



**Australian Government**  

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**Medical Services Advisory Committee**

## **Public Summary Document**

### ***Application No. 1392 – Corneal Collagen Cross Linking***

**Applicant:** **Royal Australian and New Zealand College of Ophthalmologists**

**Date of MSAC consideration:** **MSAC 69<sup>th</sup> Meeting, 6-7 April 2017**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website.](#)

#### **1. Purpose of application**

An application requesting a new Medicare Benefit Schedule (MBS) listing of Corneal Collagen Cross Linking (CCXL) as early intervention in progressive keratoconus was received from The Royal Australian and New Zealand College of Ophthalmologists (RANZCO) by the Department of Health (the Department).

#### **2. MSAC's advice to the Minister**

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported public funding of Corneal Collagen Cross Linking (CCXL) for corneal ectatic disorders with evidence of progression.

MSAC encouraged the Therapeutic Goods Administration (TGA) to continue with the Authorised Prescriber Scheme for supply of the riboflavin eye drops required to render this service.

MSAC questioned the proposed fee and requested that the Department investigate an appropriate fee and provide information to the MSAC Executive. MSAC suggested an upper limit of \$1,200 for the MBS fee - with reference to international pricing and a RANZCO recommendation.

MSAC also requested a review of the utilisation, out-of-pocket costs and basis for the MBS fee two years after MBS listing begins.

#### **3. Summary of consideration and rationale for MSAC's advice**

MSAC noted that the proposed public funding of CCXL had been considered in July 2016. MSAC recalled that it had deferred its decision to list CCXL in patients with corneal ectatic disorders due to concerns that the revised economic model had not been adequately verified and that the riboflavin drops used in rendering this service were not registered on the Australian Register of Therapeutic Goods (ARTG).

MSAC recalled that it had previously accepted the safety and clinical effectiveness of CCXL in the proposed population ([MSAC Public Summary Document \(PSD\) Application 1392, July 2016](#)).

MSAC noted that both legal advice and clarification from the TGA had been sought regarding the regulatory status of riboflavin eye drops. MSAC noted that according to this information, there were no issues from either a TGA or legal perspective with the MBS listing of a service for which some, but not all, components are listed on the ARTG. MSAC noted that the TGA encourages the use of the Authorised Prescriber Scheme to access riboflavin eye drops, which allows approved prescribers to prescribe a specific therapeutic good to a class of patients under their care. MSAC concluded that this advice addressed concerns around the individual components required to render this service.

MSAC recalled that it had requested information regarding the progress of several large, well-designed clinical trials due to report in 2016–17, which have discontinued their control arms. MSAC considered a [2015 FDA briefing document of the Joint Meeting of the Dermatological and Ophthalmic Drugs Advisory Committee and Ophthalmic Device Panel of the Medical Advisory Committee](#), which provided follow up data for three randomised sham-controlled trials. MSAC clarified that discontinuation of the control arms was the result of very high rates of crossover from sham treatment to CCXL. MSAC also considered that the information provided by the applicant alongside its pre-MSAC response reviewing each of the CCXL trials reported in [clinicaltrials.gov](#) to be helpful in considering the relevance of these trials.

MSAC also recalled that in its pre-MSAC response for the July 2016 meeting, the applicant had noted that some data were available for ectasias other than keratoconus, though these data were not included in the response. MSAC noted that the applicant had since confirmed that non-keratoconus peripheral corneal ectasias are rare conditions and, as such, valid randomised data for these conditions would be difficult to obtain.

MSAC recalled concerns regarding the use of CCXL for post-LASIK<sup>1</sup> ectasia, and noted observational studies (Poli M et al 2013; Yildirim A et al 2014) which provided evidence of favourable outcomes for use in this condition or for post-radial keratotomy ectasia. MSAC considered that the use of CCXL for these patients may be appropriate. In contrast, MSAC considered that a CCXL MBS item should exclude use for the purpose of primary prevention of post-LASIK ectasia (LASIK Xtra).

