When tear production is reduced by inflammation due to Chronic Dry Eye

Your Journey With RESTASIS®

What to know before getting started

You have a disease called Chronic Dry Eye

Chronic Dry Eye (CDE) is not a condition that comes and goes, but a disease caused by decreased tear production due to inflammation.

- Your eye doctor has determined your type of CDE requires prescription treatment—RESTASIS® (Cyclosporine Ophthalmic Emulsion) 0.05%
- RESTASIS® is the only prescription eye drop that helps increase your eyes' natural ability to produce tears for your type of CDE. RESTASIS® did not increase tear production in patients using anti-inflammatory eye drops or tear duct plugs

RESTASIS® is different from artificial tears

- Artificial tears can be helpful for temporary relief, but they do not increase your ability to produce more tears—only RESTASIS®, a prescription medicine, can do that
- You can use artificial tears, such as REFRESH OPTIVE™ Advanced Lubricant Eye Drops, with RESTASIS®. Allow 15 minutes between products

Your first use

1. Invert (turn upside down) the vial a few times to obtain a uniform, white, opaque emulsion.
2. Place 1 drop of RESTASIS® in each eye in the morning from 1 vial, then discard the vial. Repeat at night, about 12 hours later.
3. RESTASIS® is packaged in single-use vials because it doesn’t contain any preservatives. One vial should be used each time and immediately discarded after each use.
4. If you wear contact lenses, remove them before using RESTASIS®. You can put them back in 15 minutes after dosing.

What to expect

Beginning

It took time for your type of CDE to develop, so be patient, and give RESTASIS® 3 months to 6 months to improve tear production.

1 Month

Your eyes may begin producing more of their own tears. This is just the start, so keep going.

3 Months

You may notice an increase in tear production. Stick with it—more of your own tears should be on their way.

6 Months

Congratulations on reaching this milestone. You may experience a significant increase in tear production and may need artificial tears less often. Ask your eye doctor about how you are doing on RESTASIS®

With Continued Use

It’s up to you to keep your tear production going strong. You may only make more of your own real tears if you continuously use RESTASIS® so if you’re thinking about discontinuing treatment, please talk to your doctor.

Approved Use

RESTASIS® (Cyclosporine Ophthalmic Emulsion) 0.05% helps increase your eyes’ natural ability to produce tears, which may be reduced by inflammation due to Chronic Dry Eye. RESTASIS® did not increase tear production in patients using anti-inflammatory eye drops or tear duct plugs.

Important Safety Information

Do not use RESTASIS® Ophthalmic Emulsion if you are allergic to any of the ingredients. To help avoid eye injury and contamination, do not touch the vial tip to your eye or other surfaces. RESTASIS® should not be used while wearing contact lenses. If contact lenses are worn, they should be removed prior to the use.

The most common side effect is a temporary burning sensation. Other side effects include eye redness, discharge, watery eyes, eye pain, foreign body sensation, itching, stinging, and blurred vision.

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 Product Information.
When tear production is reduced by inflammation due to Chronic Dry Eye
Picking Up Your Prescription

The right supply
- Your supply of RESTASIS® (Cyclosporine Ophthalmic Emulsion) 0.05% depends on your prescription—a 90-day supply is 180 vials, a 30-day supply is 60 vials. When you receive your supply from the pharmacy, double-check to ensure you receive the right amount of vials
- A 90-day supply, compared to a 30-day supply, may be less expensive. A 90-day supply may also save you time since you won’t have to refill at the pharmacy every month*

Coverage and co-pay†
- RESTASIS® is covered for 98% of commercial and Part D patients
- $37 is the average co-pay—you may pay more or less depending on your prescription, insurance, and your eligibility to enroll in savings programs such as My Tears, My Rewards® (MTMR)*

Support for your journey
MyTears app
- Download this companion app for your treatment journey; available for iPhone® from the App Store™ or by visiting restasisapp.com
- At home or on the go, set medication reminders, track tear production, unlock trophies, access co-pay savings with MTMR, and more

MTMR
- Join the MTMR Program, a free program that rewards your commitment to staying on treatment
- Members have the opportunity to save on their co-pay costs and receive ongoing counseling and support throughout their journey with RESTASIS®
- Join by calling the RESTASIS® Support Center or visiting mytearsmyrewards.com

Online
- Visit restasis.com for valuable information about Chronic Dry Eye and RESTASIS®; and to watch educational videos featuring real RESTASIS® patients sharing their success stories

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Please see attached full Product Information.

