Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Keratoprosthesis is addressed separately in medical policy 00450.

Note: Corneal Collagen Cross-Linking is addressed separately in medical policy 00325.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider implantation of intrastromal corneal ring segments (ICRS) as a treatment of keratoconus to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for implantation of intrastromal corneal ring segments (ICRS) as a treatment of keratoconus will be considered when all of the following criteria are met:

- Patients 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; and
- Patients are 21 years of age or older; and
- Patients have clear central corneas; and
- Patients have a corneal thickness of 450 microns or greater at the proposed incision site; and
- Patients who have corneal transplantation as the only other remaining option to improve their functional vision.

Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

When Services Are Considered Investigational

Note: Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers implantation of intrastromal corneal ring segments (ICRS) when criteria are not met to be **investigational.***

Based on review of available data, the Company considers implantation of intrastromal corneal ring segments (ICRS) for all other conditions to be **investigational.***

Note: The correction of refractive errors of the eye is considered an exclusion in most member contracts.

Background/Overview

Vision Disorders

Keratoconus is a progressive bilateral dystrophy characterized by paracentral steepening and stromal thinning that impairs visual acuity.

Pellucid marginal degeneration is a noninflammatory progressive degenerative disease, typically characterized by bilateral peripheral thinning (ectasia) of the inferior cornea. Deterioration of functional vision results from irregular astigmatism induced by asymmetric distortion of the cornea, and visual acuity typically cannot be restored by using spherocylindrical lenses.

Treatment

Initial treatment for keratoconus 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 penetrating 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, although, generally, 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 penetrating keratoplasty.

Rigid gas permeable contact lenses may be used to treat pellucid marginal degeneration. Intrastromal corneal ring segments, crescentic lamellar keratoplasty, penetrating keratoplasty, and corneal wedge excision have also been proposed as treatments.

Intrastromal corneal ring segments correct myopia by flattening the center of the cornea and represent an alternative to laser in situ keratomileusis and other refractive surgeries. A proposed advantage of intrastromal corneal ring segments is 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 may be removed or replaced. However, mild myopia is effectively treated with spectacles or contact lenses.

Intrastromal Corneal Ring Segments
Intrastromal corneal ring segments are composed of microthin soft plastic inserts of variable thickness that are placed in the periphery of the cornea. They are inserted through an incision made in the cornea, into which channels have been created by rotating a lamellar dissector or by using a femtosecond laser. One or 2 segments are implanted in each channel, and various implants with a range of 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 and restoring a degree of functional vision. If required, the implants can be removed or replaced at a later date.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Intacs®‡, an intrastromal corneal ring, was approved by the U.S. Food and Drug Administration (FDA) for 2 indications. In 1999, Intacs (KeraVision, now Addition Technology) was approved by the FDA through the premarket approval process for the following labeled indication:

Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

"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 additional approval by the FDA through the humanitarian device exemption 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: The humanitarian device exemption does not require manufacturers to provide data confirming the efficacy of a device but rather data supporting its "probable" benefit. The humanitarian device exemption process is available for devices treating conditions that affect fewer than 4000 Americans per year.

Intrastromal corneal ring segments devices available outside of the United States include:

- Intacs SK
- Ferrara intrastromal corneal ring segments
- KeraRing intrastromal corneal ring segments
- MyoRing intracorneal continuous ring.

Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

FDA product code: LQE.

Rationale/Source

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

For individuals who have keratoconus who receive intrastromal corneal ring segments, the evidence includes primarily single-institution case series. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. A number of single-center case series with sample sizes ranging from 19 to 105 eyes have been published. These series have generally reported that a substantial proportion of patients with keratoconus treated with this device have improved vision at 1 to 2 years of follow-up. More limited data are available on long-term efficacy. Intrastromal corneal ring segments is associated with a number of adverse events and explantation. Although, a single case series of 572 eyes have suggested that risk of explantation may be modest (6.1%). The net health outcome is uncertain. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2009 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 functional vision was the more invasive penetrating keratoplasty. Some clinicians may opt to delay a more invasive procedure, although the success rate of this strategy is as yet unproven. Therefore, use of intrastromal corneal ring segments may be considered medically necessary in patients with keratoconus who meet the U.S. Food and Drug Administration humanitarian device exemption criteria for use of this device.

