Clinical Review Criteria
Intraocular Lens Following Cataract Extraction

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Criteria
For Medicare Members

<table>
<thead>
<tr>
<th>Source</th>
<th>Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMS Coverage Manuals</td>
<td>None</td>
</tr>
<tr>
<td>National Coverage Determinations (NCD)</td>
<td>Intraocular Lens (80.12)</td>
</tr>
<tr>
<td>Local Coverage Determinations (LCD)</td>
<td>None</td>
</tr>
</tbody>
</table>

For Non-Medicare Members
Accommodative Intraocular Lens
There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

Multifocal Intraocular Lens
Multifocal intraocular lenses will not be covered. Standard monofocal intraocular lenses are covered following cataract surgery. The patient may elect to pay for the multifocal lens.

Toric Intraocular Lens
Toric intraocular lenses to correct astigmatism are not covered. The purposes of these lenses are to reduce dependence on glasses. Improved vision with glasses is the purpose of standard cataract surgery, the additional benefit of improved vision without glasses is not a covered service.

Background
It is estimated that over 20 million Americans older than 40 years have cataract in at least one eye. It is predicted that this number will increase to 30 million by 2020. The current approach of treating cataracts is to replace the natural crystalline lens of the eye with an artificial intraocular lens (IOL). Traditionally intraocular lenses are monofocal lenses, which can provide excellent distance vision and optical quality, but they do not deliver functional vision at other ranges of distance. After their implantation most patients need spectacles at least for near vision. Bifocal and multifocal IOLs were developed to overcome the lack of accommodation in these pseudophakic patients (i.e. patients with an artificial IOL). They provide good functional distance, near, and intermediate vision without the use of corrective lenses. However, multifocal and bifocal IOLs may have optical side effects such as decreased contrast sensitivity, glare disability, and halos, which can reduce the retinal image quality and affect the patient’s visual performance (Harman 2008, Alio 2010, Alio 2011, Cochener 2011).

Accommodative Intraocular Lens
Positional accommodating IOLs were developed to avoid the optical side effects of the multifocal IOLs and provide some accommodative capability and functional near vision. The basic mechanism of these lenses is the transmission, by haptics (plastic plates or struts), of the contracting forces of the ciliary body to the flexible lens. The design of these IOLs is based on the optic-shift concept i.e. on the axial (backward and forward) movement of the optic resulting from the contraction and relaxation of the ciliary muscle. A hinge between the optic and haptics allows the lens to move forward as the eye focuses on near objects and backward as the eye focuses on distant objects, thereby increasing the dioptic power of the pseudophakic eye. The first developed accommodative IOLs were positional single optic lenses used for both cataract and surgical correction of presbyopia. Among these are the Crystalens™ (Eyeonics, Inc., 1CU [Human Optics Erlangen, Germany], and Tetraflex [KH3500, Lenstec, St Petersburg Florida]) (Marchini 2007).
The Crystalens™ AT-45 IOL is the seventh design of the Crystalens™. It consists of a single biconvex lens with a 4.5 mm optic with two plate haptics each terminating in two polyamide loops that anchor it to the capsular bag. Adjacent to the optic are grooved flexible hinges in the plates that allow forward movement of the optic during accommodative effort to provide near and intermediate vision in pseudophakic patients. The optic is square-edged and is made of silicone to maximize biocompatibility and flexibility and allow easy insertion of the lens through a 3 mm corneal incision. A newer Crystalens™ model (Crystalens HD) has a mechanism of action based on the transitional movement of the lens in anterior and posterior direction due to ciliary muscle contraction and vitreous mass displacement (Macsai 2006, Cumming 2006).

The Tetraflex (Lenstec) lens is an anteriorly vaulted, single-piece, foldable, accommodating IOL that is implanted using a custom-designed injector system through an incision as small as 3 mm. The lens' optic is 5.75 mm and is made of a highly biocompatible and extremely flexible hydrophilic acrylic material (HEMA). The IOL's two haptics, each with two footplates, sit posteriorly in the peripheral capsular bag (Sheppard 2010).

The 1CU is a foldable single-piece lens with an optic diameter of 5.5 mm and an overall length of 9.8 mm. It is made of a hydrophilic acrylic material and has a biconvex square-edged optic and 4 modified flexible haptics that are designed to bend when constricted by the capsular bag after ciliary muscle contraction. This allows anterior displacement of the optic resulting in an increase in the refractory power (Palikkaris 2011).