*Individual out-of-pocket costs may vary. Formulary status and insurance coverage may vary. Co-pay amount is based on data available as of August 2013.
†The actual savings on a member’s out-of-pocket costs for RESTASIS® will vary according to refill quantity, personal healthcare insurance coverage, and adherence to FDA dosing guidelines. Please review the My Tears, My Rewards® Program guidelines to learn about the savings you may be eligible for.

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use RESTASIS® 0.05% safely and effectively. See full prescribing information for RESTASIS®.

RESTASIS® (cyclopentolate ophthalmic emulsion) 0.05%
Initial U.S. Approval: 1983

INDICATIONS AND USAGE
RESTASIS® is a topical immunomodulator indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs. (1)

— DOSAGE AND ADMINISTRATION —
Instill one drop of RESTASIS® ophthalmic emulsion twice a day in each eye approximately 12 hours apart. (2)

— DOSAGE FORMS AND STRENGTHS —
Ophthalmic emulsion containing cyclopentolate 0.5 mg/mL. (3)

— CONTRAINDICATIONS —
• Hypersensitivity (4)

— WARNINGS AND PRECAUTIONS —
• To avoid the potential for eye injury and contamination, be careful not to touch the vial tip to your eye or other surfaces. (5,1)

ADVERSE REACTIONS
The most common adverse reaction following the use of RESTASIS® was ocular burning (17%). (6,1)

To report SUSPECTED ADVERSE REACTIONS, contact Allergan, Inc. at 1-800-433-8871 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

FULL PRESCRIBING INFORMATION: CONTENTS*
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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
RESTASIS® ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.

2 DOSAGE AND ADMINISTRATION
Invert the unit dose vial a few times to obtain a uniform, white, opaque emulsion before using. Instill one drop of RESTASIS® ophthalmic emulsion twice a day in each eye approximately 12 hours apart. RESTASIS® can be used concomitantly with artificial tears, allowing a 15 minute interval between products. Discard vial immediately after use.

3 DOSAGE FORMS AND STRENGTHS
Ophthalmic emulsion containing cyclopentolate 0.5 mg/mL.

4 CONTRAINDICATIONS
RESTASIS® is contraindicated in patients with known or suspected hypersensitivity to any of the ingredients in the formulation.

5 WARNINGS AND PRECAUTIONS
5.1 Potential for Eye Injury and Contamination
To avoid the potential for eye injury and contamination, be careful not to touch the vial tip to your eye or other surfaces.

5.2 Use with Contact Lenses
RESTASIS® should not be administered while wearing contact lenses. Patients with decreased tear production typically should not wear contact lenses. If contact lenses are worn, they should be removed prior to the administration of the emulsion. Lenses may be reinserted 15 minutes following administration of RESTASIS® ophthalmic emulsion.

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, the most common adverse reaction following the use of RESTASIS® was ocular burning (17%). Other reactions reported in 1% to 5% of patients included conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging, and visual disturbance (most often blurring).

6.2 Post-marketing Experience
The following adverse reactions have been identified during post approval use of RESTASIS®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Reported reactions have included: hypersensitivity (including eye swelling, urticaria, rare cases of severe angioedema, face swelling, tongue swelling, pharyngeal edema, and dyspnea); and superficial injury of the eye (from the vial tip touching the eye during administration).

