RESTASIS® Ophthalmic Emulsion—

Increasing tear production with RESTASIS® can be a REAL solution for certain patients with chronic Dry Eye

RESTASIS® 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.

Please see below for Important Safety Information.
1 Dispensing RESTASIS®

Patients will need 2 trays of RESTASIS® Ophthalmic Emulsion for a 1-month supply.

- Each tray contains 32 vials
- Each co-pay covers a 1-month supply (2 trays)

2 Counseling Patients About Expectations¹

Physicians should already have informed patients about what to expect when using RESTASIS® Ophthalmic Emulsion. You will still need to remind patients:

- RESTASIS® helps to increase tear production in certain patients, but it is not a quick fix
- Continued use leads to continued benefit

![Expectations during the first 6 months of therapy](image)

3 RESTASIS® Information Hotline

For any questions you may have regarding RESTASIS® Ophthalmic Emulsion, call: 1-866-572-5931
When Should Your Dry Eye Patients Ask Their Physician About RESTASIS®?

2 Simple Questions to Ask:

How many times does this patient need to instill another drop of an artificial tear throughout the day?
- Artificial tear use >3 times a day is a signal that the attention of a physician may be needed.

How many brands has this patient tried?
- A Dry Eye patient who does not find relief from different artificial tear products may not be successful in continuing this search. The attention of a physician may be needed.

Important Safety Information

RESTASIS® is contraindicated in patients with active ocular infections and has not been studied in patients with a history of herpes keratitis. The most common adverse event was ocular burning (upon instillation)—17%.

Other events 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).

Please see below for full Prescribing Information.
RESTASIS® (cyclosporine ophthalmic emulsion) 0.05% Sterile, Preservative-Free

DESCRIPTION

RESTASIS® (cyclosporine ophthalmic emulsion) 0.05% contains a topical immunomodulator with anti-inflammatory effects. Cyclosporine’s chemical name is Cyclo[(E)-(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:

![Cyclosporine Structure Formula](image)

Cyclosporine is a fine white powder. RESTASIS® appears as a white opaque to slightly translucent homogenous emulsion. It has an osmolality of 230 to 320 mOsmol/kg and a pH of 6.5-8.0. Each mL of RESTASIS® ophthalmic emulsion contains: Active: cyclosporine 0.05%, Inactives: glycercin; castor oil; polysorbate 80; carbomer 1542; purified water and sodium hydroxide to adjust the pH.

Mechanism of action:

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

Pharmacokinetics:

Blood cyclosporin 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%, BID, 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.

Clinical Evaluations:

Four multicenter, randomized, adequate and well-controlled clinical studies were performed in approximately 1200 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 infections was reported following administration of RESTASIS®.

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.

CONTRAINDICATIONS

RESTASIS® is contraindicated in patients with active ocular infections and in patients with known or suspected hypersensitivity to any of the ingredients in the formulation.

WARNING

RESTASIS® ophthalmic emulsion has not been studied in patients with a history of herpes keratitis.

PRECAUTIONS

General: For ophthalmic use only.

Information for Patients: The emulsion from one individual single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after administration.

Do not allow the tip of the vial to touch the eye or any surface, as this may contaminate the emulsion. 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.

Carcinogenesis, Mutagenesis, and Impairment of Fertility:

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 1000 and 500 times greater, respectively, than the daily human dose of one drop (28 µL) of 0.05% RESTASIS® BID into each eye of a 60 kg person (0.001 mg/kg/day), assuming that the entire dose is absorbed.

Cyclosporine has not been found 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).

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 15,000 times the human daily dose of 0.001 mg/kg/day) for 9 weeks (male) and 2 weeks (female) prior to mating.

Pharmacokinetics:

RESTASIS® is administered to a nursing woman.

The emulsion from one individual single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after use.

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

The safety and efficacy of RESTASIS® ophthalmic emulsion have not been investigated in pregnant women. RESTASIS® should be administered to a pregnant woman only if clearly needed.

Nursing Mothers:

Cyclosporine 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.

Pediatric Use:

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

Vidarabine is administered to a nursing woman.

Handling: The emulsion from one individual single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after use. The emulsion from one individual single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after use.

HOW SUPPLIED

RESTASIS® ophthalmic emulsion is packaged in single use vials. Each vial contains 0.4 mL fill in a 0.8 mL LDPE vial. 32 vials are packaged in a polypropylene tray with an aluminum peelable lid. The entire contents of this tray (32 vials) must be dispensed as one unit.

Storage: Store RESTASIS® ophthalmic emulsion at 15° to 25°C (59°-77°F).

KEEP OUT OF THE REACH OF CHILDREN.

Rx Only

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