New Drug application for:

(D&T Application Form 2022)

Surrey and Sussex NHS Healthcare NHS Trust

Drugs & Therapeutics Committee (DTC) New Drug Application

Joint Primary and Secondary Care – Drug Application

This form is to be used for all applications for a new drug, use of samples, or new use of an existing drug

Applications will be discussed by the Drugs and Therapeutics Committee if they are completed electronically in full and come from a Consultant or, in exceptional cases from a non-medical prescriber or from a pharmacist.

All sections in this form must be **completed and sent electronically** and will not be considered until received fully completed electronically.

The grey shaded areas give guidance for completion. The *Medicines Information Team* can assist with the collection and summary of unbiased information, but it is up to you to ask them for help. They can be contacted on extension [redacted] or via email to

All applicants will be invited to the next available meeting of the DTC. Applications might not be considered if the applicant or a suitable representative is not present at the meeting, at the Chairman's discretion.

A copy must also be printed and signed by applicant and the Lead Clinician

The completed form must be sent electronically to: Pharmacy Department, East Surrey Hospital

Consultant…[redacted]

Speciality…Ophthalmology

Drug Details

- Verkazia® (Ciclosporin A 0.1% / 1mg/mL) eye drops, emulsion.
- Verkazia 1 mg/mL eye drops, emulsion, in a single-dose container is administered to the ocular surface. The recommended dose is 1 drop of Verkazia 4 times a day to be applied to each affected eye during the vernal keratoconjunctivitis (VKC) season in children

Is this drug licensed? Yes for VKC in children

What are the indications?

- Verkazia 1 mg/mL ciclosporin A [CsA] is indicated for treatment of severe vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents.

For Unlicensed/off-label medicines

Is there a licensed equivalent available? **No**

Is there a licensed product that can be used 'off-label'? Yes

- Ikervis (1mg/ml ciclosporin A) which is licensed in adults is the same medication and has been used off-label in children. Concentration is the same, and the dosage is the same – in children it is recommended it is used more frequently although I rarely have.

Is this request for an individual patient? **No**

What are the main risks and contra-indications for the drug?

What are the CLINICAL RISKS/ADVERSE EVENTS to the patient?

- Verkazia is the only ocular CsA preparation supported by safety data in children and adolescents with severe VKC.
- Verkazia is an unpreserved formulation with a favourable safety profile.

VEKTIS trial

- The most common adverse reactions in the clinical trials with Verkazia were eye pain (11%) and eye

Pruritus/itching (9%) which were usually transitory and occurred during instillation.

- After 4 months of ocular instillation of Verkazia QDS (n=50), 20 patients had blood concentrations of
- Verkazia below the lower limit of detection (0.050 ng/mL) and 13 patients had values below the lower limit of quantification (0.100 ng/mL). At Month 12, (n= 68 patients) values were below the lower limit of detection for 38 patients and below the lower limit of quantification in 10 patients.

Please see the summary of product characteristics for the full list of adverse reactions, available at https://www.medicines.org.uk/emc/product/9491

Are there any TRUST/CLINICAL GOVERNANCE ISSUES that you would like raise regarding this application?

- None

Why is this drug better than other drugs currently used

- Verkazia is the first ciclosporin preparation licensed for the treatment of severe VKC in children and adolescents. Up until the licensed product, off licence and off label preparations have been used in children to good effect.
- The VEKTIS study was the first study to enrol a large number of patients with severe VKC and to demonstrate efficacy with respect to measures of VKC signs, symptoms and QoL; limiting disease progression; and reducing the use of rescue medication (corticosteroids). There was significant improvement in the most common symptoms of VKC (itching, tearing, photophobia and mucous discharge). Rescue topical steroids was used approximately 50% less frequently in children using Ciclosporin with ensuing less side effects and requirement for monitoring.
- There is evidence for its use earlier in the stepwise approach to treating severe dry eye disease in adults and extrapolating this to its use in children with VKC. There is a 2-3 week build-up of effect and so needs to be used alongside steroids in the initial period in severe cases.

Are there any disadvantages compared to other drugs currently available?

- No other licensed product is available
- Patients should be monitored for hypersensitivity to the active substances or to any of the excipients
- Is contraindicated in patients with ocular or peri-ocular malignancies or premalignant conditions.
- Is contraindicated in patients with active or suspected ocular or peri-ocular infection.

References:

1. Parvizi S, Muthusamy K, Hingorani M, Dahlmann-Noor A. Topical ciclosporin 1 mg/ml for chronic ocular surface inflammation in children. Eye (Lond). 2018 Jul;32(7):1290-1291. doi: 10.1038/s41433-018-0037-z. Epub 2018 Feb 23. PMID: 29472696; PMCID: PMC6043559.

2. Leonardi A, Doan S, Amrane M, Ismail D, Montero J, Németh J, Aragona P, Bremond-Gignac D; VEKTIS Study Group. A Randomized, Controlled Trial of Cyclosporine A Cationic Emulsion in Pediatric Vernal Keratoconjunctivitis: The VEKTIS Study. Ophthalmology. 2019 May;126(5):671-681. doi: 10.1016/j.ophtha.2018.12.027. Epub 2018 Dec 27. PMID: 30593775.