The single-optic passive shift IOLs are considered pseudoaccomodative and have limited accommodative ability as their anterior movement is insufficient to provide functionally significant amplitudes of accommodation. The limited optic power of the single optic lenses led to the development of dual-optic devices as the Synchrony (Visiogen, Irvine, California, USA), and the Sarfarazi IOL (developed by FM Safarazi of Shenasa Medical LLC, Carlsbad, CA, USA). The configuration of these devices with a high positively-powered mobile anterior optic, connected to a stationary negatively-powered posterior optic, is designed to increase the potential accommodative amplitude (Alio 2009, Sheppard 2010).

Investigators indicate that the way of measuring the range of accommodation in pseudophakic eyes is still unclear. In a recent review article, Pallikaris and colleagues state “Objective measurement of the accommodative capability offered by the accommodative IOLs is extremely difficult to obtain, and different methods such as autorefractometers, retinoscopy, and ultrasound imaging during accommodative effort, ray tracing, or pharmacological stimulation have been developed but the results are sometimes inconsistent… Pseudophakic accommodation, that is, the dynamic component of ocular refractive variation during near vision, and pseudophakic pseudoaccomodation, that is, the depth of focus and the subjective adaption to defocus during near vision, are the two core parts of pseudoaccommodation. Currently there is no consensus in the literature on the percentage of the participation of each part in the phenomenon of pseudoaccommodation. Several different methods are utilized by investigators for the study of the phenomenon thus resulting in different results.” (Palikkaris 2011).

**Multifocal Intraocular Lens**

Bifocal and multifocal intraocular lenses have optical side effects such as glare, halos, and decreased contrast sensitivity, which can reduce the retinal image quality and affect the patient’s visual performance. The Array IOL (Advanced Medical Optics [AMO], Santa Ana, CA), one of the first IOLs approved by the FDA (1997) is a typical refractive multifocal IOL. Earlier trials demonstrated that Array IOL improved distance and near visual acuity and reduced spectacle dependency after cataract extraction, but it was also associated with problems as decreased contrast sensitivity, glare, and halos. Newer generations of multifocal IOLs have been developed with the aim of providing better visual acuities at various distances with less glare and halos and without need for any spectacles. Currently in the United States, multifocal lens options include the ReZoom™ lens (Abbott Medical Optics [AMO] Inc, Santa Ana, CA), ReSTOR® lens (Alcon Laboratories Inc, Fort Worth, TX), and the Tecnis® lens (Abbott Medical Optics Inc, Santa Ana, CA) (Kawamorita 2009).

The ReZoom™ (AMO) is a second generation multifocal refractive lens that improved on the design of the Array with the aim of decreasing the symptoms of glare and halos. It is a three-piece multifocal lens made of hydrophobic acrylic material and has five refractive optical zones; each zone designed for different light and focal distances: zones 1, 3, and 5 are adjusted for far vision, while zones 2 and 4 are adjusted for near vision. The design of ReZoom is different from the Array in that the second and third zones have been enlarged, and the fourth and fifth zones have been reduced in size. An aspheric transition between zones provides balanced intermediate vision. These changes potentially reduce in night-time glare and improves uncorrected near visual acuity (Forto 2009, Kawamorita 2009, Alio 2011, Kubal 2011, Lichtinger 2012).
The ReSTOR® (Alcon Laboratories Inc) is a diffractive one-piece posterior chamber IOL. It is the first diffractive IOL to be approved by the FDA. ReSTOR® is a biconvex lens made of a soft plastic that can be folded prior to insertion, allowing placement through an incision smaller than the optic diameter of the lens. After surgical insertion into the eye, the lens gently unfolds to restore vision. The supporting arms (haptics) provide for proper positioning of the IOL within the eye. ReSTOR® lens has 12 concentric diffractive rings that cover the central 3.6 mm of the lens. The diffractive portion of the lens is apodized i.e. the height of each diffractive step decreases with increasing distance from the center. In order to create a smoother transition between focal points, the ReSTOR® is considered a hybrid of diffractive and refractive IOLs with the lens periphery functioning as a refractive zone focusing for distance vision. In 2007, the FDA approved the aspheric version of the ReSTOR® (AcrySof IO, ReSTOR), which has a 10 µm of negative asphericity, while maintaining its apodization and diffractive and refractive components. Recently, a new +3.0 diopter (D) was introduced to improve intermediate vision, which was suboptimal with the +4 D models (Alio 2011, Sood 2011, Zhang 2011, Kubal 2011, Lichtinger 2012).

