INTRASTROMAL CORNEAL RING SEGMENTS

Policy Number: 2014T0486J
Effective Date: February 1, 2014

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INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ greatly. In the event of a conflict, the enrollee’s specific benefit document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

COVERAGE RATIONALE

When provided according to U.S. Food and Drug Administration (FDA) labeled indications, intrastromal corneal ring segments (ICRS) implantation is proven for vision correction of mild myopia. Mild myopia is defined as myopia -1.0 to -3.0 diopters.

See also the Benefit Considerations section below. The enrollee-specific benefit document must be reviewed to determine coverage or exclusions.

Intrastromal corneal ring segments (ICRS) implantation is proven for treatment of keratoconus when used according to FDA labeled indications in patients who meet all of the following criteria:

- 21 years of age or older,
- Progressive deterioration of vision such that patients cannot achieve adequate functional vision with eyeglasses or contacts,
- Clear central cornea,

Related Medical Policies:
None

Policy History Revision Information
• Corneal thickness of 450 microns or greater at the proposed incision site, and
• Corneal transplantation is the only remaining option to improve vision

**Intrastromal corneal ring segments (ICRS) implantation is unproven for the following:**
• Ectasia after laser-assisted in situ keratomileusis (LASIK) or after photorefractive keratectomy (PRK) and
• All other indications not listed above as proven.

Clinical trials evaluating ICRS implantation for the correction of other visual conditions are inadequate to establish the safety and efficacy of this procedure. The long-term efficacy of ICRS implantation for ectasia after LASIK or PRK has not been established in well-designed studies. Additional research is needed to establish the role of ICRS implantation for conditions other than those described as proven. Intrastromal corneal ring segments are approved by the U.S. Food and Drug Administration (FDA) for mild myopia and keratoconus (as a Humanitarian Device Exemption). All other conditions such as post-LASIK or post-PRK ectasia are not FDA approved indications for intrastromal corneal ring segments.

**BENEFIT CONSIDERATIONS**

Most Certificates of Coverage (COC) contain an explicit exclusion for vision correction surgery. For example, intrastromal corneal ring segments (ICRS) used to treat myopia or other refractive errors may be excluded from coverage, but ICRS to treat keratoconus may be covered under the COC. The enrollee-specific benefit document must be reviewed to determine coverage or exclusions.

**BACKGROUND**

When eyes are misshapen, vision is affected due to refractive error (i.e., myopia, hyperopia or astigmatism) that prevents images from being focused on the retina. For most patients who have refractive disorders, normal vision can be obtained with corrective aids such as eyeglasses or contact lenses.

Vision may also be affected by keratoconus, a noninflammatory corneal disorder that affects less than 1% of the general population, with onset in the teen and young adult years. Persons with keratoconus have progressive myopia and astigmatism that develop due to progressive corneal steepening and thinning. Although the cause of this disorder is unknown, it can usually be treated successfully with contact lenses. For patients with more severe disease or those who cannot tolerate contact lenses, surgery may be indicated. The most common surgery for keratoconus is a corneal transplantation procedure such as penetrating keratoplasty.

To avoid the maintenance associated with eyeglasses and contact lenses and to avoid the potential complications associated with penetrating keratoplasty, a surgical procedure for the treatment of myopia or keratoconus has been developed. This procedure involves the insertion of two thin, clear, semicircular-shaped, plastic intrastromal corneal ring segments (ICRS) into the cornea of an affected eye through a single corneal incision. ICRS implantation has also been proposed to restore vision in patients with ectasia (bulging of the cornea caused by complications from laser-assisted in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) surgery). At present, the Intacs ® system is the only U.S. Food and Drug Administration (FDA)-approved ICRS.

**CLINICAL EVIDENCE**

*Myopia:*
Schanzlin et al. (2001) conducted the largest available study of intrastromal corneal ring segments (ICRS) inserts for myopia, a multicenter, uncontrolled study in which 449 patients each underwent the procedure in one eye. All eyes had low myopia and at baseline, 87% of eyes had an uncorrected visual acuity (UCVA) worse than 20/40. Two years after ICRS implantation, 97%
of eyes had a UCVA of 20/40 or better and 76% of eyes had a UCVA of 20/20 or better. This result suggests that ICRS inserts improved unaided vision, equal to that which could be achieved with eyeglasses or contacts. Comparing best-spectacle corrected visual acuity (BSCVA) at baseline and 2 years follow-up, the only result reported was that 1% of eyes lost 2 lines of BSCVA. These outcomes at 2 years follow-up did not include the 8% of eyes that underwent insert removal due to unacceptable visual symptoms, dissatisfaction with visual outcome, infection, or other problems.

