Anthem

Medical Policy

Subject: Implanted Artificial Iris Devices
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Description/Scope

This document addresses the use of artificial iris devices.

Note: for information concerning other ophthalmic implants, see:

- CG-SURG-94 Keratoprosthesis
- SURG.00061 Presbyopia and Astigmatism-Correcting Intraocular Lenses
- SURG.00113 Artificial Retinal Devices

Position Statement

Investigational and Not Medically Necessary:

The use of implanted artificial iris devices are considered**investigational and not medically necessary** for all indications, including as a treatment of congenital or traumatic aniridia.

Rationale

The CustomFlex® ArtificialIris (Clinical Research Consultants, Inc, Cincinnati, OH) received Food & Drug Administration (FDA) approval through the premarket approval (PMA) process on May 30, 2018. CustomFlex was initially granted Breakthrough Device designation. The device, which is the only FDA-approved stand-alone prosthetic iris, is indicated for those with diminished visual functioning, including glare, photophobia, decreased contrast sensitivity and decreased depth of focus, caused by partial or complete aniridia.

The FDA approval was based on a prospective, non-masked, non-randomized multicenter study composed of four cohorts with a total of 447 eyes that were followed for 12 months postoperatively. The analysis was completed on 427 eyes due to 20 eyes discontinued or dropped out prior to the 12-month follow-up. The FDA pivotal trial (Ayres, 2022) defined the primary efficacy endpoints as the decrease in severity of reported photosensitivity, improvement in health-reported quality of life (QOL) and improvement in postoperative cosmesis. At 12-month follow-up, participants reported a 59.7% decrease in daytime sensitivity and a 41.5% decrease in nighttime sensitivity. QOL was improved by 15.4 points and 93.8% of participants rated improved cosmesis. A total of 65.2% of participants gained 1 or more lines of corrected distance visual acuity (CDVA), there was no change in 23% of participants, 3.9% of participants lost 1 line and 2 or more lines were lost in 7.9% of the participants. The CDVA losses were determined to be related to the artificial iris device. The most frequently reported adverse event was an elevated intraocular pressure (IOP) over 30mm Hg. The final conditions of approval require additional follow-up studies to evaluate long-term safety (up to postoperative 3 years for adults and 5 years for pediatrics).

Spitzer and associates (2016) retrospectively evaluated the functional, cosmetic and complication outcomes in 34 individuals who received the Artificial Iris (AI) implant. Individuals with a history of a severe globe injury with total or subtotal iris loss in one eye who received an AI were included. Distance visual acuity (VA), IOP and the rate of complications (long-term inflammation and corneal decompensation leading to corneal transplantation) were evaluated. The median follow-up period was 24 months. Postoperatively, 14 individuals had a VA improvement between 0.2 and 2.1 logMAR units, 11 individuals had a VA change of less than 0.2 logMAR units, and 9 individuals (26%) had a reduction in VA (between 0.2 and 1.4 logMAR units). The median group VA was unchanged following AI implantation. A myriad of complications were reported. Postoperative hypotony was reported in 10 individuals, 7 of which had low pressure prior to AI implantation. In 2 of these individuals, the low IOP led to phthisis and blindness and ultimately enucleation. Hypertony was observed in 6 individuals, 3 of which had pre-existing glaucoma. Other complications were noted, including persistent intraocular inflammation (9%) and macular edema (12%). A total of 12 individuals required corneal transplantation following AI implantation with 6 of these cases showing endothelial decompensation post AI implantation. Suspected postoperative endophthalmitis was noted in 1 case. In several cases, additional procedures, such as keratoplasty, repositioning of the AI or strabismus surgery was required. The authors noted that several factors could have contributed to the variability in responses to the AI, including pathophysiology related to the original trauma, complications or surgeries post AI implantation which were independent from the AI, and complications resulting from the AI implantation itself. While 34 individuals were included in the case series, only 20 of these participants were available to report subjective symptoms such as discomfort and glare. The study lacks individual clinical data for the 34 participants. This does not make it possible to identify patient characteristics that might predict a good prognosis for visual recovery.

In a retrospective interventional case series, Rickmann and colleagues (2016) evaluated the long-term clinical outcome (2 years or greater) and complication spectrum after artificial iris implantation in 34 individuals with congenital, traumatic, or iatrogenic aniridia. Cases included individuals with complete and partial aniridia. Prior to implantation, 5 eyes were hypotonic, 10 eyes had glaucoma, 6 eyes had pre-existing keratopathy and in 4 eyes there was silicone oil in the anterior chamber. Complications included glaucoma (3), keratopathy (2), silicone oil in the anterior chamber (3), hemorrhage of the remnant iris (1) and retinal detachment (2). Consecutive surgery was required in 5 eyes. When the VA at baseline was compared to the final examination, 16 eyes gained two or more VA lines, 15 eyes remained stable and 3 eyes lost two or more VA lines. There was no significant difference in the mean IOP when baseline was compared to final examination. With the study being single-center and single-surgeon, there is limited generalizability of the results.

