Name of Policy:
Implantation of Intrastromal Corneal Ring Segments (ICRS®, INTACS®)

Policy #: 080 Latest Review Date: November 2013
Category: Surgical Policy Grade: B

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**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 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.

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.

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 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. This technique has primarily been investigated in patients in whom the cornea has remained transparent and who are intolerant of contact lenses.

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.

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

**Policy:**

**Effective for dates of service on or after June 4, 2013:**

**Implantation of intrastromal corneal ring segments meets** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for the treatment of **keratoconus in patients 21 years of age or older** who meet **all** 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.

**Implantation of intrastromal corneal ring segments does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage as a treatment of **myopia**.

**Implantation of intrastromal corneal ring segments does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered investigational for all other conditions.

**Effective for dates of service June 7, 2005 through June 3, 2013:**

**Intrastromal corneal ring segments (INCRS®, INTACS®) meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage only for treatment of keratoconus in patients 21 years of age or older when **all** of the following criteria are met:
- The patient is no longer able to achieve vision of at least 20/40 or better with best correction of contact lenses or spectacles; **and**
- The patient demonstrates an inability to perform activities of daily living (ADLs); **and**
- The procedure will reduce or eliminate myopia and/or astigmatism; **and**
- The procedure will restore functional vision; **and**
- The procedure will defer the need for corneal transplant procedure.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administer benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.
Key Points:
Keratoconus is an eye condition in which the shape of the cornea bulges and becomes conical, resulting in thinning and eventual scarring of the central cornea. Approximately 100 to 200 per 100,000 people have keratoconus. It occurs in all races and 85% of cases are bilateral. Onset occurs in puberty. Progression occurs slowly over decades, and often stabilizes as the patient enters his/her 40’s. The disorder affects women more often than men, and occurs more frequently in patients with Down’s syndrome (5%-8% of Down’s patients), Marfan’s syndrome, Addison’s disease, neurofibromatosis, allergies, and congenital amaurosis. Keratoconus is also associated with atopic disease (atopic or allergic dermatitis, allergic rhinitis, asthma) and connective tissue disorders.

The characteristic thinning and protrusion of the central and/or paracentral cornea results in the common symptoms of keratoconus; i.e. corneal distortion, photophobia, halos around lights, decreased vision, and monocular diplopia.

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 2011 through August 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 two-year results of this study were published in the peer-reviewed literature. 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.

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 up to a five year follow-up. 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. Approximately 10% of patients required a second procedure because of an unsatisfactory initial result.

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. 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 one 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 three (10%) eyes, and decreased in three (10%) eyes.

In 2007, Colin and Malet reported two-year follow-up from a prospective, single-center European study in 100 eyes with keratoconus (82 consecutive patients) and INTACS implantation. 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 four 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 one- and two-years’ follow-up. Central corneal thickness decreased from 478 microns preoperatively to 434 microns at one year and 421 microns at two years. The authors note that this finding may have resulted from slight stretching of the corneal tissue by the segments rather than a disease-related progressive thinning of the cornea.

Bedi et al evaluated the long-term risk of keratoconus progression in a retrospective study of 105 consecutive eyes (85 patients) that had undergone INTACS implantation. The definition of preoperative keratoconus progression was a change in steep K of 1.00 diopters (D) or greater over a 12-month period. The definition of postoperative keratoconus progression was a change in steep K of 1.00 D or greater over a period of four years between one- and five-year follow-up. At one-year follow-up, one 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. At five-year follow-up, 84 (91.3%) of the remaining 92 eyes demonstrated no postoperative progression. No significant differences were noted in mean steep, flat, and average keratometry, manifest refraction spherical equivalent, and uncorrected and corrected distance visual acuity between one- and five-year follow-up. In a sub-group analysis of the 56 eyes with documented preoperative progression, 52 (92.9%) had no postoperative progression. Of the 105 eyes, 80% retained the INTACS implant and showed no keratoconus progression over five years of follow-up. Vega-Estrada et al reported that in a series of 51 eyes, the improvement in vision obtained at six months after INTACS implantation was maintained out to five years postoperatively, although this study only included cases without significant changes in corneal topography over the 12 months before surgery.