3. Messmer EM, Ahmad S, Benitez Del Castillo JM, Mrukwa-Kominek E, Rolando M, Vitovska O, Baudouin C; a panel of European dry eye disease experts. Management of inflammation in dry eye disease: Recommendations from a European panel of experts. Eur J Ophthalmol. 2023 May;33(3):1294-1307. doi: 10.1177/11206721221141481. Epub 2022 Dec 5. PMID: 36471573; PMCID: PMC10152565.

Proposed place in therapy

1. **Where is the drug's place in therapy (refer to the evidence listed above)?**
    - There is currently no NICE treatment pathway for the management of severe VKC.
    - Topical antihistamine and mast cell stabilisers should be used alongside ciclosporin where it can be tolerated/ treatment schedule adhered to. Often in children the number of drops becomes prohibitive.
    - As mentioned above in the previous section concurrent steroid use in the initial stages is often needed in severe cases. Prolonged application of corticosteroids may cause steroid-induced cataract, glaucoma and increase susceptibility to secondary corneal infections.

- I would use Verkazia where more than one course of topical steroids is / has been needed to control the disease. Once the disease has stabilised, I ask parents to attempt tapering with a view to stopping over late autumn to early spring where possible.
- Efficacy and safety of Verkazia have not been studied beyond 12 months. Therefore, regular examination of the eye(s) is recommended, e.g. every 3 to 6 months, when Verkazia is used for more than 12 months.

2. **Will it be first / second / third line treatment (what's the evidence that supports this place?)**
   - Once diagnosed with VKC, after an initial tapering course of steroid eye drops.

3. **What patient criteria should be used for using the drug? (Please attach a treatment protocol or guideline)**
   - Any child diagnosed with symptoms of VKC – first line, or second line to steroids.

4. **Does your service have the capacity to use this drug in the current service model?** Yes

5. **What have you done to agree a new service model with the commissioners so that you can use this drug?**
   - N/A

What is the predicted usage of this drug?

1. Give the prevalence rates for indicated treatment:
- 20 patients per year

2. The proportion of patients expected to receive the drug:
- 0.01% and 0.03% of the UK population has VKC, of whom an estimated 30% have the severe form. Therefore, patient number will be relatively small; anecdotally there appears to be a more significant burden in Sussex compared to Surrey.

3. The number of patients predicted to be involved per month and per year:
- Approximately 2 per month (higher incidence in the spring/ high allergy season)

4. How many patients do you have who could be treated now?
- Currently being treated with non- licensed ciclosporin 0.01% eye drops – around 10-20 a year

5. Is there likely to be an increase in usage over the next 12-36 months – please provide an estimate
- Possibly: 24-28 children per year

6. Which other Consultants are likely to want to use this drug?

[redacted]

7. Have you liaised with the Consultants listed above?
- They have used the medication in the same patient group

What is the cost of the drug?
- £288.00 per pack (120-single dose containers), enough for 30-days supply when administered four times daily.

How does this compare to the products currently available?
- Only licensed product for this condition so cannot be compared – unlicensed product cost is the same per unit dose.

What does this new therapy replace?

1. Is this drug a new class or does it represent one of a family of drugs?

- This is a ciclosporin

2. Does this therapy replace another drug or a procedure?

- Verkazia is the only product specifically licenced for VKC however other agents such as mast cell stabilisers, antihistamines, topical mast cell stabilisers, artificial tears, steroids and unlicensed ciclosporin products have been used in the absence of a licensed indication.

3. Does this drug imply creation of a new service/procedure? No

QIPP

1. **How will this intervention improve QUALITY of patient care?**
   - Patients will be able to administer their drops themselves and be empowered to self care. They will have access to licensed medication for VKC
2. **In what way is this treatment INNOVATIVE? (How will the NHS do things differently by using this drug?)**
   - Improves self-care and patients will have access to a licensed product for VKC. Patients will have access to digital aids that they can record their symptoms via the manufacturer -SANTEN
3. **What does this treatment PREVENT? And how can we measure Patient Outcomes?**
   - This treatment will prevent repeated visits to the emergency eye clinic and paediatric outpatient clinic by reducing required follow up appointments and reduce therefore the burden to children and parents.
4. **What is the PRODUCTIVITY gain to the NHS? (How does this treatment pay for itself?)**
   - Patient will be treated with a licensed product that improves their daily quality of life The trust will be in line with any other trusts that already have access to this medication
   - It will reduce the variability in access to medications

What will the effect be on Primary Care prescribing?

1. **Do you expect to transfer prescribing and monitoring of this drug to GPs? (If no, go to the next section)**
   - Yes, once the patient has stabilised after initiation
2. **How long will you prescribe this drug before you expect GPs to take over prescribing?**
   - 3 months or once the symptoms have been stabilised (usually this length of time) – if it coincides with the end of summer then they will not need to take over prescribing
3. **What monitoring will be required by the GP? (Include frequency and criteria for action)**
   - Nothing for the GP
4. **What special precautions will the GP need to be aware of when taking on prescribing?**
   - Contraindications as above
5. **If there is any specialist monitoring required by GPs you must attach a shared care guideline when you make this application (example shared care link):**
   - N/A

What personal experience do you have of using the drug?

- I have used the unlicensed product in hospitals in London, and wrote an article with colleagues on

practice and outcomes in children at Moorfields before any licensed drop was available.

- Since Ikervis was licensed for adults) I have been using ciclosporin eye drops in both adults and children and it has been well tolerated. It has helped significantly in a few children who have been refractory to other treatment (multiple drops of antihistamine/mast cell stabiliser/ steroid/lubricants combinations).