The Tecnis® Multifocal Intraocular Lens (AMO) is an ultraviolet light-absorbing posterior chamber lens. It was first available as a 3-piece silicone lens (ZM000), then later it became available as a 3-piece acrylic (ZMA00), or a single piece acrylic (ZMB00) lens. The lens is foldable so that it can be inserted into the eye through a very small incision that is actually smaller than the diameter of the lens itself. It has an optical design based on a principle of diffraction similar to the AcrySof ReSTOR® IOL, but with the diffractive rings covering the entire posterior surface of the lens. The rings start very close to the center of the lens and then continue out toward the periphery, usually with an increasing distance between the rings. As a result, the lens achieves its multifocal effects with minimal dependence on the size of the pupil (Soood 2011, Lichtinger 2012).

The ReZoom™, AcrySof ReSTOR 3.0 and 4.0 D, and Tecnis® multifocal intraocular lenses have all received FDA clearance for the visual correction after cataract extraction in adult patients with and without presbyopia.

**Medical Technology Assessment Committee (MTAC)**

**Multifocal Intraocular Lens**

**04/11/2001: MTAC REVIEW**

**Evidence Conclusion:** A single well-done RCT provides evidence that multifocal IOL are as effective as monofocal IOL for distance acuity. Patients with monofocal IOL had better uncorrected near VA and distance-corrected near VA than monofocal IOL patients, but similar best-corrected near VA add power. A case series with long-term follow-up showed a high-rate of efficacy on visual acuity with multifocal IOL. All studies reviewed indicated that a limitation of multifocal IOL is decreased contrast sensitivity. The cohort study, which had compromised validity, found less contract sensitivity with multifocal compared to monofocal IOL in daylight and twilight with no glare and twilight with central glare. The benefits of multifocal IOL should be weighed against possible decreases in contrast sensitivity and the efficacy of monofocal IOLs with glasses for near focus.

**Articles:** The search yielded 30 articles. There were 2 RCT articles; these were based on data from the same study. The majority of the articles were case series with small numbers of patients. Evidence tables were created for three studies: The most recent report of RCT data: Javitt JC, Steinert RF. Cataract extraction with multifocal intraocular lens implantation: A multinational clinical trial evaluating clinical, functional and quality-of-life outcomes. Am Acad Ophthalmol 2000; 107: 2040-2048. See *Evidence Table*. A cohort study examining possible adverse effects of multifocal IOL: Winther-Nielsen A, Corydon L, Olsen T. Contrast sensitivity and glare in patients with a diffractive multifocal intraocular lens. J Cataract Refract Surg 1993; 19: 254-257. See *Evidence Table*. A case series with long-term follow-up data: Slagsvold JE. 3M diffractive multifocal intraocular lenses: Eight year follow-up. J Cataract Refract Surg 2000; 26: 402-407. See *Evidence Table*.

The use of multifocal Intraocular Lens in the treatment of visual correction following cataract surgery does meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

**07/2005: MTAC REVIEW**

**Intraocular Lens**

**Evidence Conclusion:** *Accommodative Intraocular Lens* The evidence on Crysalens™ is insufficient to draw conclusions about its efficacy and safety compared to standard intraocular lenses. The single published comparative study (Alio et al., 2004) had threats to validity. It was a non-randomized comparison of three case series, one on Crystalens, one on the Array multifocal lens and one on the Twinset bifocal IOL. The study is subject to selection bias because patients were not randomized and the authors did not control statistically for confounding factors. The study was also non-blinded and thus subject to observation bias. The study had four primary outcomes. Between-group differences were statistically significant for one out of the four outcomes, mean best corrected near acuity, but not for mean uncorrected distance acuity, mean best corrected distance acuity or mean uncorrected near acuity. There were two studies on the 1CU IOL by HumanOptics, a non-FDA approved
accommodative IOL. This evidence is also weak. One of the studies (Kuchle et al., 2004) was non-randomized and did not control for confounding factors, and is therefore subject to selection bias. The other study (Dogru et al., 2005) was randomized, but the study methodology was not well described, making it impossible to assess validity. There were also validity issues with the statistical analysis in the Dogru study.