MSAC noted that an assessment of the revised economic model had been undertaken by ESC. MSAC agreed with ESC that the model inputs for time horizon, age of onset of keratoconus and utility values for vision quality of life were appropriate. MSAC considered that uncertainties regarding the prevalence of keratoconus and its impact on the model had been addressed in the sensitivity analyses undertaken. MSAC noted that out-of-pocket costs were not included in the revised economic model and that these can be significant for patients accessing ophthalmologists. MSAC noted the new model:

- decreased the utility value for vision quality of life for patients with a corneal graft based upon data from the Australian Corneal Graft Registry Report 2015 (0.87 in the initial model versus 0.83 in the current model);
- decreased the number of predicted procedures in 2015/2016 (2,600 versus 2,100);
- increased corneal graft costs due to inclusion of hospital and eye bank costs (~\$1866 versus ~\$5525); and
- assumed 2 services per patient rather than 1.5.

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<sup>1</sup> LASIK: Laser-Assisted *In Situ* Keratomileusis (commonly referred to as laser eye surgery)

MSAC agreed with ESC that changes to the model were appropriate. MSAC noted that a sensitivity analysis of the MBS fee was included, with the cost of the procedure having a significant impact on the incremental cost-effectiveness ratio (ICER). MSAC concluded that revised model indicates that the CCXL treatment pathway is more effective than the current treatment pathway and is lower in cost.

MSAC considered that the number of expected procedures and the CCXL procedure fee were key drivers of the financial estimates, and that the initial surge in utilisation may be prolonged depending on the number of services provided by ophthalmologists. MSAC noted that the estimates assume that 2,426 patients are likely to access CCXL treatments in year one with the number of patients decreasing to 389 by year five. MSAC noted that the projected number of CCXL treatments is highly sensitive to an assumption that a large number of patients are currently undergoing CCXL, despite the treatment not being funded by the MBS at present. In addition, MSAC noted the assumption that listing of CCXL on the MBS would result in a reduction in corneal grafts and accepted that this was appropriate.

MSAC noted a cost sensitivity analysis was undertaken to explore the impact of variation in the MBS fee for the CCXL procedure. Listing CCXL with an MBS fee of \$1,500 was estimated to cost the MBS \$4.4 million in year one, decreasing to \$648,000 by year five. In comparison, listing CCXL with an MBS fee of \$900 was estimated to cost the MBS \$2.9 million in year one, decreasing to \$421,000 by year five. MSAC noted that varying the MBS fee may also result in variation to the associated out-of-pocket costs for patients.

MSAC recalled that the committee had requested a more detailed rationale for the \$1,500 fee proposed by the applicant at its July 2016 meeting. MSAC noted that during public consultation, consumers advised that they are currently being charged \$2,000 to \$3,000 for treatment per eye. MSAC also recalled that the Protocol Advisory Sub-Committee had suggested a value between \$900 and \$1,300 based upon current fees for cataract surgery and corneal transplant.

In its pre-MSAC response, the applicant provided estimates of equipment and personnel input costs for the UV source, riboflavin eye drops and per treatment fee. The applicant also provided comparative estimates for the time required to perform the Dresden and accelerated protocols for CCXL (80 minutes and 65 minutes, respectively). MSAC noted that Godefrooij DA et al 2016 detailed the costs associated with CCXL in clinical practice for 43 patients (86 eyes) in the Netherlands. Where delivered by an ophthalmologist, CCXL treatment costs (including consumables) equated to ~\$1,293 (€886) and decreased to ~\$1,080 if shorter UV-A radiation exposure time (5 minutes rather than 30 minutes) via an accelerated protocol was used. MSAC noted that March 2017 correspondence from RANZCO supported an MBS rebate of \$1,200.

