

**Clinical Commissioning
Policy Proposition:
Keratoprosthesis for corneal
blindness**

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Prepared by NHS England Specialised Services Clinical Reference Group for specialised ophthalmology

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1 Executive Summary

Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain Language Summary

The cornea is the clear outer layer at the front of the eyeball. It acts as a window to the eye. The coloured iris and the pupil (the black dot in the centre of the iris) can be seen through the cornea.

The cornea helps to focus light rays on to the retina (the light-sensitive film at the back of the eye). This "picture" is then transmitted to the brain.

When the cornea is damaged, it can become less transparent or its shape can change. This can prevent light reaching the retina and causes the picture transmitted to the brain to be distorted or unclear.

About Current Treatments

When the cornea becomes severely diseased it appears cloudy (opaque) resulting in very poor sight. Many people with corneal disease can benefit from corneal transplantation replacing the cloudy cornea with a clear cornea from a human organ donor.

About the new treatment - keratoprosthesis

A keratoprosthesis is an artificial cornea made from an acrylic material. These devices have been developed for use in people who have corneal blindness and for whom a normal corneal transplant and/or a limbal stem cell transplant (i.e. Holoclar) is not suitable.

The Boston Keratoprosthesis (KPro) is an artificial cornea made from acrylic (polymethyl methacrylate PMMA) and titanium. It has a PMMA front plate with a stem; this is the seeing (optical) part, and a titanium back plate with a titanium locking ring.

The Boston KPro is used with a real cornea that has been donated by an organ donor. The Boston KPro is fixed into the centre of the donated cornea, which is then stitched into place at the front of the eye. The operation is very similar to a standard corneal transplant.

What we have decided

NHS England has carefully reviewed the evidence to treat corneal blindness with a keratoprosthesis and have concluded that there is enough evidence to consider making the treatment available.

There are currently three CE-marked devices that can be used as a keratoprosthesis: Boston keratoprosthesis type 1 (Boston KPro I); KeraKlear Artificial Cornea KPro (Keramed) and Legeais BioKPro-III (FCI Ophthalmics).

A further device identified in the literature, AlphaCor (Argus, Biomedical), is no longer manufactured.

The published evidence identifies that at present, there is sufficient evidence to commission this treatment using a Boston Keratoprosthesis. Other identified devices currently have insufficient published evidence to consider them for routine commissioning by the NHS.

2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission keratoprosthesis.

This document also describes the proposed criteria for commissioning, governance arrangements and funding mechanisms.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether a keratoprosthesis for corneal blindness will be routinely commissioned is planned to be made by NHS England following a recommendation from the Clinical Priorities Advisory Group.

3 Proposed Intervention and Clinical Indication

The proposed intervention is a keratoprosthesis. It is an artificial cornea with a central prosthesis used to provide a transparent optical pathway into the eye of people with corneal blindness.

A keratoprosthesis is clinically indicated for patients with corneal blindness, who have visual acuity of 6/60 (1.0 logMAR) or worse in the better seeing eye and are unsuitable for a corneal transplant and/or a limbal stem cell transplant.

4 Definitions

Cornea – the outer layer of the eye. It is transparent in healthy people but is rendered opaque by several disease processes.

Prosthesis – an artificial replacement for a missing or defective organ or body part.

Keratoprosthesis – an artificial cornea.

Visual acuity – is measured by the ability to read lines on a chart, which is a measure of the minimum angle of resolution (MAR). It is often reported as a fraction, for example, 6/60 (or 1.0 logMAR), meaning that one can only see at 6 metres what someone with normal vision can see at 60 metres. (In the USA this would be

reported as 20/200 using feet as a measure). Visual acuity is also commonly reported as a logarithm of the minimum angle of resolution (LogMAR) as in the following conversion table.

	Snellen (UK) (measured at 6m)	Snellen (USA) (measured at 20 feet)	Log MAR value
Normal vision	6/6	20/20	0.00
	6/9.5	20/32	0.20
	6/15	20/50	0.40
	6/24	20/80	0.60
	6/38	20/125	0.80
	6/60	20/200	1.00
Poor vision	<6/60	<20/200	>1.00

5 Aims and Objectives

This policy proposition considers keratoprosthesis for the treatment of corneal blindness.

