of DED. It is a prescription eye drop that contains only a single ingredient. Perfluorohexyloctane has a unique molecular structure that effectively inhibits tear film evaporation, likely by acting as a functional substitute for the tear film lipid layer. Given that lipid layer deficiency and associated evaporative dry eye are key contributors in the majority of DED cases, MIEBO offers a targeted approach to this common condition.[4,16]

Across three phase 3 trials, MIEBO produced meaningful, consistent reductions in both signs and symptoms of DED as early as day 15, with sustained efficacy through 52 weeks. MIEBO also demonstrated a favorable safety profile and was well tolerated across the three studies. As the first and only FDA-approved drop to directly address tear evaporation, MIEBO addresses a critical unmet need in DED.

These results translate and are extremely important to our clinical practice.

Namely, symptom relief as early as two weeks, combined with the excellent tolerability, is motivating for patients with DED. It's difficult to tell someone whose eyes are already irritated that a treatment may make them feel worse, even temporarily. In MIEBO, patients have a comfortable drop* that can help ease their symptoms in as little as two weeks.

In our clinical experience, we've found that many patients who have struggled with other treatments can find relief with MIEBO, which is gratifying to see. Our observations parallel the results of clinical studies: patients report symptomatic improvement and we see evidence at the slit lamp of ocular surface healing and repair. Across a variety of presentations and stages in the DED journey, MIEBO offers targeted relief that patients can appreciate.

*Questionnaire was given on Day 1 of the GOBI and MOJAVE studies. Comfort score ranges from 0 to 10 (0 = not comfortable and 10 = very comfortable). 81% of patients treated with MIEBO reported a score of 7 or higher.

Author Bios

Alice Epitropoulos, MD, is a partner at Ophthalmic Surgeons and Consultants of Ohio in Columbus, OH. She is a paid consultant of Bausch + Lomb.

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IMPORTANT SAFETY INFORMATION (CONT'D)

- The most common ocular adverse reaction was blurred vision (1% to 3% of patients reported blurred vision and conjunctival redness)
- You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
- Please see accompanying full Prescribing Information for MIEBO on pages 14 and 15.

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Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MIEBO safely and effectively. See full prescribing information for MIEBO.

MIEBO™ (perfluorohexyloctane ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2023

---------- INDICATIONS AND USAGE ----------
MIEBO (perfluorohexyloctane ophthalmic solution) is a semifluorinated alkane indicated for treatment of the signs and symptoms of dry eye disease. (1)

---------- DOSAGE AND ADMINISTRATION ----------
Instill one drop of MIEBO four times daily into each eye. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------
Ophthalmic solution: 100% perfluorohexyloctane. (3)

---------- CONTRAINDICATIONS ----------
None. (4)

---------- ADVERSE REACTIONS ----------
Most common ocular adverse reaction was blurred vision. Blurred vision was reported in less than 4% of individuals. (6.1)

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

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 5/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
MIEBO™ (perfluorohexyloctane ophthalmic solution) is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dosage
Instill one drop of MIEBO four times daily into affected eye(s).

Contact lenses should be removed prior to and for at least 30 minutes after the administration of MIEBO.

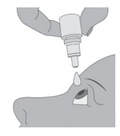
2.2 Administration Instructions
Step 1. Remove the cap from eye drop bottle.

Step 2. Holding the bottle upright, gently squeeze the bottle.

Step 3. While squeezing, turn the bottle upside down and release the pressure (drawing air into the bottle).

Step 4. Keeping the bottle upside down, place the bottle above your eye and squeeze it again to release a drop into your eye.

Repeat steps 1 - 4 for the second affected eye.



3 DOSAGE FORMS AND STRENGTHS
MIEBO (perfluorohexyloctane ophthalmic solution) is a sterile, clear and colorless ophthalmic solution containing 100% perfluorohexyloctane.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS
5.1 Use with Contact Lenses
MIEBO should not be administered while wearing contact lenses. Advise patients that contact lenses should be removed prior to and for at least 30 minutes after administration of MIEBO.

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

In patients with DED, 614 patients received at least one dose of MIEBO in two randomized controlled clinical trials across 68 sites in the United States. The most common ocular adverse reaction was blurred vision. Blurred vision and conjunctival redness were reported in 1-3% of individuals.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary

There are no adequate and well controlled studies with MIEBO in pregnant women.