Holmes-Higgin et al. (2002) performed a retrospective analysis of 263 of the patients enrolled by Schanzlin et al. who had reported adverse postoperative visual symptoms or requested removal of inserts, and found that the only statistically significant correlation with fewer symptoms was a mean keratometry greater than 45 diopters at baseline. There were also trends toward fewer symptoms in eyes with the following characteristics: manifest refractive astigmatism of 0.75 to 1.0 diopter, UCVA improvement of at least two lines more than predicted, and pretreatment use of soft contact lenses. Improved patient selection criteria may result in lower rates of insert removal in future studies.

The ability of ICRS inserts to provide equal myopia correction to that provided by eyeglasses or contacts was confirmed in a small nonrandomized controlled study. Nio et al. (2003) enrolled 28 patients with low to moderate myopia and assigned 10 patients to insert implantation while the remaining 18 patients continued to use their eyeglasses or contact lenses. Compared with eyeglasses and contact lenses, ICRS inserts provided equal improvements in BCVA or quality of vision.

The National Institute for Health and Care Excellence (NICE) issued guidance on the use of corneal implants for the correction of refractive error. The guidance for corneal implants for refractive error states that current evidence shows limited and unpredictable benefit for the use of this procedure. Therefore, corneal implants should not be used for the treatment of refractive error in the absence of other ocular pathology such as keratoconus (NICE, Corneal implants for the correction of refractive error, 2007).

Professional Societies
American Academy of Ophthalmology (AAO): A technology assessment performed by the AAO has concluded that ICRS inserts are reasonably safe and effective for the treatment of mild myopia (-1.0 to -3.0 diopters) when patients have stable manifest refraction and less than 1 diopter of astigmatism. However, the AAO assessment cautions that further research is needed to determine the long-term effectiveness of this procedure as well as its safety and effectiveness compared with other treatments such as LASIK and photorefractive keratectomy (Rapuano et al., 2001).

The AAO’s Preferred Practice Pattern for Refractive Errors and Refractive Surgery states that intrastromal corneal ring segments are now rarely utilized to correct myopia (AAO, 2012).

Keratoconus:
Vega-Estrada et al. (2013) reported the long-term refractive and optical quality outcomes of patients with intrastromal corneal ring segments (ICRS) to treat keratoconus. The uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), manifest refraction, corneal topography, and aberrometry were evaluated before and after ICRS implantation in 51 eyes (35 patients, age range 15 to 56 years) with keratoconus. The follow-up was 5 years in all cases. After 6 months, the improvement in the UDVA, CDVA, spherical equivalent, and mean keratometry (K) value was statistically significant. Five years postoperatively, these parameters remained unchanged. Anterior corneal aberrometric values decreased; however, the changes were not statistically significant. Linear regression analysis showed no correlation between the age of the patients and the changes observed in the mean K throughout the follow-up. The authors concluded that intrastromal corneal ring segment implantation in keratoconus patients provided long-term improvement of the refractive and topographic status.
Colin and Malet (2007) evaluated the use of Intacs in 100 keratoconic eyes 2 years after Intacs placement. Removal of the segments occurred in 2 eyes due to extrusion and 2 eyes due to poor visual outcome. At 2 years, of the 82 eyes available for follow-up, UCVA and best-corrected visual acuity (BCVA) improved in 80.5% and 68.3% of the eyes, respectively. The investigators concluded that significant and sustained improvements in objective visual outcomes were achieved in most patients.

A nonrandomized comparative study and analysis of retrospective data included 17 patients with keratoconus who had penetrating keratoplasty (PKP) in 1 eye and Intacs implantation in the other eye. Follow-up after PKP was at 24 hours and 6 and 24 months and after Intacs implantation, at 24 hours and 3 and 10 months. UCVA and BCVA improved in both groups. No patient lost a line of acuity. Eyes with Intacs had a shorter recovery time than eyes having PKP. The eyes with Intacs had no complications. Complications in eyes with PKP included cataract, graft rejection, and elevated intraocular pressure. The investigators concluded that Intacs may delay or prevent the need for a corneal graft, although more research with longer follow-up is needed (Rodriguez et al., 2007).


