Clinical Policy Title: Corneal implants

Clinical Policy Number: 10.03.06

Effective Date: April 1, 2017
Initial Review Date: August 17, 2016
Most Recent Review Date: September 21, 2017
Next Review Date: September 2018

Policy contains:
- Intrastromal corneal ring segments.
- Corneal inlay.
- Corneal ectasia.
- Keratoconus.

Related policies:
CP# 10.03.04 Corneal transplants (keratoplasty)
CP# 10.02.02 Therapeutic contact lenses

ABOUT THIS POLICY: AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania’s clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas Pennsylvania considers the use of Intacs® intrastromal corneal ring segments (ICRS) (Addition Technology, Lombard, Illinois) to be clinically proven and, therefore, medically necessary for treatment of keratoconus when all of the following criteria are met:

- No longer able to achieve adequate functional vision on a daily basis with either contact lenses or eyeglasses.
- Age 21 years or older.
- Clear central corneas.
- Corneal thickness of 450 µ or greater at the proposed incision site.
- Corneal transplantation is the only remaining option to improve functional vision.
Limitations:

- All other uses of Intacs are not medically necessary because the effectiveness for indications other than keratoconus has not been established.
- Absolute contraindications to Intacs implants include but are not limited to (based on product labeling):
  - Individuals who have abnormally thin corneas or who have corneal thickness of 449 µ or less at the proposed incision site.
  - Individuals with collagen, vascular, autoimmune, or immunodeficiency diseases.
  - Women who are pregnant or nursing.
  - The presence of ocular conditions, such as recurrent corneal erosion syndrome or corneal dystrophy, which may predispose the individual to future complications.
  - Individuals who are taking one or more of the following medications: isotretinoin (Accutane) and amiodarone (Cordarone).
- The use of corneal implants for treatment of presbyopia is not medically necessary.

Alternative covered services:

- Eyeglasses.
- Contact lenses.
- Contemporary keratoplasty and keratectomy procedures (e.g., penetrating [full thickness] keratoplasty, Lamellar [partial thickness] keratoplasty, endothelial keratoplasty).

Background

The cornea is the clear, dome-shaped outermost layer of the eye and a key refractive element of the eye (National Eye Institute [NEI], 2016). It is a highly organized tissue arranged in three basic layers with two thinner membranes between them. The stroma is the thickest, strongest layer of the cornea. For optimal vision, all layers of the cornea must be of normal shape and curvature and free of any cloudy or opaque areas.

Corneal ectasia encompasses primary disease conditions (e.g., keratoconus and pellucid marginal corneal degeneration) or surgically induced thinning and protrusion (e.g., after laser-assisted in situ keratomileusis [LASIK] refractive surgery). Keratoconus is a rare condition with an early age of onset (median age of 25 years) and is the most common corneal thinning disorder.

Persons with corneal ectasia suffer from varying degrees of functional disability, including glare, halos, multiple images, ghosting, reduced visual acuity, and intolerance to eyeglasses and contact lenses. The loss of visual function may result in reduced productivity and self-esteem, and difficulties performing high-skill visual tasks such as driving.
The rationale for treatment depends on disease severity and the amount of vision loss. When eyeglasses and/or contact lenses can no longer correct vision or be tolerated, surgical options (e.g., keratectomy and keratoplasty) may be considered. Corneal transplant may be indicated as a final option. Despite high graft survival rates of up to 20 years, transplant surgery requires a lengthy recovery time. In addition, corneal transplant is donor-limited and associated with potential complications from long-term steroid use following surgery, the risk of developing secondary conditions (e.g., cataracts and glaucoma) needing intervention, and residual refractive errors and astigmatism.

**Corneal implants:**

Corneal implants (also called corneal inlays or intracorneal implants) have emerged as a treatment option for corneal ectasia. Corneal implants are small segments of rings or full rings of synthetic material implanted in the corneal stroma to normalize corneal surface topography, improve contact lens tolerability, and restore visual acuity to delay or defer the need for corneal transplant. Implant placement is a minimally invasive procedure usually performed by either corneal specialists or refractive surgeons in the outpatient setting with topical anesthesia. The implants are adjustable and reversible and do not limit the performance of subsequent surgical approaches or interfere with corneal transplant. Typically one is implanted in the nondominant eye.

The United States Food and Drug Administration (FDA) has approved three premarket approval applications (PMAs) for corneal implants for commercial use in the United States (PMA product code LQE). They are (FDA, 2016a, 2015, and 1999):

- **Intacs corneal implants/prescription inserts** — Intrastromal corneal ring segments indicated for the reduction or elimination of mild myopia (-2.00 to -3.00 diopters (d) spherical equivalent at the spectacle plane) in patients: who are age 21 years or older; with documented stability of refraction as demonstrated by a change of ≤0.50 d for at least 12 months prior to the preoperative examination; and where the astigmatic components are +1.00 d or less. FDA approved Intacs through a Humanitarian Device Exemption in 2004 for use in patients with keratoconus whose corneas are not scarred, when spectacles and contact lenses no longer provide adequate visual correction.

