# Implantation of Intrastromal Corneal Ring Segments (INTACS)

**Policy Number:** 9.03.14  
**Origination:** 12/2005  
**Last Review:** 11/2016  
**Next Review:** 11/2017

## Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for implantation of intrastromal corneal ring segments (INTACS) when it is determined to be medically necessary because the criteria shown below are met.

## When Policy Topic is covered
Implantation of intrastromal corneal ring segments may be considered **medically necessary** for the treatment of keratoconus in patients 21 years of age or older who meet the following criteria:

- The patient has experienced a progressive deterioration in their vision, such that they can no longer achieve adequate functional vision with contact lenses or spectacles; **AND**
- Corneal transplantation is the only alternative to improve their functional vision; **AND**
- The patient has a clear central cornea with a corneal thickness of 450 microns or greater at the proposed incision site.

## When Policy Topic is not covered
Implantation of intrastromal corneal ring segments is considered **not medically necessary** as a treatment of myopia.

Implantation of intrastromal corneal ring segments is considered **investigational** for all other conditions.

## Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Individuals:  
- With keratoconus  
- With pellucid marginal degeneration | Interventions of interest are:  
- Intrastromal corneal ring segments | Comparators of interest are:  
- Penetrating keratoplasty | Relevant outcomes include:  
- Change in disease status  
- Functional outcomes  
- Treatment-related morbidity |
| Individuals:  
- Astigmatism | Interventions of interest are: | Comparators of interest are: | Relevant outcomes include:  
- Change in disease status |
<table>
<thead>
<tr>
<th>following penetrating keratoplasty</th>
<th>Intrastromal corneal ring segments</th>
<th>Contact lens or spectacle correction</th>
<th>Functional outcomes</th>
<th>Treatment-related morbidity</th>
</tr>
</thead>
</table>

Intrastromal corneal ring segments are composed of microthin soft plastic inserts of variable thickness that are placed in the periphery of the cornea. Intrastromal corneal ring segments have been investigated as a means of improving vision in diseases such as keratoconus and pellucid marginal degeneration, and for refractive surgery to correct mild myopia and astigmatism following penetrating keratoplasty (PK).

The evidence on intrastromal corneal ring segments in patients who have keratoconus, pellucid marginal degeneration, and astigmatism following PK includes primarily single-institution case series. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. For eyes with keratoconus there are a number of prospective series that have shown improvement in visual function from baseline to posttreatment, although data on net health outcome in the long-term are limited. For pellucid marginal degeneration and astigmatism following PK, there are very limited data at this time. The evidence is insufficient to determine the effects of the technology on health outcomes.

Although questions remain regarding the impact of this procedure on long-term health outcomes, the risk of adverse events is decreased compared with the existing alternative (corneal transplant), and there is a potential (as yet unproven) to delay the need for the more invasive procedure. In addition, clinical input strongly supported the use of intrastromal corneal ring segments in a select group of patients with advanced keratoconus whose only other option for restoration of visual function is the more invasive PK. Therefore, use of intrastromal corneal ring segments may be considered medically necessary in patients who meet the U.S. Food and Drug Administration humanitarian device exemption criteria for use of this device. Myopia can be addressed by contact lens or spectacles, therefore, intrastromal corneal ring segments are considered not medically necessary for this indication.

**Background**

Intrastromal corneal ring segments consist of microthin soft plastic inserts of variable thickness that are placed in the periphery of the cornea. An incision is made in the cornea, and channels are created in it by rotating a lamellar dissector or by using a femtosecond laser. One or 2 corneal implant segments are introduced to each channel, and various implants with a range of implant thicknesses are available for different degrees of correction. They affect refraction in the eye by physically changing the shape of the cornea (flattening the front of the eye), thereby correcting the irregular corneal shape. If required, the implants can be removed at a later date. Intrastromal corneal ring segments have been investigated as a means of improving vision in diseases such as keratoconus and pellucid marginal degeneration, and for refractive surgery to correct mild myopia and astigmatism after penetrating keratoplasty (PK).
Keratoconus is a progressive bilateral dystrophy that is characterized by paracentral steepening and stromal thinning that impairs visual acuity. Initial treatment often consists of hard contact lenses. A penetrating keratoplasty (ie, corneal grafting) was traditionally considered the next line of treatment in patients who developed intolerance to contact lenses. While visual acuity is typically improved with keratoplasty, perioperative complications are an associated risk; long-term topical steroid use is required; and endothelial cell loss occurs over time, which is a particular concern in younger patients. As an alternative, a variety of keratorefractive procedures have been attempted, broadly divided into subtractive and additive techniques. Subtractive techniques include photorefractive keratectomy or laser in situ keratomileusis (LASIK), but, in general, results of these techniques have been poor. In deep anterior lamellar keratoplasty, pathologic corneal stromal tissue is selectively removed to the level of the Descemet membrane; followed by transplantation of a donor graft. Implantation of intrastromal corneal ring segments represents an additive technique in which the implants are intended to reinforce the cornea, prevent further deterioration, and potentially obviate the need for a penetrating keratoplasty.