The objectives are to define the eligibility criteria for treatment with a keratoprosthesis; identify devices with sufficient clinical evidence for routine commissioning and define the associated commissioning arrangements.

6 Epidemiology and Needs Assessment

No evidence is directly available in England on the incidence and prevalence of patients with corneal blindness unsuitable for corneal transplant and/or a limbal stem cell transplant.

Data has therefore been drawn upon using the following:

- The experience in the USA, where the prosthesis has been available for several years, the estimated need is 2 patients per year per million population, or about 110 patients per year in England.
- NHS Blood and Transplant data on patients receiving multiple corneal grafts, which indicates there would be an expected number of 174 patients per year potentially requiring the keratoprosthesis based on them having 2 or more failed grafts.
- Clinical Consensus of Consultant corneal specialists in England.

Treatment may be considered suitable for patients of any age meeting the outlined criteria, however, it is expected that the age distribution of patients requiring this treatment would be in line with that reported by NHS Blood and Transplant for all corneal transplants, with most patients being over the age of 50 years.

7 Evidence Base

The summary of evidence for the three currently available CE-marked devices keratoprosthesis, namely, Boston keratoprosthesis type 1 (Boston KPro I), KeraKlear Artificial Cornea KPro (KeraMed) and Legeais BioKPro-III (FCIOphthalmics) is presented below. Overall, there is only sufficient clinical evidence to support the use of Boston KPro.

Boston KPro

The evidence base is contained within the NICE Interventional Procedure guidance (IPG534) (2015) and the NICE Medtech Innovation Briefing (MIB91) (2017).

There have been nine studies (n=1,202 eyes of 1,162 patients in total) published since NICE produced the interventional procedure guidance on implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes, which were considered in the NICE Medtech Information Briefing (MIB). Two of the studies were prospective and seven were retrospective. They showed that Boston KPro I improved visual acuity and was more effective than penetrating keratoplasty in patients with severe corneal opacity who have already had a failed corneal graft.

Key uncertainties around the fact that the studies do not report which version of the Boston KPro 1 was used, but most of the changes in design have been minor modifications and improvements. Most of the studies are retrospective.

The Boston KPro 1 was first licensed in 1992. There have been minor alterations to the design over the years, although the concept and basic design has stayed constant. These modifications include the introduction of holes into the back plate to improve the access of nutrients to the donor cornea, the use of a locking ring to hold the cornea and prosthesis together, a change of the assembly method from a screw

thread to a snap-fit, and most recently the use of a titanium back plate to improve biocompatibility (Salvador-Culla 2016). These changes to the design have been made to improve outcomes and reduce complications based on research and validation evidence, and have had to be approved by the Food and Drugs Administration (FDA). Although published retrospective studies have not clearly specified which version was used, clinical outcomes have improved with these modifications (Aldave 2009).

KeraKlear Artificial Cornea KPro

Two studies were identified that evaluated the clinical effectiveness of KeraKlear - one case series study (Alio et al 2015) and one case report (Alio et al 2014).

The case series (Alio et al 2015) included 11 eyes. Patients were considered for implantation with KeraKlear if they were at high risk of failure with standard penetrating keratoplasty (PK) or showed conditions with a poor prognosis following PK such as severe chemical injury. KPro was implanted intralamellar (inside a lamella/flap of the cornea) in 11 eyes and epidescemetrical (a deeper layer above Descemet's membrane) in 4 eyes. Follow-up was between 7 and 21 months and mainly for anatomical outcomes and complications. The study reported the following results:

Intralamellar implantation

- Excellent anatomical outcomes (centration inside the pocket) in 5/11 eyes with no complications.
- Complications such as deep corneal inflammatory membrane, totally vascularised cornea, extrusion of the KPro and corneal melting, all of which were managed successfully in 6/11 eyes.

Epidescemetrical implantation

- The anatomical outcome was excellent in all four eyes. No eye was lost.

The case report (Alio et al 2014) included a patient who was treated by a combined corneal graft associated with KeraKlear implantation assisted by femtosecond laser and cataract surgery with implantation of an intraocular lens. After 1 month, visual

acuity was 0.6 logMAR in both eyes with -2 sphere correction. Slit-lamp examination and anterior segment optical coherence tomography revealed that the device was centred in the pupil area with no infection. No sign of extrusion was detected.

