Miebo™ (perfluorohexyloctane ophthalmic solution)

The first and only Rx eye drop for DED that directly targets evaporation[1]

PRODUCT INFORMATION

PRODUCT TRADE: MIEBO

DELIVERY: Topical ophthalmic solution

ACTIVE INGREDIENT:
Perfluorohexyloctane 100%

INACTIVE INGREDIENTS: None

PRESERVATIVE: None

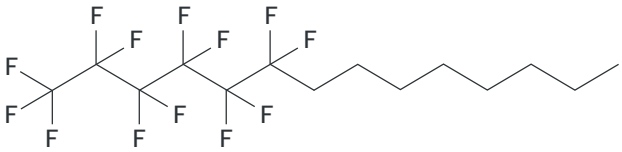
HOW SUPPLIED: Polypropylene bottles with dropper tips and screw caps in the following size: 3-mL fill in a 5-mL bottle

INDICATION AND USAGE: MIEBO is a semifluorinated alkane indicated for the treatment of the signs and symptoms of dry eye disease (DED)

FILL SIZE: 3-mL in 5-mL bottle

NO A/B GENERIC EQUIVALENT AVAILABLE

MIEBO DOSING: Instill one drop of MIEBO four times daily into affected eye(s).



PACKAGING SPECIFICATIONS

SELLING UNIT			
Unit	**NDC**	**Dimensions**	**Weight**
1	24208-0377-05	3.5 in x 1.375 in x 1.375 in	0.04 lb

SHIPPING CASE		
Pack	**Dimensions**	**Weight**
48	8.875 in x 6 in x 7.75 in	2.3 lb

BAR CODING:
3-mL fill in a 5-mL container bar-coded with NDC# 24208-0377-05

STORAGE CONDITIONS:
Store MIEBO at 15 °C to 25 °C (59 °F to 77 °F). After opening, MIEBO can be used until the expiration date on the bottle

EXPIRATION: 24 months

INNER PACK: 1

INDICATION

MIEBO™ (perfluorohexyloctane ophthalmic solution) is a semifluorinated alkane 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

Please see additional Important Safety Information on the back and full Prescribing Information in the pocket.

WHOLESALER ORDER NUMBERS

Fill	NDC	Package size	Cardinal	McKesson	Amerisource Bergen
3-mL fill in a 5-mL container	24208-0377-05	3.5 in x 1.375 in x 1.375 in	5858964	2841351	10281423

BAUSCH + LOMB CUSTOMER SERVICE DEPARTMENT

Phone orders: 1-800-321-4576, Option 1

Fax orders: 1-908-927-1926

Email orders: Ophthapharma@bausch.com

For more information about MIEBO, including our patient savings programs, please visit www.miebo-ecp.com.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- Instruct patients to instill one drop of MIEBO into each eye four times daily
- The safety and efficacy in pediatric patients below the age of 18 have not been established
- 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 additional Important Safety Information on the front and full Prescribing Information in the pocket.

Reference: 1. MIEBO. Prescribing Information. Bausch & Lomb, Inc; 2023.

BAUSCH + LOMB

Miebo™ (perfluorohexyloctane ophthalmic solution)

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

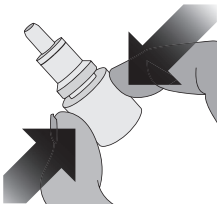
Instill one drop of MIEBO four times daily into affected eye(s).

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

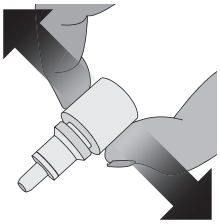
2.2 Administration Instructions

Step 1. Remove the cap from eye drop bottle.

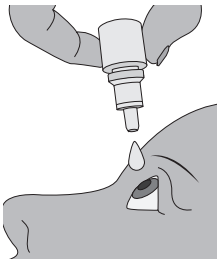
Step 2. Holding the bottle upright, gently squeeze the bottle.



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.

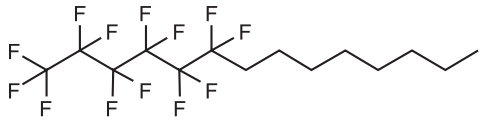
8.5 Geriatric Use

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).

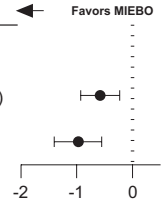
Figure 1: Mean Change (Standard Deviation) from Baseline and Treatment Difference (MIEBO-Saline) in Total Corneal Fluorescein Staining (Study Eye) in 8-Week Study in Patients with Dry Eye Disease

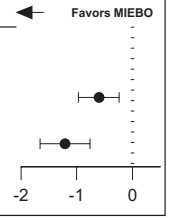
GOBI†

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

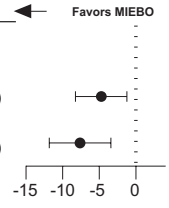
Figure 2: Mean Change (Standard Deviation) from Baseline and Treatment Difference (MIEBO-Saline) in Eye Dryness Score (Study Eye) in 8-Week Study in Patients with Dry Eye Disease

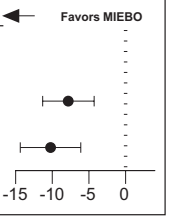
GOBI†

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

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).

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.
Bridgewater, NJ 08807 USA

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