Figueiredo and Snyder (2020) evaluated the effectiveness and safety of the CustomFlex device when used to treat photic symptoms in individuals with congenital aniridia. The retrospective single-surgeon case series involving 50 individuals and 96 eyes included those with more than 6 months follow-up (mean follow-up 44 months, 36 ± 36 months). Pre and post-operative data regarding CDVA, subjective photophobia and glare, keratopathy, glaucoma, IOP, glaucoma drops, and other comorbid pathologies was collected. Additional postoperative data regarding postoperative complications, prosthesis decentration, and further surgeries was also collected. In all cases, additional procedures were performed at the time of implantation, including phacoemulsification, intraocular

lens (IOL) implantation repositioning or replacement, limbal relaxing incision, keratectomy (superficial and lamellar) or vitrectomy. Intraoperative complications were reported in 14 eyes (14.6%). In regards to photophobia, 95.7% (89/93) reported a reduction in symptoms, 3.2% (3/93) reported no change in symptoms and 1.1% (1/93) reported worsening of symptoms. The results were similar for the subjective reporting of glare; 95.2% (79/83) reported a reduction in symptoms, 3.6% (3/83) reported no change in symptoms and 1.2% (1/83) reported worsening of symptoms. When individuals could not reliably report their symptoms, family member observations of behaviors was used to gauge functional improvement in photic symptoms. When preoperative visual acuity was compared to last measured postoperative visual acuity, 58.3% (56) of the eyes improved 2 or more lines, 32.3% (31) of the eyes stayed within two lines of preoperative measurements, and 9.4% (9) of the eyes dropped two or more lines. When compared to best measured postoperative visual acuity, there were declines during the postoperative follow-up period. These declines were attributed to underlying comorbidities, including worsening of the ocular surface, aniridia fibrosis syndrome, retinal detachment, and posterior capsule opacification. Aniridic keratopathy, which was present in 84.4% (81) of the eyes preoperatively, was present in 85.4% (82) at last visit. A total of 28.4% (23) of the eyes with preoperative keratopathy had progression of the disease. Aniridic glaucoma, which was present in 33.3% (32) of the eyes preoperatively, was present in 51.0% (49) of the eyes at last visit. A total of 53.1% (17) of the eyes with preoperative glaucoma had progression of the disease. Additional complications included aniridia fibrosis syndrome (AFS) (3.1%; 95% confidence interval (CI): 0.6 to 8.9%), prosthesis decentration (9.4%), choroidal folds/effusion secondary to ocular hypotony (2.1%), retinal detachment (1.0%), cystoid macular edema (1.0%) and vitreous hemorrhage (1.0%). During the follow-up period, 33.3% (32) eyes required additional surgical intervention with a mean of 2.97 ± 1.87 surgeries performed/eye. The authors summarize that individuals with congenital aniridia syndrome present with highly complex eyes which require an individualized approach and long-term follow-up. While the study was limited to individuals with congenital aniridia, there was significant heterogeneity related to aniridic pathology within the group.

In 2019, Mayer and colleagues reported previously unrecognized late complications associated with artificial iris implantation. Individuals with remnant iris tissue who underwent ArtificalIris implantation between June 2011 and December 2016 (n=42) were evaluated to determine the influence of the prosthesis on the residual iris. A retraction of the residual iris was detected in 7 individuals. In all cases, the syndrome was detected via photographic comparisons rather than the treating ophthalmologists or the treated individual. A total of 4 of the 7 affected individuals showed severe complications, including highly raised IOP, pigment dispersion associated with glaucoma, and recurrent bleeding into the anterior chamber. Several individuals required additional invasive procedures, including glaucoma shunt surgery and explantation of the implant. This study underscores the need for long-term data to better anticipate risks associated with specific techniques or comorbidities and to monitor for unanticipated complications.

Other implants, such as the BrightOcular (previously NewColorIris®) (Stellar Devices, New York, NY) have been used for cosmetic reasons outside of the United States. These devices are not FDA approved. These devices have been associated with a high incidence of serious complications which resulted in permanent structural damage or visual impairment (Ghaffari, 2021; Mansour, 2016; Mednick, 2018; Queiruga-Piñeiro, 2022).

Summary

Studies reported a significant number of complications including increased intraocular pressure, strands of fiber from the device in the eye, retinal hemorrhage, and corneal disruption requiring transplantation. Individuals with aniridia, congenital or acquired, present with complex cases and a myriad of significant comorbid pathologies. Other therapies, either concurrent or subsequent, may be required in addition to the artificial iris implantation, which may increase the complexity of the procedure (Crawford, 2022; Mayer, 2020). Treatment options available to these individuals are limited. Randomized, well-designed clinical trials are not a realistic expectation due to the relatively rare incidence of aniridia and the highly individualized presentation of affected individuals. However, additional experience and longer follow-up times are needed to better establish the incidence and nature of short- and long- term potential complications, allowing for more informed decisions regarding risks and benefits by providers and affected individuals. The implantation of artificial irises appears to be a promising technology, additional data can provide more information regarding the attributes of candidates with the greatest potential to benefit from this treatment.

