

**South East London Area Prescribing Committee
Formulary recommendation**

Reference	078
Intervention	Ciclosporin 0.1% (Verkazia™) eye drops for atopic keratoconjunctivitis (AKC) and vernal keratoconjunctivitis (VKC) in children aged over 4 years (Ciclosporin is an immunosuppressant)
Date of Decision	October 2017. Updated December 2018 (licensed product available)
Date of Issue	November 2017. Updated December 2018
Recommendation	Amber 2 – initiation and first prescription supplied by the ophthalmology specialist team
Further Information	<ul style="list-style-type: none"> • This recommendation has been updated to reflect the availability of a licensed ciclosporin 0.1% eyedrop product for children (Verkazia™), which is licensed for vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents. • Ciclosporin 0.1% eye drops are accepted for use in South East London for the treatment of atopic keratoconjunctivitis (AKC) and vernal keratoconjunctivitis (VKC) in children as a 3rd line treatment option. The use of the licensed preparation (Verkazia™) is preferred for both VKC and AKC. • VKC is a severe inflammatory disease that appears in children and adolescents and generally has seasonal recurrence. It is a rare form of chronic eye allergy that can lead to corneal ulcers and loss of sight. • AKC is a chronic, perennial, severe form of allergic keratoconjunctivitis that is usually self-resolving, but poses a significant risk for corneal injuries and severe sequelae. It is always associated with other atopic conditions (typically dermatitis, eczema or asthma). • First line treatment for AKC and VKC is with topical mast cell stabilisers (e.g. sodium cromoglicate eye drops) and antihistamine eye drops. • Second line treatment is with topical corticosteroid eye drops for acute exacerbations. • Ciclosporin 0.1% eye drops may be considered where: <ul style="list-style-type: none"> - the AKC or VKC symptoms are uncontrolled with topical steroid treatment or - there are more than 2 exacerbations requiring intensive topical steroid treatment within 6 months • Ciclosporin eye drops are accepted for use in children aged 4 years to adolescence. Use below 4 years is not supported by this recommendation. • The dose of ciclosporin 0.1% eye drops for both VKC and AKC is 1 drop into the affected eye twice daily, increasing to 1 drop 4 times a day into the affected eye if there is no response. It should be noted that this dosing regimen is off-label. • Maintenance treatment duration is between 3 months to 6 months. Patients should be seen by the ophthalmology specialist within that time as treatment should be reassessed at least every 6 months. The efficacy and safety of Verkazia™ have not been studied beyond 12 months. • The initiating clinician must communicate the intended treatment duration to the GP to prevent inadvertent continuous repeat prescribing of the eye drops. • Treatment should be discontinued after signs and symptoms are resolved, and reinitiated upon their recurrence. • The use of ciclosporin 0.1% eye drops (Verkazia™) in AKC is off label. The dosing regimen being employed is also off-label.
Shared Care/ Transfer of care required:	N/A but the initiating clinician must clearly communicate the intended treatment duration and review period to the GP.
Cost Impact for agreed patient group	<ul style="list-style-type: none"> • The original formulary submission estimated that 30 patients in South East London may require treatment (across GSTT and KCH) in a 1 year period. However, Trust usage data indicates that 8 patients have been treated over the last year, which is fewer than anticipated. • The product is available in packs of 120 single use dose units. The cost of 1 month's treatment with 0.1% ciclosporin eye drops per patient at a dose of 1 drop twice daily is

