Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 1/1/25**
(See policy history boxes for previous effective dates)

Title: Retinal Prosthesis

Description/Background

A retinal prosthesis replaces lost photoreceptor function by transmitting external images to an array of electrodes or via light sensors placed in the epiretinal or subretinal space. The artificial retina could restore sight to individuals with blindness secondary to retinal diseases, such as retinitis pigmentosa, hereditary retinal degeneration, and some forms of age-related macular degeneration. Several models of retinal prostheses are in development in the United States, Europe, and Asia. Only the Argus II system has been cleared for use by the U.S. Food and Drug Administration (FDA).

Two approaches are being explored to develop an artificial retina. The first is implantation of electrode arrays in the epiretinal or subretinal space to stimulate retinal ganglion cells. A second approach is the implantation in the subretinal space of light-sensitive multi-photodiode arrays, which stimulate the remaining photoreceptors in the inner retina. Use of a multi-photodiode array does not require external image processing. The latter approach is being evaluated for degenerative retinal diseases such as retinitis pigmentosa, in which outer retinal cells deteriorate, but inner retinal cells remain intact for years.

Research in the United States began with a first-generation, 16-electrode device (e.g., the Argus 16; Second Sight Medical Products), which permitted the distinction between the presence and absence of light. Three government organizations provided support for the development of the Argus II: the Department of Energy, National Eye Institute at the National Institutes of Health, and National Science Foundation. They collaborated to provide grant funding, support for material design, and other basic research for the project.

The Argus II system has three main components: a video camera attached to the frame of the individual's glasses, a video processing unit (VPU) worn on a belt at the waist, and an epiretinal micro-electrode-array implant connected to a secondary antenna. The VPU receives,

processes, and converts the visual signal captured by the video camera into a brightness map in real time, Data and power are wirelessly transmitted from the primary antenna (which is attached to the glasses) to the secondary antenna (which is sutured to the sclera in the lower temporal quadrant). The data from the secondary antenna are then sent to the micro-electrode array, which is implanted on the subject's retina. The array presents the brightness values from the video as pulse amplitudes on each of the 60 electrodes. This discrete signal is transmitted to the functioning secondary neurons, which help create a visual perception by processing and channeling the signal to the brain for final integration.

Other devices in development, none of which are approved or cleared by the U.S. Food and Drug Administration, include the following:

- The Alpha-IMS was developed at the University of Tubingen, Tubingen, Germany with the electronic chip design provided by the Institute for Microelectronics, Stuttgart (IMS) Germany. The second generation Alpha-IMS device has wireless power and signal transmission and is produced by Retina Implant AG (Germany). The microchip is implanted sub-retinally and receives input from a multi-photodiode array with 1,500 elements that moves with the eye, senses incident light, and applies a constant-voltage signal at the respective 1,500 electrodes. The multi-photodiode array transforms visual scenes into corresponding spatial patterns (38 x 40 pixels) of light intensity-dependent electric stimulation pulses with a maximum visual field of 15˚.

- The Boston Retinal Implant Project uses an external camera mounted on a pair of glasses and a 100-electrode array. The image obtained by the external camera is translated into an electromagnetic signal transmitted from the external primary data coil mounted on a pair of glasses to the implanted secondary data coil attached to the cornea. Most of the volume of the implant lies outside the eye, with transscleral cables connected to a subretinal electrode array. The Retinal Implant Project is a joint effort of MIT, the Massachusetts Eye and Ear Infirmary, the VA Boston Healthcare System, and the NanoScale Science & Technology Facility at Cornell University.

- EPIRET3 retinal implant (Philipps-University Marburg, Marburg, Germany) is a wireless system that consists of a semiconductor camera on the frame of a pair of glasses and a transmitter coil outside the eye which sends electromagnetic signals to a receiver coil in the anterior vitreous (similar to an intraocular lens), which passes them on to a receiver microchip. A stimulator chip then generates the stimulation pulses and activates a selection of 25 electrodes placed on the epiretinal surface via a connecting micro cable.

- Intelligent Retinal Implant System (Pixium Vision, Paris, France) uses an external camera integrated with a pair of glasses and linked by wire to a pocket computer. Receiver electronics connect via a scleral tunnel to an electrode array on the surface of the retina. Pixium Vision is also developing PRIMA, which uses a subretinal implant.

- Learning Retinal Implant (Intelligent Medical Implants, Zug, Switzerland) uses an external camera on the frame of a pair of glasses and wireless data and power transfer. Receiver electronics connect via a scleral tunnel to an epiretinal implant. A retinal encoder with 100 to 1000 tunable spatiotemporal filters simulates the filtering operations performed by the ganglion cell and allows individual calibration to improve each patient's visual perception.

