**INDICATIONS AND USAGE**

CEQUA (cyclosporine ophthalmic solution 0.09%) is a corticosteroid immunomodulator indicated to increase tear production in patients with keratoconjunctivitis sicca (KCS) (dry eye) (1). **DOSAGE AND ADMINISTRATION**

Instill one drop of CEQUA (0.09%) (approximately 18 microns/µ) into each eye. Discard the same container immediately after using both eyes (2).

**USES IN SPECIFIC POPULATIONS**

**Pediatric Use**

CEQUA 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 instillation of CEQUA (3).

**Lactation**

The safety and efficacy of cyclosporine ophthalmic solution have not been established in pediatric patients below the age of 18 (4).

5.2 Use with Contact Lenses

Touch the vial tip to the eye or other surfaces (5.1).

**WARNINGS AND PRECAUTIONS**

**10 Precautions for Use and Contamination**

Avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces (5).

**ADVERSE REACTIONS**

Adverse Reactions following the use of CEQUA (cyclosporine ophthalmic solution 0.09%) include instillation site pain (22%), and conjunctival hyperemia (8%) (2).

The most common adverse reactions following the use of CEQUA (cyclosporine ophthalmic solution 0.09%) are instillation site pain (N=2), conjunctival hyperemia (N=1), and localized edema (N=1) (2).

**CONTRIBUTIONS TO OTHER SYSTEMS**

CEQUA is a corticosteroid immunomodulator agent that is administered systemically. In patients whose tear production is presumed to be suppressed due to ocular surface inflammation associated with keratoconjunctivitis sicca, topical administration of cyclosporine is thought to affect a partial tolerance (3).

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Mutagenesis

In genetic toxicity tests, cyclosporine has not been found to be mutagenic/genotoxic in the Ames Test, the V79-HGPRT Test, the chromosome-aberration test in Chinese hamster, or the chromosome-aberration test 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 (1620 times higher than the maximum recommended human ophthalmic dose).

Clinical Studies

Two multicenter, randomized, double-blind, placebo-controlled clinical studies treated 1,048 patients with keratoconjunctivitis sicca (NCT # 02254265 and NCT # 02688556).

In both studies, compared to vehicle at Day 84, there was a statistically significant (p<0.01) higher percentage of eyes with increases of ≥10 mm from baseline in Schirmer wetting. This effect was seen in approximately 17% of CEQUA-treated patients versus approximately 9% of vehicle-treated patients.

<table>
<thead>
<tr>
<th>Tear Production</th>
<th>CEQUA</th>
<th>Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10-mm increase in tear production (% of eyes) at Day 84</td>
<td>N = 152</td>
<td>N = 152</td>
</tr>
<tr>
<td>OTX-101-2014-001</td>
<td>16.8%</td>
<td>8.6%</td>
</tr>
<tr>
<td>CEQUA</td>
<td>N = 371</td>
<td>Vehicle</td>
</tr>
<tr>
<td>OTX-101-2016-001</td>
<td>16.6%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>8.2% (1.9%, 14.6%)</td>
<td>7.3% (3.3%, 11.3%)</td>
</tr>
<tr>
<td>p-value versus vehicle</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

16. HOW SUPPLIED/STORAGE AND HANDLING

CEQUA ophthalmic solution is packaged in sterile, preservative-free, single-use vials. Each vial contains 0.25 mL of a 0.5% LDFPE (10 vials (2 cards of 5 vials) are packaged in a polyfoil aluminum pouch). 6 pouches are packaged in a box. The entire contents of each box of 60 vials must be dispensed intact.

Storage: Store at 20°C to 25°C (68°F to 77°F). Store single-use vials in the original foil pouch.

17. PATIENT COUNSELING INFORMATION

Handling the Vial

Advise patients not to allow the tip of the vial to touch the eye or any surface, as this may contaminate the solution. Advise patients also not to touch the tip of the vial to their eye to avoid the potential for injury to the eye (see Warnings and Precautions (5.1)).

Use with Contact Lenses

CEQUA should not be administered while wearing contact lenses. Patients with decreased tear production typically should not wear contact lenses. Advise patients that if contact lenses are worn, they should be removed prior to administration of CEQUA ophthalmic solution (see Warnings and Precautions (5.2)).

Administration

Advise patients that the solution from one individual single-use vial is to be used immediately after opening for administration in one or both eyes, and the remaining contents should be discarded immediately after administration.

Rx Only

Manufactured for Sun Pharmaceutical Industries Limited
By: Laboratory Univers Limited
1 rue de l'Arquerie
50200 Coutances
France

Cyclosporine (active ingred.) Product of Czech Republic.

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