- **KAMRA® inlay (AcuFocus™, Inc., Irvine, California)** — A dark, ring-shaped device indicated for intrastromal corneal implantation to improve near vision by extending the depth of focus in the nondominant eye of phakic, presbyopic patients between the ages of 45 and 60 years who have cycloplegic refractive spherical equivalent of +0.50 d to -0.75 d with ≤0.75 d of refractive cylinder, who do not require glasses or contact lenses for clear distance vision, and who require near correction of +1.00 d to +2.50 d of reading add.

- **Raindrop® Near Vision Inlay (REVISION OPTICS, Inc., Forest, California)** — A biocompatible hydrogel corneal inlay indicated for intrastromal implantation to improve near vision in the nondominant eye of phakic, presbyopic patients, 41 to 65 years of age, who have manifest refractive spherical equivalent of +1.00 d to -0.50 d with ≤0.75 d of refractive cylinder, who
do not require correction for clear distance vision, but who do require near correction of +1.50 d to +2.50 d of reading add.

Searches

AmeriHealth Caritas Pennsylvania searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on August 3, 2017. Search terms were: “keratoconus,” “myopia,” “presbyopia,” “nearsighted,” “astigmatism,” “Intacs,” “KAMRA,” “raindrop,” and “keravision.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

For this policy, we identified three systematic reviews (Fischer for the Ludwig Boltzmann Institut fuer Health Technology Assessment [LBIHTA], 2015; Hayes, 2012 and updated 2015; Health Quality Ontario [HQO], 2009); three individual studies (Whitman, 2016; Dexl, 2015; Vilipuru, 2015) not included in the systematic reviews; and three evidence-based guidelines (American Academy of Ophthalmology [AAO], 2013a and 2013b; National Institute for Health and Clinical Excellence [NICE], 2007). In addition, we added three FDA Summary of Safety and Effectiveness data reports that provided the basis for FDA PMA approval and product labeling instructions for the three corneal implant devices (FDA, 2016b, 2014, and 1999b).

The evidence consists of uncontrolled longitudinal cohort studies and small case series. Direct comparisons to other treatment alternatives or to no treatment are lacking. Overall, the evidence suggests corneal implants offer clinically significant improvements in corneal topography, refraction, and visual acuity. The major safety concerns include corneal perforation, infection, corneal infiltrates, corneal neovascularization, ring migration and extrusion, and corneal thinning. Reported complications were generally minor, reversible, and attributable to early surgeon experience. Treatment may result in an over- or under-correction of refraction and may induce astigmatism or asymmetry of the cornea. Other reasons for treatment failure or patient dissatisfaction include foreign body sensation and
unsatisfactory visual quality with symptoms such as double vision, fluctuating vision, poor night vision, or visual side effects related to ring edge or induced or unresolved astigmatism.

**Keratoconus:**

There is sufficient evidence and clinical experience to support ICRS (Intacs) as treatment for progressing keratoconus, and available guidelines concur. NICE recommended ICRS for treatment of progressive keratoconus and pellucid marginal degeneration (NICE; 2007, updated 2012). The AAO recommended ICRS implantation as a surgical option to improve contact lens tolerance and best-corrected visual acuity for patients with keratoconus, a clear cornea, and contact lens intolerance (AAO, 2013a). Contraindications to ICRS implantation include central corneal scarring and a corneal thickness of less than 400 μ at the incision site.

Progression of keratoconus is an indication for corneal transplant. While no study has compared the outcomes of Intacs to corneal transplant in this population, Intacs is advantageous for its ability to be removed or exchanged to improve vision without limiting subsequent interventions, particularly corneal transplant. Both eyes can be treated at once, and the treatment is adjustable and reversible. In the presence of limited corneal donors, Intacs may be considered an alternative to defer or defray corneal transplant.

**Other indications:**

Early studies reported on the safety and effectiveness of ICRS for myopia in normal eyes, but LASIK has emerged as the preferred approach (AAO, 2013b). Intrastromal corneal ring segments are now rarely used to correct myopia (AAO, 2013a and 2013b).

The evidence supporting ICRS for off-label indications such as rescue treatment for post-LASIK corneal ectasia, refractive errors following corneal transplant or combined with other surgeries, is far more limited, and long-term outcomes are lacking. Furthermore, the narrow range of approved correction specified by the FDA and inability to correct astigmatism limit the application of ICRS after refractive surgery (AAO, 2013a and 2013b).

For surgical management of presbyopia, there is strong evidence to support keratorefractive surgery for monovision or intraocular lens (IOL) implantation as the preferred surgical options (AAO, 2013b). Limited experience with the KAMRA intrastromal ring and Raindrop hydrogel inlay suggests these implants may grow in popularity for persons with presbyopia who desire spectacle-free living. KAMRA and Raindrop implants are not approved for any other indication.

