This policy statement is approved by Halton, Knowsley, Liverpool, South Sefton, Southport and Formby, St Helens, Warrington, and Wirral CCGs

Ha Kn Li SS SF SH Wa Wi

NHS
Pan Mersey
Area Prescribing Committee

CICLOSPORIN 1mg/mL eye drops (Verkazia®) for the treatment of severe vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents

The Pan Mersey Area Prescribing Committee recommends the prescribing of CICLOSPORIN 1mg/mL eye drops (Verkazia®), by specialists only, for the treatment of severe vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents.

AMBER patient retained by specialist

Severe vernal keratoconjunctivitis (VKC) is an allergic inflammatory eye condition. It causes symptoms which have a significant impact for patients and, if management is not optimal, it can lead to permanent visual impairment. VKC occurs on a seasonal basis in some patients but other patients may present at any time of year. The incidence of VKC is estimated at 1-3 in 10,000 people.[1]

Topical ciclosporin is indicated when symptoms cannot be managed with lubricant eye drops and anti-allergic eye drops. It is used alongside pulsed topical steroids in severe or very severe VKC.[2] The use of topical ciclosporin in the management of severe VKC is well established but prior to the launch of Verkazia®it was necessary to prescribe an unlicensed product or, more recently, a licensed product to be used off-label.

Treatment with Verkazia® should only be initiated by an ophthalmologist. The period of follow up for patients with severe VKC is dependent on the severity of VKC. During an acute attack patients may need to be seen by a specialist as often as every day. As symptoms begin to resolve, treatment with Verkazia® will continue but the frequency of specialist review will decrease gradually to every 8 weeks.

The cost per patient per year (assuming treatment required for 12 months per year) is £3504. The annual cost of treatment with Verkazia® per 100,000 population (assuming treatment required for 12 months per year) is £17,520.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

CICLOSPORIN 1mg/mL eye drops (Verkazia®▼)
for the treatment of severe vernal keratoconjunctivitis (VKC)
in children from 4 years of age and adolescents

EFFECTIVENESS

Following ocular administration, ciclosporin is passively absorbed by T-lymphocytes where it blocks the release of pro-inflammatory cytokines such as IL-2 and hence T-lymphocyte activation. Ciclosporin inhibits histamine release from mast cells and basophils and may reduce eosinophil recruitment and effects on the conjunctiva and cornea. Ciclosporin up-regulates the release of anti-inflammatory cytokines.[3]

In a randomised double-masked, vehicle-controlled trial, 169 patients were randomised 1:1:1 to receive ciclosporin 1mg/1mL eye drops four times a day (high dose) or ciclosporin 1mg/1mL eye drops twice a day + vehicle twice a day (low dose) or vehicle four times a day. The primary endpoint for the study was a composite score comprising a monthly assessment of keratitis (assessed by corneal fluorescein staining), need for rescue medication and occurrence of corneal ulceration. The duration of treatment was 4 months with 8 months follow up. The composite score increased in both active groups to a larger extent than with vehicle (difference in the mean vs. vehicle was 0.76 [95% CI: 0.26, 1.27] and 0.67 [95% CI: 0.16, 1.18] for the high and the low dose group, respectively) and this difference was statistically significant (p=0.007 and p=0.010). [4,5]

SAFETY

Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Active or suspected ocular or peri-ocular infection.
- Ocular or peri-ocular malignancies or premalignant conditions

Adverse Effects

- Very common – eye pain
- Common - Upper respiratory tract infection, cough, headache, eye pruritus, ocular hyperaemia, eye irritation, ocular discomfort, foreign body sensation in eyes, lacrimation increased, vision blurred, erythema of eyelid, eyelid oedema.
- Uncommon- bacterial keratitis, herpes zoster ophthalmic, blepharitis, conjunctival oedema,

COST

Based on a VKC incidence of 2 in 10,000 we would expect 5 paediatric patients with severe VKC per 100,000 population per annum.

The cost per patient per year (assuming treatment required for 12 months per year) is £3504.

Annual cost per 100,000 population (assuming treatment required for 12 months per year) = £17,520

Previously available topical ciclosporin treatments for used for VKC were either unlicensed or off-label so prescribing was via secondary care. Therefore this is considered to be a new additional cost. There may be some reduction in cost of other treatments for VKC e.g. antihistamine and steroid eye drops but this is difficult to quantify as these treatments would usually be used alongside Verkazia® and the doses adjusted according to individual patient response.

PATIENT FACTORS

- The use of Verkazia® in individuals who wear contact lenses is not recommended.
- Use Verkazia® with caution in patients with active orofacial herpes simplex infection, a history of ocular herpes, varicella-zoster, or vaccinia virus infection.
- Use Verkazia® with caution when corticosteroids are administered concomitantly.
- Regular examination of the eye(s) is recommended, e.g. every 3 to 6 months, when Verkazia® is used for more than 12 months.

Supporting information

Prescribing information

- One drop four times a day to be applied to each affected eye.
- Once adequate control of signs and symptoms is achieved the dose may be decreased to one drop twice a day.
- Treatment should be discontinued when signs and symptoms resolve, and restarted when they recur.
- Regular examination of the eye(s) is recommended, e.g. every 3 to 6 months, when Verkazia® is used for more than 12 months.
- Counsel patients/carers on method of administration. Patients should be instructed to use nasolacrimal occlusion and to close the eyelids for two minutes after instillation, to reduce the systemic absorption. This method is described in the patient information leaflet supplied with the product. If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 15 minutes apart. Verkazia® should be administered last.[3]

Implementation notes

Treatment with Verkazia® should only be initiated by an ophthalmologist. Prescribing should be retained in secondary care until signs and symptoms have improved enough that the minimum time between specialist follow up appointments is 8 weeks. Communication with the patient's GP should include details of their current dose and the date of the next follow up appointment. Any changes in dose and the decision to stop treatment should be clearly communicated to the patient's GP.

Verkazia® is supplied in single-dose containers which should be kept in the pouch in which they are supplied order to protect from light and avoid evaporation.

References

[1] European Medicines Agency (2015) Public summary of opinion on orphan designation Ciclosporin for the vernal keratoconjunctivitis. [Accessed 18.03.19]

[2] Clinical grading of vernal keratoconjunctivitis Bonini, Stefano; Sacchetti, Marta; Mantelli, Flavio; Lambiase, Alessandro (2007) Current Opinion in Allergy and Clinical Immunology: October 2007 - Volume 7 - Issue 5 - p 436–441

3 Summary of Product Characteristics – Verkazia 1 mg/mL eye drops, emulsion. Santen UK Limited. Date of first authorisation: 06 July 2018 [Accessed 18.03.19]

4 European Medicines Agency (2018) Verkazia: EPAR – Public assessment report 12/07/2018. [Accessed 20/03/19]

5 Leonardi A.; Doan S.; Amrane M.; Ismail D.; Montero J.; Nemeth J.; Aragona P.; Bremond-Gignac D. (2019) A Randomized, Controlled Trial of Cyclosporine A Cationic Emulsion in Pediatric Vernal Keratoconjunctivitis: The VEKTIS Study. Ophthalmology. 126(5):671-681. Epub 2018 Dec 27.