Amber with Guidance (Amber-G) = To be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians.*
**Specialist is defined by the APC as a clinician who has undertaken an appropriate formal qualification or recognised training programme, or who has the appropriate knowledge and competencies within the described area of practice.*

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Ciclosporin 1mg/ml eye drops (Ikervis®), for treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

Background Information[1]	• NICE TA369: Ciclosporin is recommended as an option, within its marketing authorisation, for treating severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes. • Ciclosporin (Ikervis®) is a sterile, positively charged, oil-in water, unpreserved ophthalmic emulsion that contains ciclosporin. Its formulation contains an excipient, cetalkonium chloride, which acts as a cationic agent and is specifically designed to prolong the time each eye drop stays on the epithelial layer of the eye. Ciclosporin has an anti-inflammatory effect on the cornea and the lacrimal (tear) gland. Following administration, ciclosporin blocks the expression of pro-inflammatory cytokines and subsequently enters corneal and conjunctival infiltrated T-cells, activating them. • Ciclosporin 1mg/ml eye drops (Ikervis®) are to be recommended or initiated by a specialist with follow up prescribing by primary care clinicians (monitoring should be carried out in secondary care, see monitoring section below). • Prescribe as the brand Ikervis®. Different formulations of ciclosporin 1mg/ml eye drop have different licensed indications.
BNF therapeutic class[2]	• Inflammatory eye conditions
Indication[3]	• Licensed for treatment of severe keratitis in adult patients (aged 18 and over) with dry eye disease, which has not improved despite treatment with tear substitutes.
Dosage and administration [2,3]	• The recommended dose is **one drop once daily to be applied to the affected eye(s) at bedtime**. • If a dose is missed, treatment should be continued on the next day as normal. Patients should be advised not to instil more than one drop in the affected eye(s). • Patients should be instructed to wash their hands before and after use. • Prior to administration, the single-dose container should be gently shaken. • For single use only. Each single-dose container is sufficient to treat both eyes. Any unused emulsion should be discarded immediately. • After opening of the aluminium pouches, the single-dose containers should be kept in the pouches in order to protect from light and avoid evaporation. • Patients should be instructed to use nasolacrimal occlusion and to close the eyelids for 2 minutes after instillation, to reduce the systemic absorption. This may result in a decrease in systemic undesirable effects and an increase in local activity. • If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 15 minutes apart. Ikervis® should be administered last.

Cautions and Contraindications[3]	**Contraindications** • Ikervis® is contra-indicated in patients who are hypersensitive to any of the product excipients (See SPC for full details); in patients with ocular or peri-ocular malignancies or premalignant conditions; in patients with active or suspected ocular or peri-ocular infection. **Cautions** • Ikervis® has not been studied in patients with a history of ocular herpes and should therefore be used with caution in such patients. • Contact lenses Patients wearing contact lenses have not been studied. Careful monitoring of patients with severe keratitis is recommended. Contact lenses should be removed before instillation of the eye drops at bedtime and may be reinserted at wake-up time. Also due to the cetalkonium chloride content, contact lenses should be removed prior to application and may be reinserted at wake-up time. • Cetalkonium chloride may cause eye irritation. Patients should be monitored in case of prolonged use. • Concomitant therapy There is limited experience with ciclosporin in the treatment of patients with glaucoma. Regular clinical monitoring should be exercised when treating these patients concomitantly with Ikervis®, especially with beta-blockers which are known to decrease tear secretion.
Pregnancy and breast feeding[3]	• Women of childbearing potential/contraception in females. Ikervis® is not recommended in women of childbearing potential not using effective contraception. • Pregnancy There is no data from the use of Ikervis® in pregnant women. Studies in animals have shown reproductive toxicity following systemic administration of ciclosporin at exposure considered sufficiently in excess of the maximum human exposure indicating little relevance to the clinical use of Ikervis®. Ikervis® is not recommended during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. • Breast-feeding Following oral administration, ciclosporin is excreted in breast milk. There is insufficient information on the effects of ciclosporin in new-borns/infants. However, at therapeutic doses of ciclosporin in eye drops, it is unlikely that sufficient amounts would be present in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Ikervis® therapy considering the benefit of breast-feeding for the child and the benefit of therapy for the woman.
Adverse Drug Reactions[3]	• Very common (≥1/10): eye pain; eye irritation • Common (≥1/100 to <1/10): Erythema of eyelid, lacrimation increased, ocular hyperaemia, blurred vision, eyelid oedema, conjunctival hyperaemia, eye pruritus • Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard
Monitoring[3]	• Response to treatment and examination of the eye(s) should be undertaken every 6 months by the secondary care eye specialist**.** (Ophthalmic medicinal products, which affect the immune system, including ciclosporin, may affect host defences against local infections and malignancies. Therefore, regular examination of the eye(s) is recommended, e.g., at least every 6 months, when Ikervis® is used for years)
Interactions[2,3]	• No interaction studies have been performed with Ikervis® • Co-administration of Ikervis® with eye drops containing corticosteroids could potentiate the effects of ciclosporin on the immune system. • Since systemic absorption can follow topical application, the possibility of

	interactions should be borne in mind.

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- https://www.barnsleyhospital.nhs.uk/service/ophthalmology/

References

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2. BNF. Available from: BNF (British National Formulary) | NICE Accessed 17/09/2024
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Development Process

This guidance has been produced following an AMBER-G classification status of Ciclosporin 1mg/ml eye drops (Ikervis®) by the Barnsley Area Prescribing Committee. This guidance has been subject to consultation and endorsement by the Ophthalmologists and was ratified by the Area Prescribing Committee on 9th October 2024.