Pellucid marginal degeneration is a noninflammatory progressive degenerative disease, typically characterized by bilateral peripheral thinning (ectasia) of the inferior cornea. Deterioration of visual function results from the irregular astigmatism induced by asymmetric distortion of the cornea, and visual acuity typically cannot be restored by using spherocylindrical lenses. Rigid gas permeable contact lenses may be used to treat pellucid marginal degeneration. Intracorneal ring segment implantation, crescentic lamellar keratoplasty, penetrating keratoplasty, and corneal wedge excision have also been proposed.

In myopia, intrastromal inserts correct myopia by flattening the center of the cornea and represent an alternative to LASIK and other refractive surgeries. The proposed advantages of the intrastromal corneal rings are that their insertion does not affect the central cornea and, thus, their effect is not related to the healing process in the cornea. No corneal tissue is removed, and the implants are reversible. However, mild myopia is effectively treated with either spectacles or contact lenses.

**Regulatory Status**
INTACS® represents an intrastromal corneal ring that has received approval by the U.S. Food and Drug Administration (FDA) for two indications.

In 1999, INTACS inserts were approved through a premarket approval process (PMA) for the following labeled indication:

“The KeraVision Intacs are intended for the reduction or elimination of mild myopia (-1.00 to -3.00 diopters spherical equivalent at the spectacle plane) in patients:
- Who are 21 years of age or older;
With documented stability of refraction as demonstrated by a change of less than or equal to 0.50 diopter for at least 12 months prior to the preoperative examination; and

- Where the astigmatic component is +1.00 diopter or less.”

In 2004, INTACS received an additional approval by the FDA through the humanitarian device exemption (HDE) process for the following indication:

“This device is indicated for the reduction or elimination of myopia and astigmatism in patients with keratoconus, who are no longer able to achieve adequate vision with their contact lenses or spectacles, so that their functional vision may be restored and the need for a corneal transplant procedure may potentially be deferred. The specific set of keratoconic patients proposed to be treated with INTACS prescription inserts are those patients:

- Who have experienced a progressive deterioration in their vision, such that they can no longer achieve adequate functional vision on a daily basis with their contact lenses or spectacles;
- Who are 21 years of age or older;
- Who have clear central corneas;
- Who have a corneal thickness of 450 microns or greater at the proposed incision site; AND
- Who have corneal transplantation as the only remaining option to improve their functional vision.”

Note: HDE does not require the manufacturer to provide data confirming the efficacy of the device but rather data supporting its “probable” benefit. The HDE process is available for devices treating conditions that affect fewer than 4,000 Americans per year.

Intrastromal corneal ring devices available outside of the U.S. include:

- INTACS SK
- Ferrara intrastromal corneal ring segment (ICRS)
- Keraring intrastromal corneal ring segments (ICRS)
- MyoRing intracorneal continuous ring (ICCR)

Rationale
This evidence review was created in 2005 and has since been updated periodically using the MEDLINE database. The most recent literature review was performed through February 8, 2016.

Keratoconus
The published data on Intacs for keratoconus consists primarily of single-institution case series.\(^1\,^2\) These case series indicate that a substantial proportion of patients with keratoconus treated with this device have improved vision at up to 5-year follow-up. Most studies have reported improvements (in uncorrected or corrected visual acuity) in 75% to 80% of patients in whom changes in 2 to 3 lines
of corrected or uncorrected visual acuity was considered a success.\textsuperscript{3-6} Approximately 10% of patients required a second procedure because of an unsatisfactory initial result.\textsuperscript{4,2}

For example, in 2007 Colin and Malet reported 2-year follow-up from a prospective, single-center European study in 100 eyes with keratoconus (82 consecutive patients) and Intacs implantation.\textsuperscript{8} Patients had been referred for a penetrating keratoplasty procedure due to contact lens intolerance for correction of myopia and irregular astigmatism. Intacs inserts were removed from 4 (4%) eyes due to poor visual outcome or extrusion, and 14 eyes were lost to follow-up. Of the 82 remaining eyes (68 patients), both corrected and uncorrected visual acuity remained relatively stable between 1 and 2 years of follow-up.