The National Institute for Health and Care Excellence (NICE) issued guidance on the use of corneal implants for keratoconus. The NICE guidance states that current evidence on the safety and efficacy of corneal implants for keratoconus appears adequate to support the use of this procedure (NICE, Corneal implants for keratoconus, 2007).

Post-Laser-Assisted In Situ Keratomileusis (LASIK) or Post-Photorefractive Keratectomy (PRK) Ectasia:
Intrastromal corneal ring segments have been investigated as a treatment for ectasia after LASIK or PRK. Although early results show potential (Kymionis et al. 2003: n=10 eyes and 1 year follow-up, Alio et al. (2002): 3 eyes and mean follow-up of 8.3 months, Lovisolo et al. 2002: 4 eyes and 12 to 44 months follow-up, Pokroy et al. 2004: 5 eyes and 9 month follow-up, Siganos et al. 2002: 3 eyes and mean follow-up of 8.7 months, Rodriguez et al. 2009: n=7 eyes and 9 month postoperative follow-up; Kymionis et al. 2010: 2 patients and 12 month follow-up), the long-term efficacy for this procedure has not been established. Limitations of these studies included small sample sizes, absence of controlled groups, and short follow-up.

In a retrospective study, Legare et al. (2013) compared combined intrastromal corneal ring segment implantation with same-day ultraviolet-A/riboflavin corneal collagen cross-linking (ICRS-CXL) versus ICRS implantation alone in patients with corneal ectasia. Sixty-six eyes from 54 patients with corneal ectasia were included in the study. The groups were composed of 32 eyes from 27 patients and 34 eyes from 27 patients for the ICRS-CXL and ICRS groups, respectively. The charts of all patients who underwent these procedures were reviewed for preoperative and for up to 1 year postoperative uncorrected (UDVA) and best corrected distance visual acuity (BDVA), refraction, topographical analysis. Overall, a significant improvement was seen in both groups for UDVA, BDVA, sphere, cylinder, mean refractive spherical equivalent (MRSE), mean and steepest keratometry (K), coma, spherical and total higher-order aberrations (HOA) at 12 months. Trefoil visual aberration did not improve, and higher-order astigmatism worsened in the ICRS group. There was no statistically significant difference between the 2 groups for visual acuity, sphere, cylinder, coma, trefoil, and spherical HOA. Outcomes were significantly more improved in the ICRS group for MRSE, mean K, steepest K, and total HOAs. No complications were observed. The authors concluded that ICRS-CXL and ICRS alone were both safe and effective in treating corneal ectasia. The ICRS alone group demonstrated better outcomes of MRSE, mean and steepest K, as well as total HOA. The nonrandomized design of this study and the small study population limit the validity of the conclusions of this study.
Tunc et al. (2011) evaluated the clinical outcomes of intracorneal ring segments (ICRS) (Keraring segment implantation) in 12 eyes of 10 patients with post- laser-assisted in situ keratomileusis (LASIK) ectasia. The mean preoperative uncorrected distance visual acuity (UDVA) for all eyes was 1.28 ± 0.59 logarithm of the Minimum Angle of Resolution (logMAR). At 12 months, the mean UDVA was 0.36 ± 0.19 logMAR, and the mean preoperative corrected distance visual acuity (CDVA) was 0.58 ± 0.3 logMAR, which improved to 0.15 ± 0.12 at 1 year. No significant changes in mean central corneal thickness were observed postoperatively and there were no major complications during or after surgery. The authors concluded the ICRS implantation using a unique mechanical dissection technique is a safe and effective treatment for post-LASIK ectasia. According to the authors, study limitations included small sample of treated eyes, the lack of higher-order aberration analysis, and the lack of a comparative group.