Kymionis et al reported five-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. In five patients (seven eyes), the INTACS segments were removed due to patient dissatisfaction. An additional eight patients (12 eyes) were unable to attend follow-up appointments. Five-year follow-up was reported for the remaining 17 eyes (59%). Refractive stability was obtained at the six-month follow-up (spherical equivalent error at baseline -5.54 to -2.68 at six months) and remained stable throughout the five-year follow-up (-3.02). With the exception of one eye that had a decrease of three lines, the best-corrected visual acuity was maintained to the pre-INTACS level. Keratometric values showed a mean reduction of 1.57 diopters (49.59 to 48.02 diopters).

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Ongoing randomized clinical trials are evaluating combined treatment with INTACTS and corneal collagen crow-linking to slow the progression of keratoconus.

**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 nine patients received intrastromal ring segments (Kerarings) for high astigmatism (greater than 4 diopters) after penetrating keratoplasty. Mean keratometry decreased 4.17 diopters (from 46.28 to 42.11). Of the nine patients, one reported night halos, and two 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 (three INTACS and 18 Kerarings) for pellucid marginal degeneration who had reduced best-corrected visual acuity and/or contact lens intolerance or dissatisfaction. At six months after surgery, uncorrected visual acuity had not changed; 17% of eyes lost lines of best-corrected visual acuity, and 44% of eyes gained two lines or greater of best-corrected visual acuity. Ring explantation was performed in four 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 six-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 ten patients with pellucid marginal degeneration who had reduced best-corrected visual acuity and dissatisfaction with spectacle and contact lens-corrected vision. 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 one patient.
**Adverse events**

Updated literature searches, the most recent performed through July 2012, 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. 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, six of 20 eyes had “significant” postoperative problems with regards to thinning and ring exposure, and a dense corneal infiltrate developed in one patient at seven months. Histopathologic examination of eight eyes that underwent penetrating keratoplasty after removal of INTACS inserts revealed keratocyte apoptosis. Further study long-term is needed to determine whether INTACS reduce or accelerate corneal thinning and progression of keratoconus.

**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.

**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. The guidance, based on nine case series, one 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.”

**Key Words:**

Intrastromal corneal ring segments, INCRS, INTACS, intracorneal rings, keratoconus, KeraVision Intacs, INTACS SK, Ferrara intrastromal corneal ring segment (ICRS), Keraring intrastromal corneal ring segments (ICRS), MyoRing intracorneal continuous ring (ICCR)
Approved by Governing Bodies:
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)

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: LASIK, INTACS, radial keratotomy, and other refractive services are not covered.
Pre-certification/Pre-determination requirements: Not applicable
Coding:

CPT code: 0099T  Implantation of intrastromal corneal ring segments

References:

Policy History:
Medical Policy Group, October 2002 (2)
Medical Policy Group, November 2002
Medical Policy Administration Committee, July 2003
Available for comment July 28-September 10, 2003
Medical Policy Group, December 2004 (1)
Medical Policy Group, June 2005 (1)
Medical Policy Administration Committee, July 2005
Available for comment July 28-September 10, 2005
Medical Policy Group, December 2006 (1)
Medical Policy Administration Committee, January 2007
Available for comment January 11-February 24, 2007
Medical Policy Group, February 2008 (2)
Medical Policy Administration Committee, February 2008
Medical Policy Group, September 2009 (1)
Medical Policy Administration Committee, October 2009
Available for comment October 2-November 16, 2009
Medical Policy Group, September 2011 (1) Update to Key Points, Benefit Application and References
Medical Policy Panel, September 2012
Medical Policy Group, March 2013 (2) Policy coverage statement for keratoconus revised. Non-coverage statement for myopia added. Investigational statement for all other indication added. Key Points and References updated to support Policy changes. Additional information added to Governing Body Approval and Key Words.

Medical Policy Administration Committee, April 2013
Available for comments April 18 through June 3, 2013

Medical Policy Panel, September 2013

Medical Policy Group, November 2013 (2) Policy statement unchanged. Key Points and References updated to include results of literature search.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.