Kansas City

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Implantation of Intrastromal Corneal Ring Segments (INTACS)

Policy Number: 9.03.14 **Last Review:** 11/2013
Origination: 12/2005 **Next Review:** 11/2014

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 indications.

Description of Procedure or Service

Intrastromal corneal ring segments consist of micro-thin 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.

Intrastromal corneal ring segments are flexible, crescent-shaped rings of polymethylmethacrylate 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 two 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.

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 (i.e., corneal grafting) is the next line of treatment in patients who develop 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, pathological 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 laser in situ keratomileusis (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.

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 policy was created in 2005 and has since been updated periodically using the MEDLINE database. The most recent literature update was performed for the period of August 2012 through August 13, 2013.

Literature Review

Myopia
Approval by the U.S. Food and Drug Administration (FDA) for the INTACS® device was based on the results of a multi-institutional study involving 361 subjects with mild myopia. Subsequently, the 2-year results of this study were published in the peer-reviewed literature. (1) These data suggested that the intrastromal rings predictably and effectively reduced or eliminated mild myopia (-1.00 to -3.00 diopter) and that the refractive effect was stable over time. However, mild myopia is effectively treated with either spectacles or contact lenses. Therefore, this application of INTACS is considered not medically necessary. In addition, as noted in the Benefits Applications section, many Plan benefits or contracts contain a specific exclusion for refractive eye surgeries.

Keratoconus
The published data regarding INTACS for keratoconus consists primarily of single institution case series. These case series indicate that a substantial proportion of patients with keratoconus treated with this system have improved vision at 2-5) Approximately 10% of patients required a second procedure because of an unsatisfactory initial result. (3, 6) ~~short-term~~ 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 2–3 lines of corrected or uncorrected visual acuity were considered success. (

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. (7) 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 eyes (4%) 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' follow-up.

Several retrospective studies have reported stable vision at up to 5 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. (8) 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 before surgery. (9)

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. (10) In 5 patients (7 eyes), the INTACS segments were removed due to patient dissatisfaction. Five-year follow-up was reported for 17 eyes (59%). Refractive stability was obtained at the 6-month follow-up (spherical equivalent error at baseline -5.54 to -2.68 at 6 months) and remained stable throughout the 5-year follow-up (-3.02).

One retrospective study compared outcomes between intrastromal corneal ring segments (Keraring, n=30) and deep anterior lamellar keratoplasty (DALK, n=36) in patients with advanced keratoconus. (11) One eye in the DALK group was converted to penetrating keratoplasty and was not included in the analysis. At 24 months' follow-up, compared to preoperatively, the DALK group had significantly greater improvement in uncorrected and corrected distance visual acuity and significantly greater reduction in spherical equivalent, manifest cylinder, and K values. The uncorrected distance visual acuity improved by at least 1 line in all eyes in the DALK group. In the intrastromal corneal ring segment group, uncorrected distance visual acuity improved in 24 (80%) eyes, remained unchanged in 3 (10%) eyes, and decreased in 3 (10%) eyes.

Ongoing randomized clinical trials are evaluating combined treatment with INTACS and corneal collagen cross-linking to slow the progression of keratoconus (see policy No. 9.03.28 Corneal Collagen Cross-Linking).

Astigmatism after Penetrating Keratoplasty
Several case series from Europe and South America have been identified in which intrastromal ring segments have been implanted for the correction of residual astigmatism after penetrating keratoplasty. In one of the studies 9 patients received intrastromal ring segments (Kerarings) for high astigmatism (greater than 4 diopters) after penetrating keratoplasty. (12) Mean keratometry decreased 4.17 diopters (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 intrastromal ring segments should not be used because the segments would be close to the graft-host junction.