MSAC requested that the Department investigate an appropriate fee, reviewing all reasonable cost components that contribute to setting MBS fees, and provide this information to the MSAC Executive for further consideration. Based on the information available, MSAC suggested an upper limit of \$1,200 for the MBS fee. MSAC assumed that the fee would not include capital costs for the lamp, nor the cost of the riboflavin eye drops. MSAC also noted that actual charges would be determined by the market once a MBS fee and rebate is set, especially in the out-of-hospital setting.

MSAC concluded that the MBS item descriptor should not specify details of the CCXL protocol as this may limit clinicians' ability to use the most appropriate procedure according to the best available evidence. However, given that there are variations in both the complexity and duration of the procedure, MSAC recommended it would be appropriate to review the MBS fee for CCXL two years after MBS listing. MSAC also recommended that the

explanatory notes for the CCXL MBS item should stipulate the exclusion of use of this service for LASIK Xtra.

MSAC recommended that MBS listing be linked with a requirement for mandatory recording of the types of CCXL services provided and their outcomes in a CCXL register. MSAC requested that data from the Save Sight Institute's CCXL registry and the Australian Corneal Graft Registry be collated, along with out-of-pocket expenses incurred, to inform the review of CCXL two years after MBS listing.

MSAC supported MBS funding of CCXL for corneal ectatic disorders with evidence of progression. MSAC considered that, compared with corneal transplantation, CCXL has acceptable safety and clinical effectiveness, and is probably cost-effective (subject to an appropriate MBS fee). MSAC encouraged the TGA to continue with the Authorised Prescriber Scheme for supply of the associated riboflavin eye drops. MSAC also requested a review of the utilisation, registry data, out-of-pocket costs and basis for the MBS fee two years after MBS listing begins.

#### **4. Background**

Application 1392 was considered at the July 2016 MSAC meeting. MSAC deferred its advice on public funding for CCXL in patients with corneal ectatic disorders due to concerns that the revised economic model had not been adequately verified and that the riboflavin eye drops used in rendering this service were not registered on the ARTG.

MSAC requested the following information to enable it to finalise its advice:

- A more detailed rationale for the proposed fee, including the range of applicable protocols to render the service, and how these range in both complexity and duration.
- An assessment by its Evaluation Sub-Committee (ESC) comparing the revised modelled economic evaluation with the version initially developed, and examining the sensitivity of these models to variations in the proposed fee.
- Clarification from the TGA regarding the consequences of the varying regulatory status of the codependent ultraviolet lamp device and the various riboflavin eye drop options used in rendering the service.
- Progress of the several large well-developed clinical trials due to report in 2016-17 (which have discontinued their control arms).
- Data cited in the pre-MSAC response said to be available in patients with ectasias other than keratoconus.

#### **5. Prerequisites to implementation of any funding advice**

The UVA light source devices are registered on the Australian Register of Therapeutic Goods (ARTG).

The riboflavin eye drops are not registered on the ARTG, but may be accessed via the TGA's Authorised Prescriber Scheme or Special Access Scheme.

#### **6. Proposal for public funding**

The proposed MBS item descriptor for CCXL is provided in Table 1.

The applicant proposed fee is \$1500. The PICO Advisory Sub-Committee suggested a fee of \$900-\$1300 would be appropriate (between the cost of cataract surgery and corneal transplant). During public consultation, consumers advised that they are currently being charged between \$2000–3000 per eye (\$4000–\$6000 for both eyes).

**Table 1 Proposed MBS item descriptor for corneal collagen cross-linking**

<b>Category 3 – Therapeutic Procedures – Ophthalmology Services</b>
MBS [item number] Corneal Collagen Cross Linking, for patients with corneal ectatic disorders with evidence of progression Fee: \$1500 [Applicant-proposed fee]. Anaes. <i>Explanatory Note:</i> <i>Evidence of progression in patients over the age of twenty five is determined by the patient history including an objective change in tomography or refraction over time. Evidence of progression in patients aged twenty five years or younger is determined by patient history including an objective change in tomography or refraction over time and/or posterior elevation data and objective documented progression at a subclinical level.</i>

## **7. Summary of Public Consultation Feedback/Consumer Issues**

See [Public Summary Document from July 2016 for Application 1392](#).