For individuals who have pellucid marginal degeneration who receive intrastromal corneal ring segments, the evidence includes a few case series. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. A small number of case series with fewer than 25 eyes per study have evaluated intrastromal corneal ring segments in patients with pellucid marginal degeneration. Most reports have assessed devices not available in the United States. In 1 study, which included some patients implanted with Intacs, there was no improvement in uncorrected

visual acuity 6 months after surgery. Moreover, explantation occurred in about 20% of eyes due to visual deterioration. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have astigmatism after penetrating keratoplasty who receive intrastromal corneal ring segments, the evidence includes a few case series. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. Two case series, with 9 and 54 patients, were identified; both used devices not available in the United States. Intrastromal corneal ring segments was associated with adverse events such as extrusion and Descemet membrane detachment. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Clinical Input 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. Input considered implantation of intrastromal corneal ring segments to be medically necessary for select patients with keratoconus when the only other option for improving visual acuity is corneal transplantation. Input agreed that implantation of intrastromal corneal ring segments is not medically necessary for treatment of myopia.

Practice Guidelines and Position Statements

In 2007, the National Institute for Health and Care Excellence (NICE) issued guidance on corneal implants for keratoconus. The guidance, based on 9 case series, a nonrandomized controlled trial, and specialists' 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…."

U.S. Preventive Services Task Force Recommendations

Not applicable.

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

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

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02138669	Intacs for Keratoconus	25	Dec 2021
NCT02512432	INTACS (Intrastromal Corneal Ring Segments) for Corneal Ectasia	1000	Jun 2025

NCT: national clinical trial.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Implantation of Intrastromal Corneal Ring Segments", 9.03.14, 4:2020.
2. Zadnik K, Money S, Lindsley K. Intrastromal corneal ring segments for treating keratoconus. Cochrane Database Syst Rev. 2019 May;5:CD011150. PMID 31087649
3. Vega-Estrada A, Alio JL, Brenner LF, et al. Outcomes of intrastromal corneal ring segments for treatment of keratoconus: Five-year follow-up analysis. J Cataract Refract Surg. Aug 2013;39(8):1234-1240. PMID 23747207
4. Alio JL, Shabayek MH, Belda JI, et al. Analysis of results related to good and bad outcomes of Intacs implantation for keratoconus correction. J Cataract Refract Surg. May 2006;32(5):756-761. PMID 16765791
5. Boxer Wachler BS, Christie JP, Chandra NS, et al. Intacs for keratoconus. Ophthalmology. May 2003;110(5):1031-1040. PMID 12750109
6. Colin J. European clinical evaluation: use of Intacs for the treatment of keratoconus. J Cataract Refract Surg. May 2006;32(5):747-755. PMID 16765790

7. Levinger S, Pokroy R. Keratoconus managed with intacs: one-year results. Arch Ophthalmol. Oct 2005;123(10):1308-1314. PMID 16219721
8. Siganos CS, Kymionis GD, Kartakis N, et al. Management of keratoconus with Intacs. Am J Ophthalmol. Jan 2003;135(1):64-70. PMID 12504699
9. Ziaei M, Barsam A, Shamie N, et al. Reshaping procedures for the surgical management of corneal ectasia. J Cataract Refract Surg. Apr 2015;41(4):842-872. PMID 25840308
10. Beniz LA, Queiroz GH, Queiroz CF, et al. Intrastromal corneal ring segments delay corneal grafting in patients with keratoconus. Arq Bras Oftalmol. Feb 2016;79(1):30-32. PMID 26840163
11. Heikal MA, Abdelshafy M, Soliman TT, et al. Refractive and visual outcomes after Keraring intrastromal corneal ring segment implantation for keratoconus assisted by femtosecond laser at 6 months follow-up. Clin Ophthalmol. Jan 2017;11:81-86. PMID 28096650
12. Miraftab M, Hashemi H, Hafezi F, et al. Mid-term results of a single intrastromal corneal ring segment for mild to moderate progressive keratoconus. Cornea. May 2017;36(5):530-534. PMID 27984365
13. Colin J, Malet FJ. Intacs for the correction of keratoconus: two-year follow-up. J Cataract Refract Surg. Jan 2007;33(1):69-74. PMID 17189796
14. Bedi R, Touboul D, Pinsard L, et al. Refractive and topographic stability of Intacs in eyes with progressive keratoconus: five-year follow-up. J Refract Surg. Jun 2012;28(6):392-396. PMID 22589292
15. Kymionis GD, Siganos CS, Tsiklis NS, et al. Long-term follow-up of Intacs in keratoconus. Am J Ophthalmol. Feb 2007;143(2):236-244. PMID 17184717
16. Fernandez-Vega Cueto L, Lisa C, Poo-Lopez A, et al. Intrastromal corneal ring segment implantation in 409 paracentral keratoconic eyes. Cornea. Nov 2016;35(11):1421-1426. PMID 27490048
17. Izquierdo L, Mannis MJ, Mejias Smith JA, et al. Effectiveness of Intrastromal Corneal Ring Implantation in the Treatment of Adult Patients With Keratoconus: A Systematic Review. J Refract Surg. 2019 Mar;35(3). PMID 30855097
18. Kang MJ, Byun YS, Yoo YS, et al. Long-term outcome of intrastromal corneal ring segments in keratoconus: Five-year follow up. Sci Rep. 2019 Jan;9(1). PMID 30670787
19. Nguyen N, Gelles JD, Greenstein SA, et al. Incidence and associations of intracorneal ring segment explantation. J Cataract Refract Surg. 2019 Feb;45(2). PMID 30509748

