NICE National Institute for Health and Care Excellence

Highly Specialised Technologies (HST) criteria checklist: ID6497 Polihexanide eye drops for treating acanthamoeba keratitis in people 12 years and over

Introduction

The NICE HST criteria checklist is to highlight where a technology meets/partially meets or does not meet the criteria for routing to the HST programme. Its purpose is to show the details of why a technology may not be appropriate for HST evaluation, but also where it has been identified as suitable. For more information, please see section 7 of NICE health technology evaluation topic selection: the manual

Key – Please use the colour key to advise if the technology meets the criteria

Met	There is clear and strong evidence that the criterion is met
Not met	There is some, but not enough clear evidence that the criterion is met or There is no evidence or limited evidence that the criterion is met.

MA wording: [redacted]

Number	Criterion	Description of how the technology meets the criteria	Does the technology meet the criteria?
1.	The disease is very rare defined by 1:50,000 in England	Acanthamoeba keratitis (AK) has an estimated incidence of 0.1175 cases per 50,000 people per year in the UK [1]. Acanthamoeba survive in air, soil, dust, and water. Therefore, eye trauma, poor contact lens hygiene practices or exposure to contaminated water are risk factors for infection. Estimates suggest that 87% of cases are in contact lens users.[1]	Not met

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		Acanthamoeba keratitis refers specifically to infections caused by the Acanthamoeba parasite. Infectious keratitis, which is an umbrella term for any inflammation or infection of the cornea caused by a microorganism, has an incidence of 17.35 cases per 50,000 people per year in the UK [2]. If 'the disease' is defined as infectious keratitis (IK), the criteria is not met. The company states that AK is 'clinically distinct' from IK due to distinct symptoms, clinical features and treatment approach. AK is associated with intense ocular pain (unlike AK caused by other microorganisms). There are separate guidelines provided by the Royal College of Optometrists for AK and AK has its own ICD-10 code (B60. 13). Unlike other microorganisms that can cause keratitis, Acanthamoeba can exist in two life-cycle stages, an active motile trophozoite and a resilient dormant cyst. The interchanging between these stages prevents many therapies from working, making AK more challenging to treat compared with other microbial corneal infections [3]. The company also cites the European Medicines Agency Committee for Orphan Medicinal Products, who concluded that AK was "a distinct medical entity and thus a valid condition, and there exists scientific rationale for the development of polihexanide for treatment of the condition"[4] However topical antiseptics are used for AK as well as other forms of keratitis [9]. Considering the similarities between AK and other forms of keratitis, this criterion is not met.	
2.	Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications	A 2015 study identified 124 AK cases across the UK in a 12 month period, giving an overall incidence of 2.35 per million people per year.[1] Based upon ONS population statistics where 84.2% of the UK population where based in England, this suggests around 104 people in England could be eligible for this treatment[5]. **Other indications:**	Met

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		• Polihexanide (also known as PHMB) is a broad-spectrum antimicrobial substance that has been used for 60 years in a wide range of medical and non-medical applications[6]. It is contained in solutions for the preservation of contact lenses, and other medical or industrial products. • Polihexanide 0.8mg/ml does not currently have any licensed indications in the UK. However, the medicine was designated as an orphan medicine for fungal keratitis by the EMA in August 2024 and the company has indicated its intention to pursue this, and other indications; "*this COMP positive opinion concerning orphan drug designation for fungal keratitis reinforces our commitment to further invest on polihexanide and develop it in such rare disease where there is a high unmet medical need".*	
3.	The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life	**Impact of symptoms** Symptoms of Acanthamoeba keratitis include: Severe eye pain, redness, blurred vision, sensitivity to light, sensation of something in the eye, and excessive tearing[1]. Evidence suggests that AK can lead to a reduction in vision-related quality of life during the acute phase (reading, mobility and emotional domains) [7]. People in the phase 3 ODAK trial had an average baseline utility of [redacted], which the company says is comparable to other rare diseases that have been assessed through the HST submission route (HST8 & HST10). The ODAK trial utility analysis demonstrates that the quality of life is comparable with the general population once the infection has been eradicated. **Impact of current treatment**	Not met