## **8. Proposed intervention's place in clinical management**

The current approach to treating patients with corneal ectatic disorders involves, in the first instance, attempting to improve the patient's vision with glasses, if possible. If the condition progresses and the glasses no longer improve the patient's vision, hard contact lenses are fitted. If the lenses cannot be fitted, or are unsuccessful, patients undergo penetrating corneal graft. Some patients currently access CCXL as an alternative to corneal grafting by self-funding the procedure.

Under the proposed clinical management algorithm, CCXL would be used as a first line treatment once there is evidence of progression, regardless of whether glasses or contact lenses have been tried. The proposed treatment pathway utilises CCXL as a preventative treatment (intending to halt the progress of the disease early).

## **9. Comparator**

The current treatment pathway involves attempting to improve the patient's vision with glasses or soft contact lenses, and if no improvement or deterioration then hard contact lenses. If hard contact lenses cannot be fitted or are unsuccessful, then patients undertake penetrating corneal graft.

## **10. Comparative safety**

Adverse events and complications after CCXL are not well reported in randomised trials, so there are few comparative safety data. A range of adverse events have been described but these are generally minor and transient. Corneal haze is common but resolves over time.

The assessment report stated it had not been possible to assess safety of CCXL relative to the conventional management pathway without CCXL. Therefore, at best, CCXL can be assessed to be noninferior with respect to safety.

## **11. Comparative effectiveness**

The assessment report stated it was difficult to classify the therapeutic profile of CCXL in relation to the current treatment pathway, including risk of progression to a corneal transplant, as no good quality direct or indirect comparisons were identified that would allow such an assessment to be made.

Randomised trials, nonrandomised studies and meta-analyses showed that CCXL leads to improvements in corrected visual acuity, uncorrected visual acuity, Kmax and spherical equivalent refractive error, and the improvements are maintained over at least 2 years. Data were not available to inform an assessment of the risk of progression to transplant compared with management without CCXL. The relevance of these results in terms of clinical progression of the disease is, however, difficult to assess. Comparative data for children/adolescents is scarce but where this has been attempted, the outcomes have been similar to that for adults or all ages.

Some additional, but very low quality, data on quality of life was also identified that shows possible quality of life improvements in people who had undergone CCXL compared to those with contact lenses.

The complex nature of the evidence base did not lend itself to a formal GRADE analysis. All the included Randomised Control Trials and other non-randomised studies were of low quality overall, with different protocols, outcome measures and time points. There were high levels of heterogeneity in study results. Longer-term outcome measures that would be more helpful in answering the clinical question in relation to current management without CCXL, have additional quality issues with loss to followup and low patient numbers.

An evidence summary of key results for the standard CCXL procedure over 12 months or longer is shown in Table 2.

**Table 2 Evidence profile: Overall clinical effects of standard CCXL as measured in key included systematic reviews and randomised trials with 12 months follow up or greater**