Legeais BioKPro-III

One case series study with seven patients with severe corneal scarring (Hollick et al 2006) reported on results of Legeais BioKPro implantation. The follow up was between 18-48 months. The study reported the following results:

- keratoprosthesis failed in six, because of extrusion occurring 2-28 months postoperatively.
- Retroprosthetic membranes occurred in three patients and endophthalmitis in one.
- Vision improved from hand movements to 6/12 in the only patient who retained the KPro; however the patient was troubled by mucus accumulation on the optic.

8 Proposed Criteria for Commissioning

NHS England has concluded that there is sufficient clinical evidence to support a proposal for the routine commissioning of Boston keratoprosthesis for patients who have corneal blindness.

Inclusion criteria:

Boston KPro 1 is considered suitable for patients with corneal blindness, who have:

- visual acuity of 6/60 (1.0 logMAR) or worse in the better seeing eye

AND

- are unsuitable for corneal transplant and/or a limbal stem cell transplant.

AND

- Patients whose blink and tear mechanisms are reasonably intact
- Patients with no other severe, potentially-blinding eye disease such as retinal detachment or extreme optic nerve cupping (damage due to glaucoma).
- Patients with intact nasal light projection (this is the ability to see a bright light directed onto the nasal (inner) part of the visual field).

Exclusion criteria:

Patients with the following conditions are unlikely to be suitable:

- Patients with active uncontrolled autoimmune diseases (pemphigoid, Stevens-Johnson syndrome, uveitis, Sjögren's syndrome, etc.) or other severe eye inflammation.
- Patients with longstanding severe intraocular inflammation and phthisis bulbi.
- Patients with retinal detachment or extreme optic nerve cupping
- Patients without intact nasal light projection (suggests end stage glaucoma).

9 Proposed Patient Pathway

Patients will be referred for assessment using a suitable keratoprosthesis device from corneal specialists, within NHS specialised ophthalmology services.

10 Proposed Governance Arrangements

The keratoprosthesis will be commissioned from specialised ophthalmology services with corneal specialists who have the appropriate expertise and support services to undertake and implant a keratoprosthesis and who are able to collect and report audit data on the outcome of the keratoprosthesis for at least 5 years after implantation.

Corneal specialists undertaking procedures to implant a keratoprosthesis must also be undertaking at least 20 corneal transplants per year and must be registered with the manufacturers of the keratoprosthesis device.

11 Proposed Mechanism for Funding

The treatment costs associated with keratoprosthesis will be commissioned and funded by NHS England Specialised Commissioning under existing contractual arrangements for the provision of specialised ophthalmology services.

12 Proposed Audit Requirements

The following information will form the audit requirement for all patients treated with a keratoprosthesis; Retention of device; Complications (includes infection); Visual acuity (annually); Quality of life (annually).

13 Documents That Have Informed This Policy Proposition

National Institute for Health and Care Excellence (NICE) (2017) Medtech Innovation Briefing. Boston Keratoprosthesis Type I for corneal blindness. MIB 91
<https://www.nice.org.uk/advice/mib91>

National Institute for Health and Care Excellence (2015) Implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes IPG 534 and
<https://www.nice.org.uk/guidance/ipg534>

Literature search and clinical opinion regarding alternate keratoprosthesis excluding Boston KPro. (NHS England, 2017)

14 Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned.

15 References

Aldave, A. J., et al. (2009). "The Boston type I keratoprosthesis: improving outcomes and expanding indications." Ophthalmology **116**(4): 640-651

Alio JL, et al . A new epidescemetic keratoprosthesis: pilot investigation and proof of concept of a new alternative solution for corneal blindness.. Br J Ophthalmol 2015;99:1483–1487. doi:10.1136/bjophthalmol-2014-306264

Alio JL, Abbouda A, Vega-Estrada A. An innovative intrastromal keratoprosthesis surgery assisted by femtosecond laser. Eur J Ophthalmol. 2014 24(4):490-3.

Hollick et al. Legeais BioKpro III keratoprosthesis implantation: long term results in seven patients. Br J Ophthalmol 2006;90:1146–1151

Salvador-Culla, B. and P. E. Kolovou (2016). "Keratoprosthesis: A Review of Recent Advances in the Field." J Funct Biomater **7**(2).

END

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