**Articles: Accommodative Intraocular Lens** There was one study comparing the FDA approved accommodative IOL, Crystalens, to other types of IOLs. There were two studies comparing the non-FDA approved 1CU accommodating IOL (HumanOptics; Erlangen, Germany) to other IOLs. Like Crystalens, the 1CU IOL has a hinge-like design which allows for forward and backward movement. These three empirical studies were critically appraised. In addition, there was a small case series (n=14) reporting on the initial phase of the Crystalens FDA clinical trial. This study was excluded from further review. Evidence tables were created for the following studies: Crystalens™ Alio JL, Tavalato M, De la Hoz F et al. Near vision restoration with refractive lens exchange and pseudoaccommodating multifocal and refractive and diffractive intraocular lens. J cataract Refract Surg 2004; 30: 2494-2503. See **Evidence Table**. Human Optics 1CU. Dogru M, Honda R, Omoto M. Early visual results with the 1CU accommodating intraocular lens. J Cataract Refract Surg 2005; 31: 895-902. See **Evidence Table**. Kuchle M, Seitz B, Langenbacher A et al. Comparison of 6-month results of implantation of the 1CU accommodative intraocular lens with conventional intraocular lens. Ophthalmology 2004; 111: 318-324. See **Evidence Table**.

The use of Accommodative Intraocular Lens in the treatment of visual correction following cataract surgery does not meet the Kaiser Permanente Medical Technology Assessment Criteria.

**04/16/2012: MTAC REVIEW**

Intraocular Lens

**Evidence Conclusion:** Accommodative Intraocular Lens Crystalens™: AT-45 The literature search did not reveal any published large good quality RCTs that compared the implantation of the accommodative Crystalens™ with multifocal or monofocal intraocular lenses after cataract extraction. The best published evidence on Crystalens™ comes from the FDA multicenter clinical trial with 12 months follow-up (Evidence table 1). The initial study was a phase II trial that evaluated the efficacy and safety of the CrystalensTM AT-45. It was a prospective cohort study with no control or comparison group. The results of 12 months follow-up of 263 patients receiving the implant in the primary eye showed that the accommodating CrystalensTM AT-45 provided good uncorrected near and distance visual acuity with minimal adverse effects. In a substudy the authors compared contrast sensitivity under mesopic conditions with and without glare in a subgroup of patients who received the Crystalens versus a matched population of 64 patients who received standard IOL. The results of this substudy showed that the difference in contrast sensitivity between the two groups of patients was clinically irrelevant.