Background/Overview

Congenital aniridia syndrome is a relatively uncommon disorder, occurring in approximately 1/60,000-100,000 live births in the United States (National Organization for Rare Disorders, NORD). Mutations in the PAX6 gene can result in in the production of a nonfunctional PAX6 protein that disrupts eye formation during embryonic development (National Institute of Health). The syndrome represents a wide variety of presentations, from minimal iris alterations to an apparent complete absence of the iris (Figueiredo, 2020; Romano, 2023). Congenital aniridia syndrome causes a reduction in visual acuity and increased photophobia; both eyes are typically equally affected. The syndrome is associated with other ophthalmic manifestations such as aniridic keratopathy, glaucoma, cataract, zonular laxity, capsule fragility, foveal and optic nerve hypoplasia, nystagmus, and ptosis (Figueiredo, 2020). Acquired aniridia results from injuries to the eye and is typically limited one eye. Traumatic aniridia can result in a variety of symptoms, including spherical and chromatic aberrations, subjective diplopia, significant photophobia, cosmetic defects, photopic retinal damage, and reduced visual acuity (Qiu, 2015). Large iris defects following ocular trauma is one of the major indications for surgical intervention (Doroodgar, 2017).

Due to the spherical aberration caused by light rays passing through the periphery of the optical system, aniridia and iris defects can adversely affect visual acuity, depth of focus and contrast sensitivity. As individuals with aniridia or iris defects lack an adequate miotic light reaction, photophobia is a common symptom (Koch, 2014). Mayer (2018) notes “iris atrophy and pupil size can deteriorate the visual function of an increase of higher order aberrations”.

Alternative, conservative treatments to replace the iris include noninvasive techniques, such as sunglasses or tinted contact lenses. Tinted contact lenses or aniridic contacts may be a safer option than more intensive therapies for some individuals, but is not a feasible option for many affected individuals (Qiu, 2015). Lamellar intrastromal corneal tattooing is an early treatment which is associated with few complications, but may be limited in those with keratopathy (Calvão-Pires, 2014). Corneal tattooing is considered minimally invasive, largely successful and the current pigments have a low incidence of complications (Lian, 2020) Suture techniques, such as iridopathy or iridopexy side-to-side iris sutures may be an option in those with some portion of iris remaining. Iris suturing is widely available and is reversible, however, sutures have the potential to cause endothelial damage (Lian, 2020). Iris cautery is also an option. The procedure is similar to iris suturing but no sutures are needed. Early studies have reported complications associated with cautery including iris pigment dispersion and diathermy site disconnection (Lian, 2020). Previous intraocular iris replicas include black-diaphragm intraocular (BDI) lenses, aniridia rings and iris prosthesis systems (Spitzer, 2016). Currently, there are no other FDA approved iris replica devices.

The ArtificialIris device, which is known as CustomFlex in Europe, is a custom-made, hand-colored, foldable iris prosthesis made of biocompatible hydrophobic silicone elastomer, which may or may not be sutured in place (Figueiredo, 2020). The posterior surface of the implant contains black pigmentation, which prevents light transmission. Suturing is usually required in individuals with partial aniridia or with no capsular support. The CustomFlex can be implanted into the capsular bag or in the ciliary sulcus (Spitzer, 2016). The implantation of the device is frequently done concurrently with additional surgical procedures (Figueiredo, 2020).

Definitions

Aniridia: Partial or complete absence of the iris.

Aniridia fibrosis syndrome: A condition characterized by the development of a progressive fibrotic membrane in the anterior chamber of the eye which can occur in individuals with congenital aniridia who have undergone previous intraocular surgery. Membrane growth can cause anterior displacement of posterior chamber intraocular lenses (PCIOLs) into the cornea and hypotony by posterior extension of the membrane over the ciliary body.

Iris: Colored portion of the eye which contains muscles to expand and contract to control the amount of light which enters the eye.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
For the following procedure codes; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT	
0616T	Insertion of iris prosthesis, including suture fixation and repair or removal of iris, when performed; without removal of crystalline lens or intraocular lens, without insertion of intraocular lens
0617T	Insertion of iris prosthesis, including suture fixation and repair or removal of iris, when performed; with removal of crystalline lens and insertion of intraocular lens
0618T	Insertion of iris prosthesis, including suture fixation and repair or removal of iris, when performed; with secondary intraocular lens placement or intraocular lens exchange
HCPCS	
C1839	Iris prosthesis
ICD-10 Procedure	
08RC3JZ	Replacement of right iris with synthetic substitute, percutaneous approach
08RD3JZ	Replacement of left iris with synthetic substitute, percutaneous approach
ICD-10 Diagnosis	
	All diagnoses

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Government Agency, Medical Society, and Other Authoritative Publications:

1. HumanOptics CustomFlex® Artificial Iris Professional Use Information. 2018. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170039d.pdf. Accessed on May 25, 2023.
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Websites for Additional Information

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ArtificialIris
BrightOcular
CustomFlex
Human Optics
NewColorIris

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	08/10/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, Background and References sections.
Reviewed	08/11/2022	MPTAC review. Updated Rationale and References sections.
Reviewed	08/12/2021	MPTAC review. Updated Description, Rationale, Discussion and References sections.
New	08/13/2020	MPTAC review. Initial document development.

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Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.