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

VEVYE (cyclosporine ophthalmic solution) 0.1%,
for topical ophthalmic use
Initial U.S. Approval: 1983

----------RECENT MAJOR CHANGES----------
Dosage and Administration (2.2) 9/2025

----------INDICATIONS AND USAGE----------
VEVYE (cyclosporine ophthalmic solution) 0.1% is a calcineurin inhibitor immunosuppressant indicated for the treatment of the signs and symptoms of dry eye disease. (1)

----------DOSAGE AND ADMINISTRATION----------
Instill one drop of VEVYE twice a day in each eye approximately 12 hours apart. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Ophthalmic solution containing cyclosporine 0.1%. (3)

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

----------WARNINGS AND PRECAUTIONS----------
Care should be taken to not touch the eye or other surfaces with the bottle tip to avoid potential for eye injury and/or contamination. (5.1)

----------ADVERSE REACTIONS----------
The most common adverse reaction following the use of VEVYE were instillation site reactions (8%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Harrow at 1-833-4HARROW(427769) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Revised: 9/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
VEVYE indicated for the treatment of the signs and symptoms of dry eye disease.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage
Instill one drop of VEVYE twice a day in each eye approximately 12 hours apart.

2.2 Administration Instructions
Wash hands before using.

Gently pull the lower eyelid downward. Tip the bottle upside down over the eye to allow one drop to dispense on its own into the eye. If a drop does not dispense after a few seconds, gently apply slight pressure to the sides of the bottle while holding over the eye.

Note: You may not feel the drop falling into your eye.

If VEVYE is used with other eye drops, a 15-minute interval between products should occur.

3 DOSAGE FORMS AND STRENGTHS
Clear, colorless non-preserved ophthalmic solution containing cyclosporine 0.1% (1 mg/mL), delivering 0.01 mg of cyclosporine per one drop (0.01 mL).

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Eye Injury and Contamination
To avoid the potential for eye injury and/or contamination, patients should not touch the bottle tip to the eye or other surfaces.

5.2 Use with Contact Lenses
VEVYE should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of VEVYE ophthalmic solution.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the 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 clinical trials with 738

subjects receiving at least 1 dose of VEVYE, the most common adverse reactions were instillation site reactions (8%) and temporary decreases in visual acuity (3%).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of VEVYE administration in pregnant women to inform a drug-associated risk. Oral administration of cyclosporine to pregnant rats or rabbits did not produce teratogenicity at clinically relevant doses VEVYE doses are approximately 4,700 times lower than recommended oral doses, with blood concentrations being undetectable after topical administration.

Data

Animal Data

Oral administration of cyclosporine oral solution to pregnant rats or rabbits was teratogenic at maternally toxic doses of 30 mg/kg/day in rats and 100 mg/kg/day in rabbits, as indicated by increased pre- and postnatal mortality, reduced fetal weight and skeletal retardations. These doses (normalized to body weight) were approximately 7,250 and 48,000 times higher than the daily maximum recommended human ophthalmic dose (MRHOD) of 0.67 mcg/kg/day, respectively.

No adverse embryofetal effects were observed in rats or rabbits receiving cyclosporine during organogenesis at oral doses up to 17 mg/kg/day or 30 mg/kg/day, respectively (approximately 4,100 and 14,500 times higher than the MRHOD, respectively).

An oral dose of 45 mg/kg/day cyclosporine (approximately 10,900 times higher than MRHOD) administered to rats from Day 15 of pregnancy until Day 21 postpartum produced maternal toxicity and an increase in postnatal mortality in offspring. No adverse effects in mothers or offspring were observed at oral doses of up to 15 mg/kg/day (3600 times greater than MRHOD).

8.2 Lactation

Risk Summary

Cyclosporine is known to be excreted in human milk following systemic administration but excretion in human milk after topical treatment has not been investigated. VEVYE doses are approximately 4,700 times lower than recommended oral doses of cyclosporine, with blood concentrations being undetectable after topical administration. However, caution should be exercised when VEVYE is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

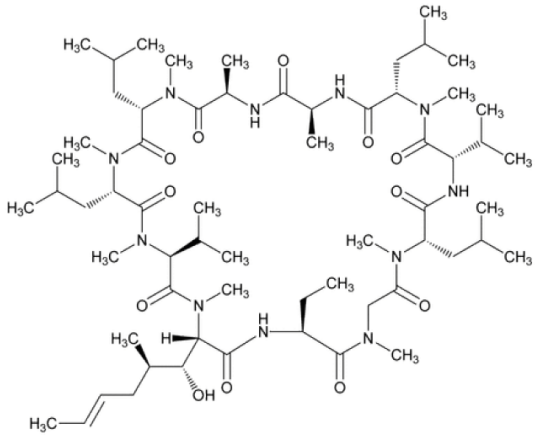
8.5 Geriatric Use

No overall difference in safety or effectiveness has been observed between elderly and younger patients.