Pellucid Marginal Degeneration
In 2009, Pinero and colleagues published a European multicenter retrospective analysis of 21 consecutive eyes in 15 patients with intrastromal corneal ring implantation (3 INTACS and 18 Kerarings) for pellucid marginal degeneration who had reduced best-corrected visual acuity and/or contact lens intolerance or dissatisfaction. (13) At 6 months after surgery, uncorrected visual acuity had not changed; 17% of eyes lost lines of best-corrected visual acuity, and 44% of eyes gained 2 lines or greater of best-corrected visual acuity. Ring explantation was performed in 4 eyes (19%) due to visual deterioration during the follow-up. Mean keratometry decreased 1.76 diopters, from 44.95 diopters to 43.19 diopters at 6-months postoperatively.

A 2010 publication from Europe reported a retrospective analysis of intrastromal ring segment implantation (210-degree arc length Keraring) in 16 consecutive eyes of 10 patients with pellucid marginal degeneration who had reduced best-corrected visual acuity and dissatisfaction with spectacle and contact lens-corrected vision. (14) At 12 months after implantation, uncorrected visual acuity improved from 1.69 logMAR 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 spectacle-corrected visual acuity. There was a statistically significant reduction in manifest spherical refraction from -2.43 diopters to -0.72 diopters. For the 11 patients who completed 36-month follow-up, there was no significant change in outcome measures between 12 and 36 months. No intraoperative or postoperative complications were noted aside from white deposits around the segments in 1 patient.

Adverse events
Updated literature searches have identified a number of case reports of adverse events following implantation of intrastromal corneal ring segments, including persistent pain, extrusion, traumatic shattering, bacterial keratitis, fungal keratitis, corneal edema, deep corneal vascularization, Descemet membrane's detachment, and alterations of extracellular matrix components and proteinases. In a multicenter series of 251 intrastromal corneal ring segment implantations, 58 eyes of 47 patients had the devices explanted. (15) The main cause was found to be 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” postoperative problems with regards to thinning and ring exposure, and a dense corneal infiltrate developed in 1 patient at 7 months. (16) Histopathologic examination of 8 eyes that underwent penetrating keratoplasty after removal of INTACS inserts revealed keratocyte apoptosis. (17) Further study long-term is needed to determine whether INTACS reduce or accelerate corneal thinning and progression of keratoconus.

Ongoing Clinical Trials
A search of online site ClinicalTrials.gov in August 2013 identified 2 large randomized trials on the treatment of keratoconus with combined use of intrastromal corneal ring segments and collagen cross-linking. A Phase II/III randomized trial (NCT01081561) will compare corneal collagen cross-linking in eyes with INTACS compared to eyes without INTACS. The study has an estimated enrollment of 400 subjects with estimated completion in 2015. Another Phase III trial (NCT01112072) will randomly assign subjects to receive collagen cross-linking immediately after, or 3 months after, INTACS implantation. Estimated enrollment is 160 subjects, with an estimated completion date of December 2014 April 2011.

Clinical Input Received through 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.

Summary
Clinical input strongly supports 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 penetrating keratoplasty. Although questions remain regarding the impact of this procedure on long-term health outcomes, the risk of adverse events is decreased in comparison with the existing alternative (corneal transplant), and there is a potential (as yet unproven) to delay the need for the more invasive procedure. Therefore, use of intrastromal corneal ring segments may be considered medically necessary in patients who meet the FDA-HDE criteria for use of this device.

There is insufficient evidence to evaluate health outcomes in patients with pellucid marginal deterioration. Therefore, intrastromal corneal ring segments in this population are considered investigational.

Practice Guidelines and Position Statements
The United Kingdom’s National Institute for Health and Clinical Excellence (NICE) issued guidance in 2007 on corneal implants for keratoconus. (18) The guidance, based on 9 case series, 1 nonrandomized controlled trial, and specialist advisors’ opinion concluded that “current 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.”

Medicare National Coverage
There is no national coverage determination.

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Billing Coding/Physician Documentation Information

0099T Implantation of intrastromal corneal ring segments
66999 Unlisted procedure, anterior segment of eye

Additional Policy Key Words

N/A

Policy Implementation/Update Information

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