	<p>£144 (excluding VAT). This rises to £288 per month at a dose of 1 drop four times a day.</p> <ul style="list-style-type: none"> Assuming: (i) Total of 8 patients estimated for treatment, 4 patients in each treatment group (ii) VKC patients – are treated with twice daily dosing regimen, rising to four times a day if needed (iii) AKC patients – all treated with twice daily dosing, the cost implication for 12 months treatment equates to ~£17,000 per annum (excluding VAT).
<p>Usage Monitoring & Impact Assessment</p>	<p>Acute Trusts:</p> <ul style="list-style-type: none"> Monitor use and submit usage data and audit reports (against this recommendation) upon request to the APC. <p>CCGs:</p> <ul style="list-style-type: none"> Monitor ePACT data. Exception reports from GPs if inappropriate prescribing requests are made to primary care.
<p>Evidence reviewed</p>	<p>References (from evidence evaluation)</p> <ol style="list-style-type: none"> Bremond-Gignac D, Donadieu J, Leonardi A, et al. Prevalence of vernal keratoconjunctivitis: a rare disease? <i>British Journal of Ophthalmology</i> 2008; 92:1097. Clinical Knowledge Summaries: Conjunctivitis – allergic. Available online here (accessed 02/10/2017) Leonardi A. Management of Vernal Keratoconjunctivitis. <i>Ophthalmology and Therapy</i> 2013 2 (2) p73-88 Gonzalez-Lopez J, Lopez_Alcalde J, Morcillo L et al. Topical cyclosporine for atopic keratoconjunctivitis (review). <i>Cochrane Database of Systematic Reviews</i> 2012 Issue 9. Uchio E, Kimura R, Migita H, et al. Demographic aspects of allergic ocular diseases and evaluation of new criteria for clinical assessment of ocular allergy. <i>Graefes Arch Clin Exp Ophthalmol</i> 2008; 246:291. Ikervis (cyclosporin 0.1%) eye drops. Summary of Product Characteristics. Available online here (accessed 02/10/2017) Moorfields Eye Hospital Medicines Formulary. Available online here (accessed 02/10/2017) Lallemand F, Schmidt M, Bourges JL et al. Cyclosporine A delivery into the eye: a comprehensive review of academic and industrial efforts. <i>European Journal of Pharmaceutics and Biopharmaceutics</i> 2017 117 p14-28 Wan K, Chen L, Rong S et al. Topical cyclosporine in the treatment of allergic conjunctivitis, a meta-analysis. <i>Ophthalmology</i> 2013 120 (11) p2197-2203 Akpek E, Dart J, WWatson S et al. A randomised trial of topical cyclosporine 0.05% in topical steroid-resistant atopic keratoconjunctivitis. <i>Ophthalmology</i> 2004 111 (3) p476-482 Daniell M, Contantinou M, Vu H et al. Randomised controlled trial of topical cyclosporin A in steroid dependent allergic conjunctivitis. <i>British Journal of Ophthalmology</i> 2006 90 p461-464 Hingorani M, Calder V, Buckley R et al. The immunomodulatory effect of topical cyclosporin A in atopic keratoconjunctivitis. <i>Investigative Ophthalmology and Visual Science</i> 1999 40 (2) p392-399 Keklikci U, Dursun B, Cingu A. Topical cyclosporine A 0.05% eye drops in the treatment of Vernal Keratoconjunctivitis – randomized placebo-controlled trial. <i>Advances in Clinical and Experimental Medicine</i> 2014 23 (3) p455-461 Lambiase A, Leonardi A, Sacchetti M et al. Topical cyclosporine prevents seasonal recurrences of vernal keratoconjunctivitis in a randomised, double masked controlled 2 year study. <i>Journal of Clinical Immunology</i> 2011 128 (4) p896-897 De Smedt S, Nkurikiye J, Fonteyne Y. Topical cyclosporin in the treatment of vernal keratoconjunctivitis in Rwanda, Central Africa: a prospective randomised double masked controlled clinical trial. <i>British Journal of Ophthalmology</i> 2012 96 (3) p323-328 Ebihara N, Ohashi Y, Uchio E et al. A large prospective observational study of novel cyclosporine 0.1% eye drops in the treatment of severe allergic conjunctivitis. <i>Journal of Ocular Pharmacology and Therapeutics</i> 2009 25 p365-372 Leonardi A, Doan S, Amrane M et al. Topical cyclosporin A 1mg/mL cationic emulsion in the treatment of active severe vernal keratoconjunctivitis (VKC): results of the phase 3 vektis study. Abstract – European Academy of Allergy and Clinical Immunology Congress 2017 Papmichael E, Parvizi S, Gadhvi K et al. Is cyclosporine 0.1% useful in children with severe ocular surface inflammation? – Abstract European Paediatric Ophthalmology Annual Meeting 2017 Summary of Product Characteristics (SPC). Ikervis. Available online here (accessed 06/10/2017) Added December 2018: SPC for Verkazia. Available online here (last accessed 06.12.18)

NOTES:

- Area Prescribing Committee recommendations and minutes are available publicly on the APC website.
- This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
- Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**