- The Microelectrode-STS (suprachoroidal-transretinal stimulation) system (Osaka University, Japan) places the 9-electrode retinal prosthesis in a scleral pocket with a reference electrode in the vitreous cavity. A video camera is used to detect a visual object. Because the electrodes are at a greater distance from the retina, the resolution of the image may be lower than other devices. A proposed advantage of the STS prosthesis over epi- or subretinal prostheses is the safety of the surgical procedure, since the electrodes do not touch the retina.

Regulatory Status

In 2013, the Argus® II retinal prosthesis system (Second Sight Medical) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through a humanitarian use device exemption. This exemption is limited to devices that treat or diagnose fewer than 4,000 people in the United States each year. The Argus® II system is intended for use in adults, age 25 years or older, with severe-to-profound retinitis pigmentosa who have bare light perception (can perceive light, but not the direction from which it is coming) or no light perception in both eyes, evidence of intact inner layer retina function, and a history of the ability to see forms. Patients must also be willing and able to receive the recommended post-implant clinical follow-up, device fitting, and visual rehabilitation. Food and Drug Administration product code: NBF.

Medical Policy Statement

The intraocular retinal prosthesis is considered experimental/investigational. It has not been scientifically demonstrated to be safe and effective.

Inclusionary and Exclusionary Guidelines

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

0100T	0472T	0473T	C1841*	L8608	V2799

** Codes are for facility use only*

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice. The following is a summary of the key literature to date.

RETINAL PROSTHESES

Clinical Context and Therapy Purpose

The purpose of implanting a retinal prosthesis in individuals who have blindness due to retinal diseases is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICOs were used to select literature to inform this review.

Populations

The relevant population(s) of interest are individuals with blindness secondary to retinal diseases, such as retinitis pigmentosa, hereditary retinal degeneration, and some forms of age-related macular degeneration.

Interventions

The treatment being considered is the use of a retinal prosthesis. The Argus II Retinal Prosthesis System (Argus II) is the second-generation device, which has 60 electrodes. The retinal prosthesis, with the electrode array, is surgically implanted in and on the eye. The system's external components include a small external video camera, held on eyeglass frames, that captures images then processed by an externally worn microcomputer. These signals are transmitted to an antenna in the prosthesis, an electronics package in the superior temporal quadrant and an electrode array implanted in the back of the eye, which in turn stimulates the optic nerve. It has been suggested that future-generation devices, containing more than 1000 electrodes, will provide more detailed vision.

Comparators
Standard treatment of retinal diseases; medical therapies in early stage of some conditions and adaptive interventions.

Outcomes
The general outcomes of interest are symptoms, change in disease status, functional outcomes and quality of life. More specific outcomes include: visual function, visual acuity, laboratory-based visual performance measures, and day-to-day function.

Follow-up of at least 6 months would be desirable to assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A 2016 technology assessment prepared for the Agency for Healthcare Research and Quality included a systematic review of the literature on retinal prostheses.(1) Reviewers included studies on the Argus II, the only retinal prosthesis cleared for marketing in the United States, as well as other retinal prostheses. Outcomes of interest were visual function, visual acuity, laboratory-based visual performance measures, day-to-day function, and quality of life. In their qualitative summary of the literature on retinal prostheses, reviewers concluded that the strength of evidence was insufficient for all outcomes.

One single-arm study with 30 subjects (NCT00407602) has evaluated the Argus II retinal prosthesis; numerous articles have been published on its findings and on subgroup studies conducted on some or all of the participants. The study was prospective and multicenter, with sites in the United States and Europe. It included individuals with retinitis pigmentosa (U.S.) or outer retinal degeneration (Europe) who had bare light perception or no light perception in both eyes. Articles based on this study are described next.

Humayan et al (2012) reported interim (minimum 6-month) results on 3 types of visual acuity tasks using a computer and 2 types of real-world utility tests.(2) The computer tasks included square localization (locating a high-contrast white square of light on a black background), direction of motion (indicating the direction of a high-contrast bar moving across the screen), and grating discrimination (discriminating among square-wave gratings of different special frequencies presented on a monitor). Patients performed better on all 3 computer tasks with the system on than off. In terms of the 2 real-world utility tests, with the system on, subjects had a 54% success rate in finding a door compared with a 27% success rate with the device off and had a 68% success rate in following a white line on a dark floor compared with a 23%

success rate with the device off. Although all subjects were able to perceive light when the system was stimulated, the Argus II did not affect full-field light perception.

Da Cruz et al (2016) reported on 3- and 5- year results of the visual acuity tests.(3) Subjects performed significantly better on the 3 computer tasks with the device on than off. For the simplest task, square localization, 89% (25/28) of individuals tested did better with the device on and, at year 5, 81% (17/21) of individuals tested did better with the device on. For grating discrimination, the most difficult assessment, 33% (9/27) of individuals tested at year 3 did better with the device on and 38% (8/21) of individuals tested at year 5 did better with the device on.

