

Practical guidance for prescribing topical ciclosporin for ocular surface disease in Australian clinical practice

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Guidance for prescribing topical ciclosporin (CsA) for ocular surface disease in Australia

1. Prior to prescribing topical CsA for dry eye disease, assess for symptoms (e.g. with the Ocular Surface Disease Index (OSDI) questionnaire) and clinical signs (e.g. corneal fluorescein staining using Oxford scale, or equivalent) to determine the patient's:
 - a. Suitability for topical CsA treatment;
 - b. Eligibility for a Pharmaceutical Benefits Scheme (PBS) subsidy for the drug; and
 - c. Expected response to treatment.
2. Topical ciclosporin may be considered when dry eye disease symptoms and/or signs are not adequately controlled using preservative-free artificial tear monotherapy.
3. Use commercially available CsA products (Ikervis[®], Cequa[®] and Restasis[®]), per the Australian Therapeutic Goods Administration (TGA) product information, to ensure acceptable standard of quality with respect to efficacy, tolerability and dosing schedules. Restasis[®] is available via the TGA Special Access scheme.
4. Use topical CsA with preservative-free artificial tears, allowing about a 5-15 minute interval between eye drop instillations.
5. Commercially available CsA products are preservative-free, where each ampoule is intended for single use. Patients should be advised to discard the ampoule immediately after a single dose.
6. For patients to access PBS subsidised product pricing for **initial** treatment (i.e., for first 180 days of treatment), they need to meet the PBS guidelines for the available CsA products (Ikervis[®] (CsA 0.1%) and Cequa[®] (CsA 0.09%)) in Australia, including:
 - a. Ocular Surface Disease Index score >23; and
 - b. Corneal fluorescein staining of at least Grade 4 using the Oxford scale, or equivalent; and
 - c. Inadequate control of their dry eye disease with monotherapy with a preservative-free artificial tear substitute; and
 - d. Concomitant treatment with a preservative-free artificial tear substitute.

For patients to access **continuing** PBS subsidised treatment, they need to meet the PBS guidelines, including:

- 7.
- a. Having received PBS-subsided initial treatment with topical CsA; and
 - b. Improvement (reduction) in both OSDI score by $\geq 30\%$ from baseline (i.e., the grade stated in the initial authority application) and corneal fluorescein staining by ≥ 3 grades (measured using the same scale as at treatment initiation); and
 - c. Follow up of at least every six months, to assess treatment response and provide further prescriptions (if indicated); and where
 - d. The maximum number of repeat prescriptions on each script that can be provided for PBS scripts is five.

For a private prescription of topical CsA, patients:

- 8.
- a. Do not need to meet the criteria in the PBS guidelines; and
 - a. Should be advised that they will not be able to access the PBS subsidy.

Topical CsA should be dosed in accordance with the relevant product information:

- 9.
- a. Ikervis® once daily as final medication at bedtime
 - b. Cequa® twice daily
 - c. Restasis® twice daily

- 10.
- Compounded CsA, preserved or preservative free, may be considered if a higher concentration (e.g., 0.5%, 1% or 2%) is needed such as if there is no response to a low dose, or if there is a sensitivity to excipients in commercial products.

- 11.
- Topical CsA may be used after short term (e.g. 2-4 weeks) low potency topical corticosteroids (e.g. Fluorometholone 0.1%, Loteprednol etabonate 0.5%) if there is moderate to severe ocular surface inflammation/keratitis (ocular surface staining ≥ 4 using Oxford scale or equivalent).

When prescribing topical CsA, counsel patients that:

- 12.
- a. A response to treatment can take 4-12 weeks;
 - b. Evidence suggests that adverse effects are mostly mild, and primarily related to local reactions upon eye drop instillation, including ocular stinging, irritation and transient blurred vision that do not usually require treatment discontinuation, and may be more frequent with topical CsA formulated in oil or at higher concentrations;
 - c. Close monitoring is required due to a risk of elevated intraocular pressure and cataract if topical corticosteroids are used concurrently, as informed by the propensity of the specific corticosteroid agent to induce this change.

Response to treatment should be reassessed at least every six months.

- 13.
- a. Save Sight Dry Eye Registry can be used to monitor patients' disease status by tracking their dry eye symptoms (Ocular Surface Disease Index (OSDI) questionnaire), clinical signs (corneal fluorescein staining using Oxford scale, or equivalent) and treatments. <https://savesightregistries.org/fight-corneal-blindness/>

Topical CsA **may** also be considered for use in patients with:

- 14.
- a. Dry eye disease associated with autoimmune disease, such as Sjögren's syndrome;
 - b. Dry eye disease related to ocular surface disease conditions such as trachoma, post-refractive surgery (laser in situ keratomileusis (LASIK) surgery), post-cataract surgery;
 - c. Other ocular surface diseases, including posterior blepharitis, ocular rosacea, graft-versus-host disease (GVHD), allergic keratoconjunctivitis and viral conjunctivitis (specifically, epidemic keratoconjunctivitis).

For these ocular surface conditions, patients should be counselled that the PBS subsidy does not apply, a treatment effect may take at least 12 weeks, and that evidence is **limited** on the outcomes of treatment.

Contraindications and cautions:

- 15.
- a. The use of topical CsA has not satisfied the TGA categories A, B, C, D and X system for prescribing in pregnancy. Potential risks associated with prescribing topical CsA during pregnancy, or when planning a pregnancy or lactating, are based primarily on preclinical evidence and should be carefully weighed against the expected benefit for an individual patient.
 - b. Topical CsA is neither TGA approved, nor PBS listed for use in individuals under 18 years. Topical CsA 0.05% (Restasis®) and 0.1% (Ikervis®) have been indicated as steroid sparing agents for non-infective severe conjunctivitis for children >3 years in the in-house medication resource called Meds4Kids under the Sydney Children's Hospital Network.
 - c. Topical CsA should not be used while wearing contact lenses; patients should be advised to remove contact lenses prior to administering topical CsA and to reapply their contact lenses at least 15 minutes following topical CsA instillation.
 - d. Patients should be advised not to touch the CsA drug ampoule tip to the eye, or other surfaces, to minimise the potential for eye injury and/or contamination.
 - e. Topical CsA should not be prescribed for patients with a known hypersensitivity to the active substance or to any of the excipients.
 - f. Topical CsA should not be prescribed for patients with active or suspected ocular or peri-ocular infection, peri-ocular malignancies or premalignant conditions.