Pinero et al. (2010) evaluated and compared visual, refractive, and corneal aberrometric outcomes after implantation of 2 types of intrastromal corneal ring segments (ICRS) in eyes with early to moderate ectatic disease in a retrospective analysis over a 6 month follow-up. The study included consecutive eyes with grade I or grade II corneal ectasia (keratoconus, pellucid marginal degeneration, ectasia after laser in situ keratomileusis) that had Intacs (Group I) or KeraRings (Group K) ICRS implantation using femtosecond technology. Group I had 17 eyes and Group K, 20 eyes. One month postoperatively, there was a statistically significant reduction in sphere in both groups. At 6 months, there was a statistically significant reduction in manifest cylinder in Group K that was consistent with the significant reduction in corneal astigmatic aberration. The uncorrected distance visual acuity increased significantly in Group K but not in Group I; 41.18% of eyes in Group I and 52.94% in Group K gained 1 or more lines of corrected distance visual acuity. Both groups had significant corneal flattening. At 1 month, the mean primary spherical aberration was 0.17 microm +/- 0.52 (SD) in Group I and 0.40 +/- 0.35 microm in Group K; the difference was statistically significant. The investigators concluded that astigmatism correction in early to moderate ectatic corneas was more limited with the Intacs ICRS, which induced negative primary spherical aberration in the initial postoperative period. This study is limited by short-term follow-up.

Torquetti and Ferrara (2010) evaluated the clinical outcomes of implantation of Ferrara intrastromal corneal ring segments (ICRS) in patients with corneal ectasia after refractive surgery. Charts of patients with corneal ectasia after refractive surgery were retrospectively reviewed. Twenty-five eyes (20 patients) with corneal ectasia (20 after laser in situ keratomileusis, 4 after radial keratotomy, 1 after photorefractive keratectomy) were evaluated. Postoperatively, the mean uncorrected distance visual acuity (UDVA) increased from 20/185 to 20/66 and the mean corrected distance visual acuity (CDVA), from 20/125 to 20/40. The investigators concluded that intrastromal corneal ring segment implantation significantly improved UDVA and CDVA in patients with corneal ectasia. The short-term follow-up in this study did not allow for assessment of intermediate and long-term outcomes.

Kymionis et al. (2006) reported on the long-term follow-up (5 years) of Intacs for the management of post-LASIK corneal ectasia in 8 eyes of 5 patients. Refractive stability was maintained for up to 5 years in the treatment of post-LASIK corneal ectasia after Intacs implantation. There was no evidence of progressive time-dependent corneal ectasia, late regression, or sight-threatening complications in this study. The limitation of this study was its small sample size.

Pinero et al. (2009) evaluated the refractive and aberrometric changes in corneas with post-LASIK keratectasia implanted with intracorneal ring segments (ICRS) during a 2-year follow-up in a retrospective, consecutive case series of 25 patients (34 eyes). Uncorrected visual acuity did not improve after surgery. Best spectacle-corrected visual acuity increased significantly at 6 months. Thirty-nine percent of eyes gained 2 or more lines of best spectacle-corrected visual acuity (BSCVA) at 6 months, and this percentage increased to 60% at 24 months. There was a nonsignificant reduction of sphere at 6 months. Segment ring explantation was performed in 6 eyes, and ring reposition was performed in 2 eyes. The apical curvature gradient was significantly higher in the group of explanted eyes. The investigators concluded that intracorneal ring segment
Implantation is a useful option for the treatment of coma-like aberrations and astigmatism in post-LASIK corneal ectasia. These findings require confirmation in a larger study. The retrospective nature of this study limits its validity.

**Professional Societies**

**American Academy of Ophthalmology (AAO):** The AAO's Preferred Practice Pattern for Refractive Errors and Refractive Surgery states that management options for ectasia after LASIK include intrastromal corneal ring segments (ICRS). ICRS are FDA-approved for use in keratoconus and have been used off-label for ectasia after LASIK. Reported techniques vary in the size, number, and symmetry of the implant as well as the location of the incision. The AAO states that long-term efficacy of this procedure for ectasia remains to be determined (AAO, 2012).

**Other Conditions:**

Intrastromal corneal ring segment implantation has been investigated for other conditions including pellucid marginal corneal degeneration (Kubaloglu, 2010: n=16 eyes; Ertan and Bahadir, 2006: n=9 eyes; Mularoni, 2005: n=8 eyes) or high astigmatism after penetrating keratoplasty (Coscarelli et al. 2012, Arriola-Villalobos, 2009). However, because of limited studies, small sample sizes and weak study designs, there is insufficient data to conclude that intrastromal corneal ring segment implantation is safe and/or effective for treating these indications. Further clinical trials demonstrating the clinical usefulness of this procedure are necessary before it can be considered proven for these conditions.