Several retrospective studies have reported stable vision at up to 10 years after Intacs implantation. Bedi et al evaluated the risk of keratoconus progression in a study of 105 consecutive eyes (85 patients) that had undergone Intacs implantation.\textsuperscript{9} At 1-year follow-up, 1 eye had extrusion and 12 (11.4%) had undergone removal of Intacs because of unsatisfactory results; these eyes were managed by penetrating or deep lamellar keratoplasty. Of the 105 eyes, 80% retained the Intacs implant and showed no keratoconus progression over 5 years of follow-up. Vega-Estrada et al reported that, in a series of 51 eyes, the improvement in vision obtained at 6 months after Intacs implantation was maintained out to 5 years postoperatively, although this study only included cases without significant changes in corneal topography over the 12 months prior to surgery.\textsuperscript{10} Kymionis et al reported 5-year follow-up on 28 patients (36 eyes) who had initially participated in a clinical trial for safety and efficacy of Intacs implantation in patients with keratoconus.\textsuperscript{11} In 5 patients (7 eyes), the Intacs segments were removed due to patient dissatisfaction. Five-year follow-up was reported for 17 (59%) eyes. Refractive stability was obtained at the 6-month follow-up and remained stable throughout the 5-year follow-up. Ten-year follow-up of 30 patients (36 eyes) with keratoconus treated with the Ferrara ring was reported in 2014.\textsuperscript{12} Only patients who returned for follow-up were included in the study and exactly how many patients had undergone the procedure was not reported. Excluding 2 eyes that had Ferrara ring exchange and 2 that underwent keratoplasty, mean corrected distance visual acuity improved from 20/55 at baseline to 20/35 at 5 years and 20/38 at 10 years. There was no significant change between 5 years and 10 years (p=0.292), suggesting stabilization of keratoconus.

**Pellucid Marginal Degeneration**

In 2009, Pinero et al published a European multicenter retrospective analysis of 21 consecutive eyes in 15 patients who had been implanted with ICRS (3 Intacs, 18 KeraRings) for pellucid marginal degeneration. All subjects had experienced reduced best spectacle-corrected visual acuity (BSCVA) and/or contact lens intolerance or dissatisfaction prior to implantation.\textsuperscript{13} At 6 months after surgery, uncorrected visual acuity had not changed; 17% of eyes lost lines of BCVA, and 44% of eyes gained 2 or more lines of BSCVA. Ring explantation was performed in
4 eyes (19%) due to visual deterioration during the follow-up. Mean keratometry decreased 1.76 D, from 44.95 to 43.19 D at 6 months postoperatively (p<0.01).

A 2010 publication from Europe reported a retrospective analysis of ICRS implantation (210° arc length KeraRing) in 16 consecutive eyes of 10 patients with pellucid marginal degeneration who had reduced BSCVA and dissatisfaction with spectacle and contact lens-corrected vision. At 12 months after implantation, uncorrected visual acuity improved from 1.69 to 0.83 logMAR. At the 36-month follow-up, patients (n=11) had gained a mean of 2.4 lines uncorrected visual acuity and 3.3 lines of BSCVA. There was a statistically significant reduction in manifest spherical refraction from -2.43 to -0.72 D. For the 11 patients who completed 36-month follow-up, there was no significant change in outcome measures between 12 months and 36 months. No intraoperative or postoperative complications were noted aside from white deposits around the segments in 1 patient.

Astigmatism After Penetrating Keratoplasty
Several case series from Europe and South America have been identified in which ICRS were implanted to correct residual astigmatism after penetrating keratoplasty. In 1 of the studies, 9 patients received ICRS (KeraRings) for high astigmatism (>4 diopters [D]) after the procedure. Mean keratometry decreased 4.17 D (from 46.28 to 42.11). Of the 9 patients, 1 reported night halos and 2 had the implant removed due to compulsive eye rubbing and vascularization in the stromal tunnel. The authors noted that in patients with a corneal transplant with a diameter of 7.5 mm or smaller, Intacs implants should not be used because the segments would be in close proximity to the graft-host junction.