Ho et al (2015) reported on safety up to 3 years.(4) At 3 years post implantation, 23 serious adverse events were reported in 11 individuals; the most commonly reported were conjunctival erosion (n=4), hypotony (n=4), conjunctival dehiscence (n=3), and presumed endophthalmitis (n=3). Five-year safety was reported by da Cruz et al (2016).(3) As reported by da Cruz, only 1 additional serious adverse event, a case of a rhegmatogenous retinal detachment, occurred after the 3-year follow-up (≈4.5 years).(3) Three devices were explanted, 1 each at 14 months, 3.5 years, and 4.3 years after implantation. Two individuals had experienced recurrent conjunctival erosion and the third experienced chronic hypotony and ptosis.

Several publications have reported on additional functional outcomes in individuals participating in the Argus II study. Subjects served as their own controls; performance was compared with the device in the on versus off position. Geruschat et al (2016) reported on observer-rated assessments of visual function using the multicomponent Functional Low-Vision Observer Rated Assessment (FLORA), which evaluates performance of 35 tasks.(5) Tasks were grouped into four domains: visual orientation, mobility, daily life, and interaction with others. Twenty-six (87%) of the 30 enrolled subjects were included in the analysis at a mean of 36 months (range, 18-44 months) after device implantation. All subjects performed significantly better ($p<0.05$) in each of the four domains with the device on versus off, ranging from 19% to 38% improvement. Twenty-four (69%) of 35 tasks had statistically significant improvements in outcomes (i.e., they were easier to perform) with the device turned on versus off.

A 2013 study reported on letter and word reading at 20 months in 21 individuals participating in the Argus II study.(6) Correct letter reading ranged from 51.7% to 72.3% with the device on, compared with 15.3% to 17.7% with the device off. The average time to correctly identify letters with the device on ranged from 47.7 to 68.6 seconds. Subjects who successfully completed the letter identification task proceeded to the next task. Six subjects were able consistently to read letters of reduced size. The smallest letter identified was 0.9 cm for 1 subject, but preferred letter size was as much as 22.6 cm. Four subjects were able to correctly identify 2-, 3-, and 4- letter words.

Kotecha et al (2014) reported on further testing of 6 patients from 1 of the Argus II study sites that had at least 3 years of follow-up; reaching and grasping outcomes were assessed.(7) The test consisted of picking up a white cube from a table covered with black felt and illuminated from above, and was conducted with the electrode array on, array off, and scrambled (i.e., array stimulated with a random, scattered input), in a random order. Also randomized was the location of the object, which could be placed in 1 of 4 positions. To eliminate the use of any residual vision among participants, certain patients had both eyes taped shut during the test.

After 4 to 6 weeks, individuals were retested to examine repeatability of performance. The percentage of successful grasps was significantly higher with the device on (69%) compared with off (0%); this finding was maintained at the second visit. With the signal scrambled, success rates were 59% at the first visit and 28% at the second visit. There were no significant differences between “on” or “scrambled” conditions for movement onset, time to object contact, or path deviation ratio, which was defined as the “deviation of the movement trajectory from a straight route between the starting and object contact wrist positions.”

Dagnelie et al (2017) evaluated performance on several functional tasks in 28 of 30 study participants who had been implanted with the device between 6 months and 3 years earlier.(8) The 3 tasks were intended to have real-world application. Performance was compared with the retinal prosthesis device on and off. Task 1 was sock sorting; task 2 was sidewalk tracking; and task 3 was walking direction discrimination.

On all 3 tasks, subjects performed significantly better with the device on than off ($p<0.05$). (For the sock sorting task, results were presented in figures, hence precise data were not available.) With a cloth-covered table, subjects sorted approximately 70% of the socks correctly with the device on and 30% correctly with the device off. With a bare table, subjects sorted approximately 50% of socks correctly with the device and 30% with the device off. For the sidewalk task, subjects walked out of bounds a mean of 6.85 times with the device off and a mean of 4.93 times with the device on. For the walking direction discrimination task, 15 (56%) of 27 subjects performed significantly better than chance with the device on and 4 performed significantly better than chance with the device off. Although statistically significant, the clinical significance of the differences in performance on the 3 tasks is uncertain.