In a prospective randomized study, Birnbaum et al. (2011) evaluated the efficacy and safety of an intrastromal corneal ring after penetrating keratoplasty. The study included 20 patients, 10 of whom received an intracorneal ring (group 1) and 10 who did not (group 2 or control group). Mean follow-up time was 27.6 ± 5.3 months. Mean astigmatism (Orbscan) was 4.4 diopters in group 1 and 4.4 diopters in group 2. Spontaneous suture rupture occurred in 5 patients with corneal ring but in none of the patients in the control group. Three immune reactions were observed in 3 patients with corneal ring, whereas group 2 experienced no rejection. The authors concluded that the use of the intrastromal corneal ring after penetrating keratoplasty caused no reduction in postoperative astigmatism. According to the authors, its use was significantly associated with adverse events.

**U.S. Food and Drug Administration (FDA)**

The Intacs intrastromal corneal ring system is regulated by the FDA as a Class III device that is subject to the most extensive regulations enforced by the FDA via the premarket approval process. The 1999 approval letter for Intacs inserts limits its use to patients with myopia of -1.0 to -3.0 diopters who are at least 21 years of age with an astigmatic component of no more than +1.0 diopter and with stable refraction as shown by a change of no more than 0.5 diopter in the preceding year. See the following Web site for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf/P980031b.pdf. Accessed October 2013.

In 2004, the FDA issued a humanitarian device exemption (HDE) approving Intacs implantation for the reduction or elimination of myopia and astigmatism in patients with keratoconus in patients who meet the following criteria: at least 21 years of age, progressive deterioration of vision, inadequate vision correction with eyeglasses or contacts, clear central cornea, corneal thickness of 450 microns or greater at the proposed incision site, and corneal transplantation is the only option other than Intacs to improve vision. See the following Web site for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf4/h040002a.pdf. Accessed October 2013.

HDE is a special regulatory marketing approval that makes the device available on a limited basis provided that: (1) The device is to be used to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States; (2) the device would not be available to a person with such a disease or condition unless the exemption is granted; (3) no comparable device (other than a device that has been granted such an exemption) is available to treat or diagnose the disease or condition; and (4) the device will not expose patients to an unreasonable...
or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

Humanitarian use devices may only be used in facilities that have obtained an institutional review board (IRB) approval to oversee the usage of the device in the facility, and after an IRB has approved the use of the device to treat or diagnose the specific rare disease. Additional information may be obtained directly from the U.S. Food and Drug Administration (FDA) [Website] - Center for Devices and Radiological Health (CDRH) at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm. Accessed October 2013.

The FDA issued the following precautions in conjunction with its 1999 approval order for Intacs inserts: See the following Web site for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf/P980031b.pdf Accessed October 2013.

Patients treated with the 0.35-mm insert may have worse outcomes than those treated with 0.25- or 0.30-mm inserts.

- Overcorrection is more likely for patients with -1.0 diopter myopia.
- Intacs inserts may have long-term effects on endothelial cell density but this has not been determined.
- Intacs implantation causes a temporary decrease in corneal sensation for some patients, although this effect does not seem to be clinically significant.
- Patients are predisposed to low-light visual symptoms if they have dilated pupil diameters 7.0 mm.
- Patients may experience some loss of contrast sensitivity in low-light conditions.
- The efficacy and safety of other procedures to modify refraction have not been established for patients who have undergone Intacs implantation and removal.

In addition to the precautions listed above, Intacs implantation is contraindicated under the following circumstances: use of Accutane® (isotretinoin), Cordarone® (amiodarone) or Imitrex® (sumatriptan), recurrent corneal erosion syndrome, corneal dystrophy, or other ocular disorders that might cause complications in the future; and known autoimmune, immunodeficiency, or collagen vascular disease. Intacs implantation is not recommended for patients who have systemic diseases that can affect wound healing or for patients who have had ocular Herpes simplex or Herpes Zoster infections. See the following Web site for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf/P980031b.pdf. Accessed October 2013.

### CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for intrastromal corneal ring segments (ICRS) procedure. Local Coverage Determinations (LCDs) do exist. Refer to the LCDs for Noncovered Services, Category III Codes, Category III CPT Codes, Non-Covered Category III CPT Codes and Services That Are Not Reasonable and Necessary. (Accessed October 16, 2013)

### APPLICABLE CODES

The codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. Coverage is determined by the benefit document. This list of codes may not be all inclusive.

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REFERENCES


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