Adverse Events
Literature searches have identified case reports of adverse events following implantation of ICRS, including persistent pain, extrusion, traumatic shattering, bacterial keratitis, fungal keratitis, corneal edema, deep corneal vascularization, Descemet membrane detachment, and alterations of extracellular matrix components and proteinases. In a multicenter series of 251 ICRS implantations, 58 eyes of 47 patients had the devices explanted. The main cause was extrusion (48%), followed by poor refractive outcome (38%), keratitis (7%), and corneal melting and perforation (7%). The time from implantation to explantation ranged from 0.1 to 82 months.

In another study, 6 of 20 eyes had “significant” problems at 3 to 6 months postoperatively regarding corneal thinning and subsequent ring exposure, and a dense corneal infiltrate developed in 1 patient at 7 months. Histopathologic examination of 8 eyes that underwent penetrating keratoplasty after removal of Intacs implants revealed keratocyte apoptosis. Further study is needed to determine whether Intacs reduces or accelerates corneal thinning and progression of keratoconus over the long term.
Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.

- **Table 1. Summary of Key Trials**

<table>
<thead>
<tr>
<th>No.</th>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ongoing</td>
<td>Randomized Study of Safety and Effectiveness of Corneal Collagen Crosslinking and Intacs for Treatment of Keratoconus and Corneal Ectasia</td>
<td>160</td>
<td>Dec 2016</td>
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<tr>
<td></td>
<td>NCT01112072</td>
<td></td>
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<tr>
<td></td>
<td>INTACS (Intrastromal Corneal Ring Segments) for Corneal Ectasia</td>
<td>1000</td>
<td>Jun 2025</td>
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<td></td>
<td>NCT02512432</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Unpublished</td>
<td>Randomized Study of Corneal Collagen Cross-Linking With the UV-X System for the Treatment of Keratectasia in Eyes With Intacs Compared to Eyes Without Intacs</td>
<td>400</td>
<td>Jun 2015</td>
</tr>
<tr>
<td></td>
<td>NCT01081561</td>
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</tbody>
</table>

NCT: national clinical trial.

Summary of Evidence
The evidence for intrastromal corneal ring segments (ICRS) in individuals who have keratoconus, pellucid marginal degeneration, or astigmatism following penetrating keratoplasty (PK) includes primarily single-institution case series. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. For eyes with keratoconus, a number of prospective series have shown improvement in functional vision from baseline to posttreatment, although data on net health outcome in the long term are limited. For pellucid marginal degeneration and astigmatism following PK, there are very limited data at this time. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received through 1 physician specialty society and 3 academic medical centers while this policy was under review in 2009. The input considered implantation of intrastromal corneal ring segments to be medically necessary for selected patients with keratoconus when the only other option for improving visual acuity is corneal transplantation. The input agreed that implantation of intrastromal corneal ring segments is not medically necessary as a treatment of myopia.
Practice Guidelines and Position Statements
The U.K.’s National Institute for Health and Clinical Excellence issued guidance in 2007 on corneal implants for keratoconus. The guidance, based on 9 case series, 1 nonrandomized controlled trial, and specialist advisors’ opinions, concluded that “[c]urrent evidence on the safety and efficacy of corneal implants for keratoconus appears adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance.”

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

References


Billing Coding/Physician Documentation Information

0099T  Implantation of intrastromal corneal ring segments (Deleted code 1/1/2016)

65785  Implantation of intrastromal corneal ring segments (New code 1/1/2016)

66999  Unlisted procedure, anterior segment of eye

ICD-10 Codes

H18.601-  Keratoconus code range

H18.629

Additional Policy Key Words

N/A

Policy Implementation/Update Information

12/1/05  New policy. Added to Surgery section.

6/1/06  No policy statement changes.

12/1/06  No policy statement changes.

6/1/07  No policy statement changes.

12/1/07  No policy statement changes.

6/1/08  No policy statement changes.

12/1/08  No policy statement changes.

6/1/09  No policy statement changes.

9/10/09  Policy statement revised; may be medically necessary in specified conditions.

11/1/10  No policy statement changes.

11/1/11  No policy statement changes.

11/1/12  No policy statement changes.

11/1/13  No policy statement changes.

11/1/14  No policy statement changes.

11/1/15  No policy statement changes.

11/1/16  No policy statement changes.

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational
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