In animal reproduction studies with oral administration of perfluorohexyloctane during the period of organogenesis, no adverse maternal or developmental effects were observed in rats at doses up to 162 times the recommended human ophthalmic dose (RHOD) (*see Data*). Maternal toxicity, miscarriages and reduced fetal weights were observed in rabbits at all doses tested, with the lowest dose as 41 times the RHOD.

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

Data

Animal Data

An embryofetal study was conducted in pregnant rabbits administered perfluorohexyloctane by oral gavage on gestation days 6 to 19, to target the period of organogenesis. Perfluorohexyloctane produced maternal toxicity, characterized by reduced body weight gain and food consumption, and miscarriages at all doses tested, with the lowest dose as ≥ 250 mg/kg/day (41 times the RHOD based on body surface area). Reduced fetal weights were also observed at ≥ 250 mg/kg/day but no fetal mortality or malformations. A no observed adverse effect level (NOAEL) for maternal toxicity was not established in rabbits.

An embryofetal study was conducted in pregnant rats administered perfluorohexyloctane by oral gavage on gestation days 6 to 17, to target the period of organogenesis. There was no evidence of embryofetal toxicity or teratogenicity at doses up to 2,000 mg/kg/day (162 times the RHOD).

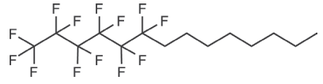
8.2 Lactation
There are no data on the presence of perfluorohexyloctane in human milk, the effects on the breastfed infant, or the effects on milk production. The lack of clinical data during lactation precludes a clear determination of the risk of MIEBO to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MIEBO.

8.4 Pediatric Use
The safety and effectiveness of MIEBO in pediatric patients below the age of 18 years have not been established.

8.5 Geriatric Use
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION
MIEBO™ (perfluorohexyloctane ophthalmic solution) is a sterile, clear and colorless liquid containing 100% perfluorohexyloctane, for topical ophthalmic use.

The active ingredient is 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorotetradecane and is a semifluorinated alkane. It has a molecular formula of $C_{14}H_{17}F_{13}$ and a molecular weight of 432.26 g/mol. The chemical structure is:



Perfluorohexyloctane is practically immiscible with water. It is miscible with ethanol and most organic solvents. Each multiple-dose bottle contains 3 mL of perfluorohexyloctane, 1.338 g/mL as a clear and colorless liquid.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Perfluorohexyloctane, a semifluorinated alkane, contains 6 perfluorinated carbon atoms and 8 hydrogenated carbon atoms. Perfluorohexyloctane forms a monolayer at the air-liquid interface of the tear film which can be expected to reduce evaporation. The exact mechanism of action for MIEBO in DED is not known.

12.3 Pharmacokinetics
The pharmacokinetics of perfluorohexyloctane following topical ocular administration of MIEBO has not been quantitatively characterized in humans. A single pharmacokinetic (PK) study was conducted that showed low systemic perfluorohexyloctane blood levels after topical ocular administration. Perfluorohexyloctane was not metabolized by human liver microsomes in vitro.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been conducted to evaluate the carcinogenic potential of perfluorohexyloctane.

Perfluorohexyloctane was not mutagenic or clastogenic in a standard battery of genotoxicity tests, including a bacterial mutagenicity assay (Ames assay), an in vitro chromosome aberration assay using human peripheral lymphocytes, and an in vivo bone marrow micronucleus assay in rats.

14 CLINICAL STUDIES
In two randomized, multicenter, double-masked, saline-controlled trials (GOBI and MOJAVE), a total of 1,217 patients with a history of DED and clinical signs of meibomian gland dysfunction were randomized to MIEBO or saline 0.6% (1:1 ratio) to evaluate safety and efficacy after receiving MIEBO four times daily (QID) for 57 days.The mean age of the 614 patients who received MIEBO was 57 years (range, 19-87 years). The majority of patients were female (76%).

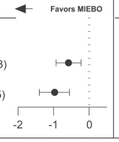
Effects on Signs of Dry Eye Disease

Total corneal fluorescein staining (tCFS) was recorded at each study visit using a standardized grading system of 0-3 for each of the five areas on the cornea (inferior, superior, central, nasal, and temporal), totaling a maximum tCFS score for each eye of 15. The average baseline tCFS was approximately 6.7 in GOBI and 7.0 in MOJAVE. At Days 15 and 57, a statistically significant reduction in tCFS favoring MIEBO was observed in both studies (Figure 1).