11 DESCRIPTION

VEVYE (cyclosporine ophthalmic solution) 0.1% contains the immunomodulatory agent cyclosporine. Cyclosporine's chemical name is Cyclo[[€-(2S,3R,4R)-3-hydroxy-4-methyl-2-(methylamino)-6-octenoyl]-L-2-aminobutyryl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl] and it has the following structure:

Structural Formula



Formula: $C_{62}H_{111}N_{11}O_{12}$, Molecular weight: 1202.6

Cyclosporine is a white powder that is solubilized in perfluorobutylpentane, a semi-fluorinated alkane vehicle. VEVYE is supplied as a 2 mL sterile, clear, colorless, non-aqueous ophthalmic solution for topical ophthalmic use. VEVYE® contains:

- Active: cyclosporine 0.1%
- Inactives: perfluorobutylpentane, ethanol (anhydrous).

The solution does not contain water or anti-microbial preservatives. As a water free product, there is no associated pH and no osmolarity.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cyclosporine, a calcineurin inhibitor, is a relatively selective immunomodulatory drug.

12.3 Pharmacokinetics

Following bilateral topical ocular dosing of one drop of VEVYE twice daily, the blood concentrations of cyclosporine were below the limit of quantification (0.1 ng/mL) at all timepoints.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Evaluation of the potential carcinogenicity of cyclosporine was conducted in male and female mice and rats. In a 78-week oral (diet) mouse study, at doses of 1, 4, and 16 mg/kg/day, evidence

of a statistically significant trend was found for lymphocytic lymphomas in females, and the incidence of hepatocellular carcinomas in mid -dose males significantly exceeded the control value.

In a 24-month oral (diet) rat study, conducted at 0.5, 2, and 8 mg/kg/day, pancreatic islet cell adenomas significantly exceeded the control rate in the low dose level. The hepatocellular carcinomas and pancreatic islet cell adenomas were not dose related. The low doses in mice and rats were approximately 120 times higher than the maximum recommended human ophthalmic dose (0.67 mcg/kg/day), normalized to body surface area.

Mutagenesis

In genetic toxicity tests, cyclosporine has not been found to be mutagenic/genotoxic in the Ames Test, the V79 HGPRT Test, the micronucleus test in mice and Chinese hamsters, the chromosome-aberration tests in Chinese hamster bone-marrow, the mouse dominant lethal assay, and the DNA-repair test in sperm from treated mice. Cyclosporine was positive in an in vitro sister chromatid exchange (SCE) assay using human lymphocytes.

Impairment of Fertility

Oral administration of cyclosporine to rats for 12 weeks (male) and 2 weeks (female) prior to mating produced no adverse effects on fertility at doses up to 15 mg/kg/day (approximately 3,600 times higher than the maximum recommended human ophthalmic dose).

14 CLINICAL STUDIES

The safety and efficacy of VEVYE were assessed in a total of 1369 patients with dry eye disease, of which 738 received VEVYE.

In two multicenter, randomized, adequate and well-controlled clinical studies, patients with dry eye disease (CYS-002: NCT02617667 and CYS-004: NCT04523129), treated with VEVYE® were compared to patients treated with vehicle. At Day 29, there was a statistically significant higher percentage of eyes with increases of ≥ 10 mm from baseline in Schirmer wetting. This effect was seen in approximately 10% of VEVYE-treated patients versus approximately 6% of vehicle-treated patients.

Percent of Patients Achieving ≥ 10 mm Improvement from Baseline in Schirmer's Tear Test Score in Study Eyes in Patients with Dry Eye Disease

	CYS-002 Day 29		**CYS-004 Day 29**	
	VEVYE N=51	**Vehicle N=51**	**VEVYE N=409**	**Vehicle N=395**
≥ 10 mm increase in tear production (% patients)	8%	0%	11%	7%
Difference (95% CI)	7.8% (0.5%, 15.%)		3.9% (0.02%, 7.8%)	
p-value versus vehicle	0.04		0.05	

16 HOW SUPPLIED/STORAGE AND HANDLING

VEVYE is a sterile, clear, colorless non-aqueous ophthalmic solution packaged in multiple-dose eye drop bottles delivering single drops of approximately 0.01 mL volume. Each unit contains 2 mL of VEVYE in a 5 mL transparent squeezable polypropylene bottle with a transparent polyethylene tip and a white polyethylene cap with tamper-evident ring.

NDC 82667-900-02

Storage and Handling

Do not use if tamper-evident ring attached to the white cap is not intact. After first opening the tamper-evident ring of the cap remains on the bottle neck. Retain the cap and keep the bottle tightly closed when not in use.

Store at 15°C to 25°C (59°F to 77°F). Do not freeze or refrigerate. After opening, VEVYE can be used until the expiration date on the bottle.