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		•Current treatment requires hourly eye drops through the day and night for first 2-3 days (which can require hospitalisation). Less frequent treatment often required for several months after diagnosis. A 2024 UK study found that the cure rate for one of the currently used treatments in the NHS is 86.6%. Company said ~1 in 5 people with unresolved AK following medical therapy undergo therapeutic surgery, which is associated with stress, anxiety and additional complications. Therapeutic surgery includes penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK), can indeed help restore vision, especially when performed early in the disease progression. DALK has a graft survival rate of 89.5% and better visual acuity outcomes three years post-surgery [12]. **Lasting impact** If not diagnosed early and treated promptly, the advanced stages of the condition can potentially result in vision loss.[7] It is estimated that AK results in prolonged morbidity and significant loss of visual acuity for up to 15% of patients [8]. AK is usually unilateral, but it can occur in one or both eyes[9]. Taking into account the vision set out for the HST programme, the criteria is not met in this case. The HST Programme is designed to be used in exceptional circumstances.	
4.	There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options.	There are no treatments which are specifically licenced for this indication in the UK, but treatments are widely used in the NHS.[3, 10] Current treatment includes antiseptic eyedrops such as polihexanide 0.2mg/mL (PHMB), chlorhexidine, propamidine or hexamidine[7]. Polihexanide eye drops (0.2mg/mL), chlorhexidine eye drops and hexamidine eye drops are all unlicensed products. Propamidine eye drops are licensed for minor eye	Not met

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		infections. However, the dosing regimen used to treat AK is more aggressive than the dosing regimen specified in the summary of product characteristics (off-label use). Clinical experts estimated that 98.9% receive medical treatment following diagnosis in UK. No standard treatment pathway; company and clinical experts report heterogenous treatment. The NICE health technology evaluations manual states that the committee can consider as comparators technologies that do not have regulatory approval for the population defined in the scope when they are considered to be part of established clinical practice for the population in the NHS. Clinical experts explained that there can be delays accessing treatment. Polihexanide 0.2mg/mL may only be available in tertiary hospitals and may need to be compounded for individual patients. SIFI-conducted Delphi Panel reported typical time of [redacted] between AK initial diagnosis and medical treatment initiation in the UK. Polihexanide 0.8mg/ml does not require regular administration overnight. Current treatment requires hourly treatment day and night, for the first 2-3 days therefore this new treatment may reduce treatment regimen burden. A trial comparing the efficacy of 0.2mg/ml polihexanide + propamidine and 0.8mg/ml polihexanide monotherapy demonstrated non-inferiority of 0.8mg/ml polihexanide. The adjusted cure rate within 12 months was 86.6% for 0.2mg/ml polihexanide + propamidine and 86.7% for polihexanide 0.8mg/ml [11].	

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		The study notes that PHMB 0.2mg/ml may not be routinely available 'off-the-shelf' in NHS pharmacies. So, it is sometimes necessary for the treatment to be compounded specifically for individual patients. The study authors suggest this may result in treatment delays [11]. The company notes that polihexanide 0.8 mg/ml offers a less burdensome dosing regimen vs currently used treatments, requiring the administration of eyedrops every hour in the daytime only in the initial treatment stage (avoiding the need to disrupt sleep). It is unclear if 0.8mg/ml polihexanide offers clinical benefits compared to the propamidine monotherapy (licensed eye drops which are used off-label in this population). Taking this into account along with the availability and number of other treatments, this criterion is not met.	

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9. CDC. *Clinical Overview of Acanthamoeba Keratitis*. Acanthamoeba Infections 2024; Available from: https://www.cdc.gov/acanthamoeba/hcp/clinical-overview-acanthamoeba-keratitis/index.html.
10. NHS, T.R.W.T., *What is Acanthamoeba Keratitis (AK)?*, T.R.W. Trust, Editor. 2024.

11. Dart, J.K.G., et al., *The Orphan Drug for Acanthamoeba Keratitis (ODAK) Trial: PHMB 0.08% (Polihexanide) and Placebo versus PHMB 0.02% and Propamidine 0.1%.* Ophthalmology, 2024. **131**(3): p. 277-287.

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