Outcomes (units)	Participants (studies)	Type of study	Quality of evidence (GRADE)	Effect (summary)
Corrected visual acuity (logMAR)	Craig 2014; Meiri 2016	Meta-analysis (RCTs and NRS)	Low	-0.1 at 12&24 months -0.09 at >36 months
	Li 2015	Meta-analysis (RCTs)	Low	-0.1 (3-36 months)
	#997 Seyedian 2015 #1204,1205 Wittig-Silva 2008 and 20014	RCTs	Low	-0.1 at 12 months
Uncorrected visual acuity (logMAR)	Craig 2014; Meiri 2016	Meta-analysis (RCTs and NRS)	Low	-0.1 to -0.2 at 12&24 months -0.1 at >36 months:
	Li 2015	Meta-analysis (RCTs)	Low	-0.18 (3-36 months)
	#1204,1205 Wittig-Silva 2008 and 20014	RCTs	Low	-0.1 at 12 months
Max K (D)	Craig 2014; Meiri 2016	Meta-analysis (RCTs and NRS)	Low	Relative to baseline/preCCXL: -1 at 12&24 months -0.4 at > 36 months
	Li 2015	Meta-analysis (RCTs)	Low	Relative to controls: -2.05 D (3-36 months)
	#997 Seyedian 2015 #1204,1205 Wittig-Silva 2008 and 20014	RCTs	Low	Relative to baseline and/or controls (up to 36 months): -1 to -2 D
Spherical equivalent refractive error (D)	Craig 2014; Meiri 2016	Meta-analysis (RCTs and NRS)	Low	Relative to baseline: 0.1-0.5 at 12 months 0.7 at 24 months 0.5 at >36 months

Outcomes (units)	Participants (studies)	Type of study	Quality of evidence (GRADE)	Effect (summary)
	Li 2015	Meta-analysis (RCTs)	Low	Relative to controls: -0.96 (3–36 months)
	#997 Seyedian 2015 #1204,1205 Wittig-Silva 2008 and 20014	RCTs	Low	Little change to baseline and/or controls
Quality of life	NRS		Very low	Some improvements for people with CCXL compared to those with rigid contact lenses

On the basis of this evidence profile, it is suggested that, relative to the current treatment pathway, CCXL has non-inferior safety and non-inferior (possibly superior) effectiveness. Considerable further comparative data would be required to make a more definitive conclusion relative to the conventional management pathway.

Keratoconus and other corneal ectasias present specific challenges for conducting well-designed randomised controlled trials. The disease progression of keratoconus is often slow, and 10-20 years may elapse between diagnosis and corneal transplant, which is difficult to capture in a clinical trial. The applicant has advised that additional long-term trials with an untreated control arm would be unlikely to be approved by an ethics committee, and investigators on trials that are currently under way have presented preliminary reports at ophthalmic meetings that the trials have discontinued their control arms. Further data is more likely to come from registry studies. A CCXL register has recently been set up at the University of NSW but has not yet collected any data.

#### Clinical claim

The complication rate of cross linking is relatively low and certainly much less than corneal transplantation. Overall visual loss from the condition should be significantly reduced.

## **12. Economic evaluation**

The application presented a cost utility analysis. The model was calibrated against the number of corneal grafts currently occurring (between 300 and 400 per year) and the current number of CCXL treatments per year (around 2 000 per year).

The overall costs and outcomes, and incremental costs and outcomes as calculated for the intervention and comparator in the model, and using the base case assumptions, are shown in Table 3. This indicates that CCXL treatment pathway has a lower cost and higher incremental benefits compared to the current treatment pathway.

**Table 3 Incremental cost effectiveness ratio, discounted**

	Cost	Incremental Cost (\$)	Effectiveness (QALYs)	Incremental effectiveness	ICER
Intervention	21,926,707		145,145		
Comparator	23,057,646	-1,130,939	144,877	268	-4,215

The application noted that with respect to CCXL, the Incremental Cost Effectiveness Ratio (ICER) is an imperfect measure of value because it results in improved outcomes at a lower cost. Although the CCXL treatment pathway ‘front loads’ treatment costs, there is an incremental saving as it avoids corneal transplants which are significantly more expensive due to hospital and eye bank fees. The benefit attributed to CCXL is also likely understated as the utility measures do not reflect the improved quality of life from not undergoing an

invasive surgical procedure, or experiencing life as a young person without deteriorating vision. Data limitations prevent allowances being made for these factors in the analysis.