17 PATIENT COUNSELING INFORMATION

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

Risk of Contamination

Advise patients to wash their hands well before each use. Advise patients not to allow the dropper tip to touch the eye or any other surface, as this may contaminate the solution *[see Warning and Precautions (5.1)]*.

Contact Lens Wear

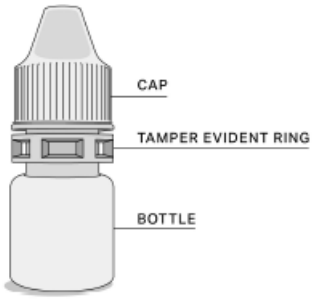
Contact lenses should be removed prior to instillation of VEVYE and may be reinserted 15 minutes following administration *[see Warning and Precautions (5.2)]*.

Distributed by
Harrow Eye, LLC
Nashville, TN 37215
USA

INSTRUCTIONS FOR USE
VEVYE® [vee vye']
(cyclosporine ophthalmic solution) 0.1%
for topical ophthalmic use

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

VEVYE ophthalmic solution parts:

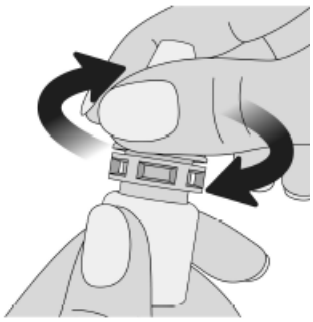


Important information you need to know before using VEVYE:

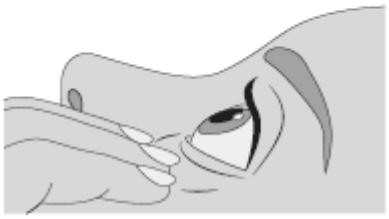
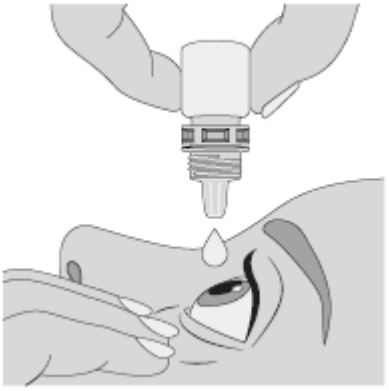
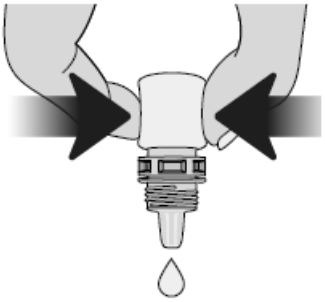
- **For topical use in the eye**.
- Before using VEYVE, be sure the tamper-evident ring is not broken. **Do not** use if the tamper-evident ring attached to the white cap is broken.
- **Do not** let the VEVYE dropper tip touch your eyes, fingers, or any other surfaces to avoid contamination or injury to your eyes.
- Use 1 drop of VEYVE in each eye, 2-times each day, about 12 hours apart.
- If you are using VEYVE with other eye (ophthalmic) medicine(s), you should wait at least 15 minutes between using VEYVE and the other medicine(s).
- If you wear contact lenses, remove them before using VEVYE. Wait at least 15 minutes after using VEYVE before placing the contacts back in your eyes.

Preparing to Use VEVYE

- Wash your hands before using VEVYE.
- After first opening the tamper-evident ring, the white cap should remain on the bottle neck until you are ready to use the medicine.



Using VEVYE

Step 1.	Remove the white cap on the bottle by twisting it to the left (counterclockwise) to open the bottle. **Do not** throw away the white cap (see Figure A).	 Figure A
Step 2.	Gently pull the lower eyelid downward before giving the drop (see Figure B).	 Figure B
Step 3.	Holding the bottle upright, tilt your head back and look up. Tip the bottle upside down over the eye allowing a drop to dispense on its own into your eye (see Figure C).	 Figure C
	If a drop does not come out of the bottle after a few seconds, gently apply slight pressure to the sides of the bottle while holding over the eye. If a drop misses your eye, try again (see Figure D). **Note:** You may not feel the drop falling into your eye.	 Figure D

Step 3.	Repeat Step 1 and Step 2 for your other eye.	
Step 4.	Place the white cap back on the bottle and twist it to the right (clockwise) to close the bottle. Keep the bottle tightly closed when not in use (see Figure E).	 Figure E

Storing VEVYE

- Store VEVYE at room temperature between 59ºF to 77ºF (15ºC to 25ºC).
- Keep the bottle tightly closed when not in use.
- **Do not** freeze or refrigerate.
- After opening, VEVYE can be used until the expiration date on the bottle.

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

Manufactured for Harrow Inc by:
Alliance Medical Products, Inc. (DBA Siegfried Irvine), 9342 Jeronimo Road, Irvine, CA 92618 (USA)

This Instructions for Use has been approved by the U.S. Food and Drug Administration.
Approved: 9/2025