The evidence is insufficient to conclude that emerging alternative treatment strategies, such as collagen cross-linking aimed at strengthening the underlying corneal tissue, might prove more effective or increase the effectiveness of the implants, particularly in advances stages of corneal thinning.
Policy updates:

In 2017, we found one update to the Hayes report (2012, updated 2016) and one updated practice recommendation (AAO, 2013a, updated 2016), but there were no changes to their conclusions. No policy changes are warranted at this time.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tr>
<td><strong>Whitman (2016)</strong></td>
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</table>
| Raindrop Post-approval results (ClinicalTrials.gov identifier, NCT01373580) | Key points:  
  - At one-year follow-up (340 of 373 nondominant eyes).  
  - Device provides significant improvement in near and intermediate visual performance, with no significant change in binocular distance vision or contrast sensitivity.  
  - Adverse events were treatable and resolved.  
  - Eighteen inlays replaced, usually soon after implantation because of decentration.  
  - Inlay explantation in 11 cases, 100% achieved a corrected distance visual acuity of 20/25 or better by three months after explant.  
  - Significantly improved patient satisfaction with minimal ocular or visual symptoms. |
| **Dexl (2015)** |  |
| KAMRA | Key points:  
  - Single-site prospective cohort (32 emmetropic presbyopic eyes).  
  - One inlay was removed after 36 months because of patient dissatisfaction with vision after a hyperopic shift in the surgical eye, with no loss of corrected distance visual acuities or corrected near vision acuities two years after removal.  
  - Long-term results (timeframe unclear) of monocular corneal inlay implantation indicate increased UNVA and UIVA and slightly compromised UDVA in emmetropic presbyopic eyes. |
| **Hayes (2012, updated 2016)** |  |
| Intacs | Key points:  
  - Systematic review of two prospective cohort studies, six retrospective cohort studies, two uncontrolled studies, and one comparison study (range: 19 to 255 patients per study).  
  - Overall quality: low.  
  - Intacs is reasonably safe and provides some improvements in visual outcomes for patients who have keratoconus.  
  - No studies compared Intacs with corneal transplantation.  
  - Clinical acceptance will depend on its utility versus corneal transplant and a paucity of suitable donors for corneal transplantation. |
| **Fischer (2015) for the LBIHTA** |  |
| Intacs | Key points:  
  - Systematic review of five uncontrolled studies (627 total eyes).  
  - Insufficient evidence of equal or superior efficacy or safety compared to either corneal transplantation or no intervention for treating keratoconus or post-LASIK corneal ectasia.
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tbody>
<tr>
<td>Vilipuru (2015)</td>
<td>Before-and-after study results suggest clinically relevant improvement of visual acuity in a large proportion of patients. Recommend inclusion in the catalog of benefits with restrictions: - Unable to tolerate or wear contact lens. - Consider product labeling restrictions (e.g., adequate thickness of cornea). - Procedure offered only in specialty centers. - Monitor and record device safety in a national database.</td>
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<td>KAMRA versus IOL Key points:</td>
<td>- Indirect comparison of a previous nonrandomized multicenter clinical trial results of KAMRA (507 patients) to a trial randomizing 78 subjects to one of three presbyopia-correcting IOLs. - Patients with KAMRA inlay showed improved intermediate and near vision with minimal to no change to distance vision, better contrast sensitivity in the inlay eye versus multifocals, and better binocular contrast sensitivity versus all three IOLs. - Versus KAMRA, Crystalens AO was superior in uncorrected intermediate vision, but not in distance-corrected intermediate vision, and worse in near vision. Multifocal IOLs were superior in near vision at their respective optimal near focus points, but worse in intermediate vision versus both KAMRA inlay and Crystalens AO. - Should consider device performance, subjects’ visual demands and expectations, degree of crystalline lens dysfunction, and other ocular characteristics in guiding device selection to correct presbyopia.</td>
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<td>HQO (2009)</td>
<td>Systematic review of two previous technology assessments in Australia and the United Kingdom and 10 pre-/post-longitudinal cohort studies of Intacs (cohorts included 608 patients with 754 total eyes with keratoconus). - High technical success rates. - Overall complication rate 4.6% (29/636), mainly reversible minor complications such as segment migration. Major complications (e.g., infection and vascularization) were uncommon. - Limited reporting of outcome data, data on durability of treatment effects on underlying disease processes and patient satisfaction. - For patients unable to achieve functional vision due to keratoconus, Intacs provides a useful alternative to corneal transplant. - Limited evidence suggests role for patients who acquire corneal thinning after undergoing refractive surgery (e.g., LASIK for myopia correction) and to correct residual refraction and astigmatism recurring after corneal transplant.</td>
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References

Professional society guidelines/other:


Peer-reviewed references:


**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local Coverage Determinations (LCDs):**


**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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<td>Implantation of intrastromal corneal ring segments</td>
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<td>Q13.4</td>
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