Summary of Evidence

For individuals who have blindness secondary to retinal diseases who receive a retinal prosthesis, the evidence includes a prospective single-arm study evaluating the device approved by the U.S. Food and Drug Administration and a systematic review of studies on various devices. Relevant outcomes are functional outcomes, quality of life, and treatment-related morbidity. A 2016 systematic review included studies on the Food and Drug Administration—approved retinal prosthesis as well as devices unavailable in the United States; the overall conclusion was that the evidence on retinal prostheses is insufficient on all outcomes of interest. One study with 30 individuals has evaluated the single Food and Drug Administration—approved device (Argus II); numerous articles on this study have been published. Primary outcomes included 3 computer-based visual acuity tests. At 3 and 5 year follow-up visits, individuals performed significantly better on the 3 computer tasks with the device on vs off. Performance on the most difficult task (grating discrimination) was still relatively low with the device on. Subgroup studies have tested performance on more practical tasks. These studies have tended to find significantly better performance with the device on but differences between groups may not be clinically meaningful. The same 30 patients have been evaluated multiple times and, as a result of multiple testing, their performance may differ from other individuals with the device. Additional prospective studies and additional evaluations of the ability to perform practical tasks that have a clinically meaningful impact on health outcomes are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome

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
Unpublished			
NCT01864486[a]	Restoring Vision With the Intelligent Retinal Implant System (IRIS V1) in Patients With Retinal Dystrophy (Title in France: Compensation of Vision With the Intelligent Retinal Implant System (IRIS V1) in Patients With Retinal Dystrophy)	20	Oct 2017 (updated 10/17/17)
NCT02303288[a]	Post-Market Study of the Argus® II Retinal Prosthesis System -France	18	Nov 2018 (updated 06/22/20)

NCT: national clinical trial
[a] Denotes industry-sponsored or cosponsored trail

Supplemental Information

PRACTICE GUIDELINES AND POSITION STATEMENTS

No practice guidelines related to retinal prostheses were identified.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

Government Regulations
National/Local:

There is no National or Local Medicare coverage determination.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References

1. Fontanarosa J, Treadwell JR, Samson DJ, et al. Retinal Prostheses in the Medicare Population (AHRQ Technology Assessment). Rockville, MD: Agency for Healthcare Research and Quality; 2016 September.
2. Humayun MS, Dorn JD, da Cruz L, et al. Interim results from the international trial of Second Sight's visual prosthesis. Ophthalmology. Apr 2012;119(4):779-788. PMID 22244176
3. da Cruz L, Dorn JD, Humayun MS, et al. Five-year safety and performance results from the Argus II Retinal Prosthesis System Clinical Trial. Ophthalmology. Oct 2016;123(10):2248-2254. PMID 27453256

4. Ho AC, Humayun MS, Dorn JD, et al. Long-Term Results from an Epiretinal Prosthesis to Restore Sight to the Blind. Ophthalmology. Aug 2015;122(8):1547-1554. PMID 26162233
5. Geruschat DR, Richards TP, Arditi A, et al. An analysis of observer-rated functional vision in patients implanted with the Argus II Retinal Prosthesis System at three years. Clin Exp Optom. Jan 24 2016. PMID 26804484
6. da Cruz L, Coley BF, Dorn J et al. The Argus II epiretinal prosthesis system allows letter and word reading and long-term function in patients with profound vision loss. Br J 97(5):632-6. Ophthalmol 2013; 97(5):632-6.
7. Kotecha A, Zhong J, Stewart D, et al. The Argus II prosthesis facilitates reaching and grasping tasks: a case series. BMC Ophthalmol. 2014;14:71. PMID 24885164
8. Dagnelie G, Christopher P, Arditi A, et al. Performance of real-world functional vision tasks by blind subjects improves after implantation with the Argus(R) II retinal prosthesis system. Clin Exp Ophthalmol. Aug 06 2016. PMID 27495262

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 8/13/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
12/9/05	12/9/05	12/1/05	Joint policy established
3/1/08	12/11/07	1/23/08	Routine maintenance
3/1/09	12/9/08	12/21/08	Routine maintenance
7/1/11	4/19/11	5/3/11	Routine maintenance
1/1/13	10/16/12	10/16/12	Routine maintenance; description, rationale and reference sections revised
7/1/14	4/10/14	4/15/14	Routine maintenance
7/1/15	4/21/15	5/8/15	Routine maintenance
7/15/16	4/16/16	4/16/16	Routine approval
9/1/16	6/21/16	6/21/16	Routine maintenance
9/1/17	6/20/17	6/20/17	• Routine maintenance; updated title, background, codes, rationale, regulatory status and references • Added codes: C1841, V2799, 0472T and 0473T
9/1/18	6/19/18	6/19/18	• Routine maintenance
9/1/19	6/18/19		• Routine maintenance • Added codes: C1841 and L8608
1/1/20	10/15/19		• Routine maintenance
1/1/21	10/20/20		• Routine maintenance
1/1/22	10/19/21		• Routine maintenance
1/1/23	10/18/22		• Routine maintenance (slp)
1/1/24	10/17/23		• Routine maintenance (slp) • Vendor Managed: N/A
1/1/25	10/15/24		• Routine maintenance (slp) • Vendor Managed: N/A

Next Review Date: 4th Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: RETINAL PROSTHESIS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	Refer to the Medicare information under the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.