20. Pinero DP, Alio JL, Morbelli H, et al. Refractive and corneal aberrometric changes after intracorneal ring implantation in corneas with pellucid marginal degeneration. Ophthalmology. Sep 2009;116(9):1656-1664. PMID 19643482
21. Kubaloglu A, Sari ES, Cinar Y, et al. A single 210-degree arc length intrastromal corneal ring implantation for the management of pellucid marginal corneal degeneration. Am J Ophthalmol. Aug 2010;150(2):185-192 e181. PMID 20570241
22. Arriola-Villalobos P, Diaz-Valle D, Guell JL, et al. Intrastromal corneal ring segment implantation for high astigmatism after penetrating keratoplasty. J Cataract Refract Surg. Nov 2009;35(11):1878-1884. PMID 19878819
23. Coscarelli S, Ferrara G, Alfonso JF, et al. Intrastromal corneal ring segment implantation to correct astigmatism after penetrating keratoplasty. J Cataract Refract Surg. Jun 2012;38(6):1006-1013. PMID 22624900
24. Ferrer C, Alio JL, Montanes AU, et al. Causes of intrastromal corneal ring segment explantation: clinicopathologic correlation analysis. J Cataract Refract Surg. Jun 2010;36(6):970-977. PMID 20494769
25. Kanellopoulos AJ, Pe LH, Perry HD, et al. Modified intracorneal ring segment implantations (INTACS) for the management of moderate to advanced keratoconus: efficacy and complications. Cornea. Jan 2006;25(1):29-33. PMID 16331037
26. Samimi S, Leger F, Touboul D, et al. Histopathological findings after intracorneal ring segment implantation in keratoconic human corneas. J Cataract Refract Surg. Feb 2007;33(2):247-253. PMID 17276265
27. National Institute for Health and Care Excellence (NICE). Corneal implants for keratoconus [IPG227]. 2007; https://www.nice.org.uk/guidance/IPG227.

Policy History

Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

04/05/2005	Medical Director review
04/27/2005	Medical Policy Committee review
05/23/2005	Managed Care Advisory Council approval
02/01/2006	Medical Director review
02/15/2006	Medical Policy Committee review. Coverage changed from investigational to eligible with criteria.

Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

02/23/2006	Quality Care Advisory Council approval
07/07/2006	Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
04/04/2007	Medical Director review
04/18/2007	Medical Policy Committee approval
06/13/2007	Medical Director review
06/20/2007	Medical Policy Committee approval. When services are considered not medically necessary section was deleted. Myopia was deleted from the statement "BCBS considers ICRS as a treatment of any other condition except keratoconus and myopia to be investigational".
06/13/2007	Medical Director review
06/20/2007	Medical Policy Committee approval
07/02/2008	Medical Director review
07/16/2008	Medical Policy Committee approval. No change to coverage eligibility.
06/04/2009	Medical Director review
06/17/2009	Medical Policy Committee approval. No change to coverage eligibility.
06/03/2010	Medical Policy Committee review
06/16/2010	Medical Policy Implementation Committee approval. Title changed to "Implantation of Intrastromal Corneal Ring Segments."
06/02/2011	Medical Policy Committee review
06/15/2011	Medical Policy Implementation Committee approval. No change to coverage.
06/14/2012	Medical Policy Committee review
06/20/2012	Medical Policy Implementation Committee approval. No change to coverage.
06/06/2013	Medical Policy Committee review
06/25/2013	Medical Policy Implementation Committee approval. No change to coverage.
06/05/2014	Medical Policy Committee review
06/18/2014	Medical Policy Implementation Committee approval. No change to coverage.
06/04/2015	Medical Policy Committee review
06/17/2015	Medical Policy Implementation Committee approval. No change to coverage.
06/02/2016	Medical Policy Committee review
06/20/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
06/01/2017	Medical Policy Committee review
06/21/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

06/07/2018 Medical Policy Committee review
06/20/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/06/2019 Medical Policy Committee review
06/19/2019 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/04/2020 Medical Policy Committee review
06/10/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 06/2021

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Implantation of Intrastromal Corneal Ring Segments

Policy # 00164
Original Effective Date: 05/23/2005
Current Effective Date: 07/13/2020

Code Type	Code
CPT	65785
HCPCS	C1780
ICD-10 Diagnosis	H18.601-H18.629

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.