## Key points on this medicine

- Ikervis is the first and only ciclosporin eye drops licensed in the UK
- Ikervis costs £72 for 30 days
- Ikervis improves corneal damage and ocular surface inflammation
- NICE recommends ciclosporin as an option for treating severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes
- The Scottish Medicines Consortium has accepted ciclosporin 1 mg/mL (0.1%) eye drops emulsion for use within NHS Scotland.

## Drug name

**Ikervis® (ciclosporin 0.1% / 1 mg/mL eye drops)**

## Indication

- Ikervis is indicated for the treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes
- Treatment must be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology.

## Presentation and administration

- Eye drops, milky white emulsion in a single-dose container
- One drop in the affected eye(s) once daily at bedtime
- Patients should be instructed to use nasolacrimal occlusion and to close the eyelids for 2 minutes after instillation
- Response to treatment should be reassessed at least every 6 months, but no specific monitoring is required.

## Budgetary implications

- Ikervis costs £72 for 30 days.

## Evidence for use

- The innovative formulation of Ikervis (ciclosporin in a cationic emulsion) targets ciclosporin to the cornea
- A phase III study compared ciclosporin in a cationic emulsion with an identical emulsion without ciclosporin and found that over 12 months Ikervis:
  - continuously improved corneal damage
  - continuously improved ocular surface inflammation
  - had an overall favourable tolerability profile
- After 6 months of treatment, the patients in the cationic emulsion without ciclosporin group had on average 50% more superficial punctate keratitis than those in the group receiving Ikervis
- A real-world evaluation has shown that Ikervis improved dry eye symptoms after 1 month in 47% of patients (n=63/133), and the improvement was sustained over a 12-month evaluation.

## Guidance recommendations

- NICE states that 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
- The Scottish Medicines Consortium has published the following advice:
  - ciclosporin 1 mg/mL (0.1%) eye drops emulsion (Ikervis®) is accepted for use within NHS Scotland
  - indication under review: treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes
  - ciclosporin eye drops, compared to vehicle, improved signs of corneal surface damage but not symptoms in patients with severe keratitis associated with dry eye disease.
Ophthalmology

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(ciclosporin 1 mg/mL) eye drops

Safety profile

- The most common adverse reactions in clinical studies were eye pain, eye irritation, lacrimation, ocular hyperaemia and eyelid erythema.
- The majority of adverse reactions reported in clinical studies with the use of Ikervis were ocular, mild to moderate in severity and usually transient.
- See summary of product characteristics for further details on adverse effects and contraindications.

Prescribing Information

Please refer to the product Summary of Product Characteristics for full details.

Product Name: IKERVIS® 1 mg/mL eye drops, emulsion.
Composition: One ml of emulsion contains 1 mg of ciclosporin and 0.05mg cetalkonium chloride as an excipient. Please refer to the Summary of Product Characteristics (SmPC) for a full list of excipients.
Indication: Treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes.
Dosage and administration: IKERVIS® treatment must be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology. The recommended dose is one drop of IKERVIS® once daily to be applied to the affected eye(s) at bedtime. Response to treatment should be reassessed at least every 6 months. To reduce systemic absorption, advise patients to use nasolacrimal occlusion and to close the eyelids for 2 minutes after instillation.
If more than one topical ophthalmic product is used, 15 minutes should separate their administration. IKERVIS should be administered last.
Contraindications: Hypersensitivity to any of the ingredients. Active or suspected ocular or peri-ocular infection.

Warnings and Precautions: Use with caution in patients with a history of ocular herpes. Contact lenses: Patients wearing contact lenses have not been studied. Monitor carefully in patients with severe keratitis. Contact lenses should be removed before instillation of the eye drops at bedtime and may be reinserted at wake-up time. Concomitant therapy: Use with caution in patients with glaucoma, especially in those receiving concomitant beta-blockers which are known to decrease tear secretion. Immune system effects: Medicinal products which affect the immune system, including ciclosporin, may affect host defences against infections and malignancies. Contains cetalkonium chloride which may cause eye irritation.

Interactions with other medicinal products: Coadministration with eye-drops containing corticosteroids may potentiate effects on the immune system.
Pregnancy and Breast Feeding: Not recommended in women of childbearing potential not using effective contraception or during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. Benefits of treatment must be weighed against the benefits of breast feeding.

Driving and using machines: Moderate influence on the ability to drive and use machines. If blurred vision occurs on instillation, the patient should be advised to not drive or use machines until their vision has cleared.

Undesirable Effects: Consult SmPC for full details. The most common adverse reactions in clinical studies were eye pain, eye irritation, lacrimation, ocular hyperaemia and eyelid erythema. Patients receiving immunosuppressive therapies including ciclosporin, are at an increased risk of infections.

Special Precautions for Storage: Do not freeze. After opening of the single-dose containers should be kept in the pouches in order to protect from light and avoid evaporation. Discard any opened individual single-dose container with any remaining emulsion immediately after use.

Package quantities and basic NHS cost: 30 x 0.3ml single-dose containers £72.00.

Product Licence Holder: Santen Oy, Nittyhaankatu 20, 33720 Tampere, Finland (PL 16058/0012) (EU/1/15/990/001 & 002)

Date of Authorisation: March 2015
Legal Category: POM
Date of last revision of Prescribing Information: 14/04/2016.

Ikervis® is a registered trademark of Santen Pharmaceuticals Co., Ltd.
Job code: STN 0418 IKV 00004c

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Santen UK Limited (Email medinfo@santen.co.uk or telephone: 0345 075 4863).

References

5. Scottish Medicines Consortium. Ciclosporin 1 mg/mL (0.1%) eye drops emulsion (Ikervis®). SMC No. (1089/15), www.scottishmedicines.org.uk/SMC_Advice/Advice/1089_15_ciclosporin_Ikervis

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Guidelines

in practice