Figure 1: Mean Change (Standard Deviation) from Baseline and Treatment Difference (MIEBO-Saline) in Total Corneal Fluorescein Staining (Study Eye) in 8-Week Study in Patients with Dry Eye Disease

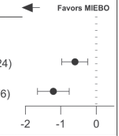
GOBI†

Visit	MIEBO (n=303)	Saline (n=294)	Difference (95% CI)
Baseline	6.7 (1.8)	6.7 (1.9)	
Day 15	-1.7 (2.1)	-1.1 (2.2)	-0.58 (-0.93, -0.23)
Day 57	-2.0 (2.6)	-1.0 (2.7)	-0.97 (-1.40, -0.55)



MOJAVE†

Visit	MIEBO (n=311)	Saline (n=309)	Difference (95% CI)
Baseline	7.0 (2.0)	7.1 (1.9)	
Day 15	-1.9 (2.3)	-1.3 (2.4)	-0.60 (-0.97, -0.24)
Day 57	-2.3 (2.8)	-1.1 (2.9)	-1.21 (-1.66, -0.76)



† A Phase 3, Multi-Center, Randomized, Double-Masked, Saline-Controlled Trial to Evaluate the Effect of NOV03 (Perfluorohexyloctane) on Signs and Symptoms of Dry Eye Disease Associated with Meibomian Gland Dysfunction

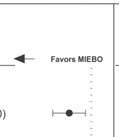
Effects on Symptoms of Dry Eye Disease

Eye dryness score was rated by patients using a visual analogue scale (VAS) (0=no discomfort, 100=maximal discomfort) at each study visit. The baseline VAS eye dryness average score was approximately 67 in GOBI and 65 in MOJAVE. At Days 15 and 57, a statistically significant reduction in VAS eye dryness score favoring MIEBO was observed in both studies (Figure 2).

Figure 2: Mean Change (Standard Deviation) from Baseline and Treatment Difference (MIEBO-Saline) in Eye Dryness Score (Study Eye) in 8-Week Study in Patients with Dry Eye Disease

GOBI†

Visit	MIEBO (n=303)	Saline (n=294)	Difference (95% CI)
Baseline	66.5 (19.1)	66.8 (18.7)	
Day 15	-18.0 (24.0)	-13.4 (23.3)	-4.72 (-8.25, -1.20)
Day 57	-27.4 (27.9)	-19.7 (26.7)	-7.61 (-11.82,-3.40)



MOJAVE†

Visit	MIEBO (n=311)	Saline (n=309)	Difference (95% CI)
Baseline	64.7 (19.5)	64.3 (19.8)	
Day 15	-18.5 (23.6)	-10.5 (23.9)	-7.79 (-11.28, -4.29)
Day 57	-29.5 (28.6)	-19.0 (27.2)	-10.24 (-14.35,-6.08)

† A Phase 3, Multi-Center, Randomized, Double-Masked, Saline-Controlled Trial to Evaluate the Effect of NOV03 (Perfluorohexyloctane) on Signs and Symptoms of Dry Eye Disease Associated with Meibomian Gland Dysfunction

16 HOW SUPPLIED/STORAGE AND HANDLING
MIEBO™ (perfluorohexyloctane ophthalmic solution) is supplied as a sterile, clear and colorless liquid in multiple-dose 5 mL polypropylene bottles with dropper tips and screw caps, packaged in a carton - NDC 24208-377-05.

Storage
Store MIEBO at 15ºC to 25ºC (59ºF to 77ºF). After opening, MIEBO can be used until the expiration date on the bottle.

17 PATIENT COUNSELING INFORMATION
Use with Contact Lenses

Advise patients that contact lenses should be removed prior to and for at least 30 minutes after administration of MIEBO.

Administration Instructions

Advise patients to instill one drop of MIEBO four times daily into each eye as depicted in the Administration Instructions *[see Dosage and Administration (2.2)]*.

Distributed by:
Bausch & Lomb Americas Inc.
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REF-MBO-0025

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