A sensitivity analysis showed:

- The incremental cost of the CCXL treatment pathway is highly sensitive to the discount rate used because, compared to the current treatment pathway, under CCXL a larger proportion of treatment costs are incurred on diagnosis.
- Increasing the number of treatments for individuals previously diagnosed with corneal ectatic disorders, has a significant impact on the costs of the CCXL pathway.
- Changing the costs of CCXL treatment has significant impacts on the results. Applying a range of 30 per cent either side implies costs could be between \$4.1 million lower under the CCXL pathway or \$7.1 million higher in present value terms (over 50 years).

Overall, the application stated that the service generally has incremental benefits (increased QALYs) across the range of scenarios tested.

### 13. Financial/budgetary impacts

An epidemiological approach was been used to estimate the financial implications of the introduction of CCXL.

The estimated potential patient population for people who might receive CCXL at some point in their lives is around 12,000. Forecasts change in line with expected population growth and changes in the stage of the disease for each person.

Given CCXL activity to date, 1,642 treatments are estimated to occur in 2016-17 and then taper down substantially as much higher levels currently being treated are not believed to be sustainable.

The financial implications to the MBS resulting from the proposed listing of CCXL are summarised in Table 4. The estimated cost to the MBS of CCXL is \$2.5 million, which tapers off and stabilises around \$600,000 thereafter. This is reducible by approximately \$65,000 annually as a result of avoided corneal grafts and associated complications.

**Table 4 Total costs to the MBS associated with CCXL**

	2016-2017	2017-2018	2018-2019	2019-2020	2020-2021
<b>Preliminary consultations</b>	\$140,473	\$38,583	\$30,883	\$32,338	\$33,279
<b>CCXL procedures</b>	\$2,134,600	\$586,300	\$469,300	\$491,400	\$505,700
<b>Follow up consultations after 1 year</b>	\$211,818	\$58,179	\$46,569	\$48,762	\$50,181
<b>Total cost to the MBS</b>	\$2,486,891	\$683,062	\$546,753	\$572,500	\$589,160

The financial cost to the MBS depends on the listed cost of CCXL. This has been subject to sensitivity testing by increasing the listed price from \$1,300 to \$1,500, and reducing it to \$900. This results in costs to the MBS of \$4.4 million in 2016-17, falling to \$648,000 in 2020-21 if the listed price is \$1,500. If the listed price is \$900 then the cost to the MBS is \$2.9 million in 2016-17, falling to \$421,000 in 2020-21.

The applicant's pre-MSAC response noted that the saving in "grafts avoided" may be underestimated. Throughout a lifetime patients may require more than one graft per eye but the corneal graft registry from which the data is derived may record failed previous graft as



the graft indication rather than go back to the fundamental diagnosis of Keratoconus. Other surgery subsequent to the graft may include cataract surgery, refractive keratoplasty [for high degrees of post graft astigmatism] and glaucoma surgery [there is a significant increase in the incidence of glaucoma post corneal graft].

#### **14. Key issues from ESC for MSAC**

ESC noted that MSAC had previously accepted the safety and clinical effectiveness of CCXL in the proposed population at its July 2016 meeting. In addition, ESC noted that MSAC had deferred its advice on public funding and had requested the following information to enable it to finalise its advice:

- a more detailed rationale for the proposed fee;
- an assessment by ESC comparing the revised modelled economic evaluation with the version initially developed, and examining the sensitivity of these models to variations in the proposed fee;
- clarification from the TGA regarding the consequences of the riboflavin eye drops, used in rendering this service, not being listed on the ARTG;
- an update on why several large well-designed clinical trials have discontinued their control arms; and
- data cited in the pre-MSAC response said to be available in patients with ectasias other than keratoconus.

ESC noted that both legal advice and clarification from the TGA had been sought regarding the status of riboflavin eye drops and the consequences of the product not being registered on the ARTG. ESC noted advice that there is neither an issue with the TGA nor a legal issue with a service being listed on the MBS for which not all components are listed on the ARTG. ESC noted that the policy area also has no issues with the listing of the service without any brand of riboflavin being listed on the ARTG. ESC considered that this advice addressed concerns around the individual components required to render this service.