1CU (Human Optics) Several randomized and nonrandomized trials compared the performance of 1CU with monofocal and multifocal intraocular lenses (IOLs) (Evidence tables 2-4). The results of the studies showed that distance corrected near vision was significantly better in the 1CU group versus other groups receiving non-accommodating IOLs. Two small studies showed that the accommodative ability of the lens may decrease by time (8 months in Sauder and colleagues’ trial and 12 months in Dogru and colleagues’ study) leading to a reduction in the near vision acuity. The studies had some limitations and long-term follow-up is needed to determine the long-term safety and efficacy of the lens. In a large prospective, controlled, but non-randomized trial with potential biases (Evidence table 3), Uthoff and colleagues found that 1CU had a minor statistical advantage of half a reading step towards monofocal IOLs measured with subjective methods in near point, defocusing curve, and near visual acuity with BSCVA. They explained that this could be due to the pseudophakic accommodation by the optic shift or as a result of the additional pseudophakic pseudoaccommodation. The accommodative effect differed between patients and was unpredictable. Tetraflex: The prospective nonrandomized US Food and Drug Administration trial (Sanders 2010) on Tetraflex accommodative IOL is ongoing. In this study 255 patients received Tetraflex IOLs and 101 received monofocal IOLs. Interim results of 12 months follow-up of 239 patients in the Tetraflex arm and 96 controls show that the Tetraflex patients read better than the controls at print sizes of 20/80 (P=.04), 20/63 (P=.01), 20/50 (P<.001), 20/40 (P=.001), 20/32 (P<.001), and 20/25 (P=.001). The proportion of patients reading at a speed of ≥80 words per minute was significantly higher with the Tetraflex IOL (P=.003). Ninety-six percent of Tetraflex patients reported never wearing glasses for distance compared with 80% of control patients (P<.001). Seventy-five percent of the Tetraflex patients reported that they did not or occasionally needed to wear glasses for near reading small print and/or dim light compared with 46% of control patients (P<.001). The trial had its limitations and the study groups were not randomly assigned to type the IOL implanted which is a source of selection bias. They were also not blinded to the IOL received, which is another source of bias especially with subjective outcomes as self reporting of use of spectacles. Moreover, the reading ability and speed is dependent on many factors in addition to visual acuity. In conclusion, large randomized, controlled, and blinded trials with long-term follow-up are needed to determine the long-term efficacy, durability of benefit, and safety of the accommodative intraocular lenses.
Multifocal Intraocular Lens: A Cochrane meta-analysis with valid methodology (Leyland et al, 2008, evidence table 1) pooled the results of ten randomized controlled trials that compared visual outcomes of multifocal IOLs versus monofocal IOL implantation after cataract surgery. There were variations between the studies in population sizes, measures and outcomes reported, as well as follow-up durations. The main pooled results of the analysis showed no significant differences between multifocal and monofocal IOLs in uncorrected distance visual acuity or the proportion of patients achieving distance 6/6 best-corrected distance visual acuity. The uncorrected near vision was improved with the multifocal IOLs, and the rate of freedom from use of glasses was also higher with the multifocal IOLs. Contrast sensitivity was lower among participants receiving multifocal IOL implants who also experienced significantly higher rates of glare and halos. The results of another meta-analysis (Cochener et al 2011, Evidence table 2) that had the limitation of pooling results of observational studies together with randomized controlled trials, also showed that multifocal IOLs provided better uncorrected near visual acuity and less need for spectacles compared to monofocal IOLs. The results of the analysis also showed that diffractive multifocal lenses led to better results than the refractive IOLs, and that ReSTOR® had better uncorrected near visual acuity, uncorrected distance visual acuity, and higher spectacle independence rates compared with other multifocal IOLs. The incidence of halos was higher with multifocal lenses versus monofocal IOLs, but there was no significant difference between the different multifocal IOLs. No sensitivity analysis including only RCTs was made, and the results of the meta-analysis should be interpreted with caution. A more recent randomized controlled trial by Alió and colleagues (2011, Evidence table 3) compared the visual performance of 4 different IOLs: monofocal Acri.Smart, multifocal Acrysof ReSTOR® SN6AD3, multifocal Acri.Lisa 366D, and multifocal ReZoom refractive IOL. The same type of lens was implanted bilaterally in each of the 152 participants (304 eyes). After six moths of follow up, the results showed that all patients had postoperative significant improvement in uncorrected and corrected visual acuities. Patients with the ReSTOR® and Acri.Lisa multifocal lens implants had significantly better uncorrected reading acuity than those in the monofocal or the refractive ReZoomTM groups. The monofocal group had the greatest uncorrected reading distance at 1 and 6 months postoperatively. The authors did not evaluate patient satisfaction with the different types of IOLs, nor did they assess the contrast sensitivity, or presence of glare and halos. Studies comparing ReSTOR® +3.0 D versus ReSTOR® +4.0 D were not critically appraised in this report, but their overall results showed better intermediate visual acuity, but more glares with the +3.0 D vs.+4.0 D IOLs. Conclusion: There is good evidence from the published literature that multifocal intraocular lenses improve near visual acuity when compared to monofocal lenses, without compromising distance visual acuity. There is good evidence that patients undergoing multifocal IOLs implantation have higher rates of spectacle independence compared to those with monofocal lens implants. There is evidence that patients with multifocal IOL implants experience more halos and glare and have lower contrast sensitivity than those with monofocal implants. There is fair evidence that optical outcomes are better with diffractive versus refractive multifocal IOLs, and that improvement in near vision without use of glasses and patient satisfaction are more evident with ReSTOR® compared to other multifocal IOLs. There is insufficient evidence to determine any significant difference in contrast sensitivity, glare, or halos between multifocal IOLs.


Multifocal Intraocular Lens The literature search revealed a large number of studies on multifocal intraocular lenses. The majority were prospective or retrospective observational studies and case series with different population sizes and follow-up durations and no comparison or control groups. There were also a number of published randomized or nonrandomized controlled trials that evaluated the visual function, and/or quality of life after the implantation of monofocal versus multifocal lenses. The search also indentified three meta-analyses that pooled the results of trials comparing multifocal versus monofocal intraocular lenses, one meta-analysis of studies compared different IOLs, as well as a pooled analysis of two non-randomized trials that compared outcomes of ReSTOR vs. monofocal IOLs lenses. The most recent meta-analysis comparing outcomes of monofocal versus

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