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Teratogenic Effects: Pregnancy Category C
Adverse effects were seen in reproduction studies in rats and rabbits only at dose levels toxic to dams. At toxic doses (rats at 30 mg/kg/day and rabbits at 100 mg/kg/day), cyclopentolate oral solution, USP, was embryo- and fetotoxic as indicated by increased pre- and postnatal mortality and reduced fetal weight together with related skeletal retardations. These doses are 5,000 and 32,000 times greater (normalized to body surface area), respectively, than the daily human dose. Higher doses were lethal to the dams at doses up to 70 mg/kg/day respectively, during organogenesis. These doses in rats and rabbits are approximately 1,000 and 10,000 times greater (normalized to body surface area), respectively, than the daily human dose.

8.2 Lactation
Cyclopentolate is known to be excreted in human milk following systemic administration, but excretion in human milk after topical treatment has not been investigated. Although blood concentrations are undetectable after topical administration of RESTASIS® ophthalmic emulsion, caution should be exercised when RESTASIS® is administered to a nursing woman.

8.3 Nursing Mothers
Cyclopentolate is known to be excreted in human milk following systemic administration, but excretion in human milk after topical treatment has not been investigated. Although blood concentrations are undetectable after topical administration of RESTASIS® ophthalmic emulsion, caution should be exercised when RESTASIS® is administered to a nursing woman.

8.4 Pediatric Use
The safety and efficacy of RESTASIS® ophthalmic emulsion have not been established in pediatric patients below the age of 16.

8.5 Geriatric Use
No overall difference in safety or effectiveness has been observed between elderly and younger patients.
Cyclosporine is a fine white powder. RESTASIS® appears as a white opaque to slightly translucent homogeneous emulsion. It has an osmolality of 320 to 320 mOsmol/kg and a pH of 6.5-8.0. Each mL of RESTASIS® ophthalmic emulsion contains: Active: cyclosporine 0.05%. Inactives: glycerin; castor oil; polysorbate 80; carbomer copolymer type A; purified water; and sodium hydroxide to adjust pH.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Cyclosporine is an immunosuppressive agent when administered systemically. In patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca, cyclosporine emulsion is thought to act as a partial immunomodulator. The exact mechanism of action is not known.

12.3 Pharmacokinetics
Blood cyclosporine A concentrations were measured using a specific high pressure liquid chromatography-mass spectrometry assay. Blood concentrations of cyclosporine, in all the samples collected, after topical administration of RESTASIS® 0.05%, twice daily, in humans for up to 12 months, were below the quantitation limit of 0.1 ng/mL. There was no detectable drug accumulation in blood during 12 months of treatment with RESTASIS® ophthalmic emulsion.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: Systemic carcinogenicity studies were carried out in male and female mice and rats. In the 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 the 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 are approximately 80 times greater (normalized to body surface area) than the human dose of one drop (approximately 28 mcL) of 0.05% RESTASIS® twice daily into each eye of a 60 kg person (0.001 mg/kg/day), assuming that the entire dose is absorbed.

Mutagenesis: 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. A study analyzing sister chromatid exchange (SCE) induction by cyclosporine using human lymphocytes in vitro gave indication of a positive effect (i.e., induction of SCE).

Impairment of Fertility: No impairment in fertility was demonstrated in studies in male and female rats receiving oral doses of cyclosporine up to 15 mg/kg/day (approximately 2,000 times the human daily dose of 0.001 mg/kg/day normalized to body surface area) for 9 weeks (male) and 2 weeks (female) prior to mating.

14 CLINICAL STUDIES
Four multicenter, randomized, adequate and well-controlled clinical studies were performed in approximately 1,200 patients with moderate to severe keratoconjunctivitis sicca. RESTASIS® demonstrated statistically significant increases in Schirmer wetting of 10 mm versus vehicle at six months in patients whose tear production was presumed to be suppressed due to ocular inflammation. This effect was seen in approximately 15% of RESTASIS® ophthalmic emulsion-treated patients versus approximately 5% of vehicle-treated patients. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.

No increase in bacterial or fungal ocular infections was reported following administration of RESTASIS®.