ESC considered the revised economic evaluation and noted concerns around the uncertainty of the prevalence of keratoconus and its impact on the model. ESC considered that these concerns were addressed in the sensitivity analysis.

ESC considered the time horizon and the age of onset of keratoconus appropriate in the revised economic model.

ESC noted that it was assumed that successful CCXL treatment halts corneal ectatic disorders' progression but does not lead to disease improvement and hence the utility weights after CCXL remain constant. ESC considered that there may be utility benefits in stopping progression but that this was hard to quantify. ESC noted the utility values for vision quality of life and considered them to be appropriate as they were closely linked to actual scores of patients reported in the data sources identified.

ESC questioned why no out-of-pocket costs were included in the revised economic model. ESC noted that out-of-pocket costs for ophthalmologists can be significant.

ESC noted that the revised economic model assumed that there was no backlog of cases and questioned the impact of this assumption on expected future financial costs.

ESC noted that the costs of glasses and other incidentals were not included in the revised economic model. ESC considered that inclusion of such costs is likely to favour CCXL.

ESC questioned the presentation of both discounted and undiscounted costs of the different treatment pathways. ESC noted that guidelines for preparing applications for MSAC specify

that costs and benefits should be discounted at an annual rate of 5% which was used in the base case.

ESC noted that calculation of QALYs uses vision-related quality of life instruments rather than more global measures.

ESC noted that the revised model indicates that the CCXL treatment pathway is more effective and lower cost than the current treatment pathway.

ESC noted that the revised assessment report failed to provide comparative information on the economic model initially developed and the revised model. On manual inspection ESC noted the new model:

- decreased the utility value for vision quality of life for patients with a corneal graft based upon data from the Australian Corneal Graft Registry Report 2015 (0.87 in the initial model versus 0.83 in the current model);
- decreased the number of predicted procedures in 2015/2016 (2,600 versus 2,100);
- increased corneal graft costs due to inclusion of hospital and eye bank costs (~\$1866 versus ~\$5525); and
- assumed 2 services per patient rather than 1.5.

ESC considered the changes identified to be appropriate. ESC also noted that a sensitivity analysis on the MBS fee was included with the cost of the procedure having a significant impact on the model.

ESC requested that MSAC be provided with a table clearly outlining changes made to the initial model by the contracted assessment group responsible for this application. ESC advised that the table should also include responses to the information requirements specified by MSAC at its July 2016 meeting.

ESC noted that a key driver of the financial estimates is the number of expected procedures. ESC considered that this was an area of uncertainty with inputs based on estimates and prevalence and population data. ESC noted that the potential for earlier diagnosis of patients with corneal ectatic disorders may increase the number of procedures undertaken.

ESC noted that the MBS item was not restricted to a specific CCXL procedure. ESC considered that this was appropriate as the methodology for CCXL appears to be evolving with variations in the procedure performed under the same name. ESC noted that as the variations relate to both the complexity and duration of the procedure it would be appropriate to review the fee for CCXL two years post listing or if trial evidence on new procedures becomes available.

ESC noted that MSAC's question regarding the rationale for the proposed fee remained unaddressed.

ESC noted comments from the applicant in its pre-ESC response that the control arms of recent clinical trials have likely been discontinued due to investigator concern that they are denying patients potentially effective treatment. ESC considered that while further information is required to answer MSAC's question it is unlikely that the outcome will affect the cost-effectiveness of CCXL.

ESC noted that no further data on patients with ectasias other than keratoconus has been provided.

From a consumer perspective, CCXL was noted to be an important and valued procedure. ESC noted that consumers may question why riboflavin is not registered on the ARTG.

**15. Other significant factors**

Nil

**16. Applicant's comments on MSAC's Public Summary Document**

The applicant had no comments.

**17. Further information on MSAC**

MSAC Terms of Reference and other information are available on the MSAC Website:  
[visit the MSAC website.](#)