Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 11/1/23**
(See policy history boxes for previous effective dates)

Title: Intraocular Radiation Therapy for Age-Related Macular Degeneration

Description/Background

Intraocular radiation, including brachytherapy, proton beam therapy, and stereotactic radiotherapy, are being evaluated to treat choroidal neovascularization associated with age-related macular degeneration.

Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is the leading cause of legal blindness in individuals older than age 60 in developed nations. AMD is characterized in its earliest stages by minimal visual impairment and the presence of large drusen and other pigmentary abnormalities on ophthalmoscopic examination. Two distinctive forms of degeneration may be observed. The first, called the atrophic or areolar or dry form, evolves slowly. Atrophic AMD is the most common form of degeneration and may be a precursor of the more visually impairing exudative neovascular form, also referred to as disciform or wet AMD. The wet form is distinguished from the atrophic form by the development of choroidal neovascularization (CNV) and serous or hemorrhagic detachment of the retinal pigment epithelium. Risk of developing severe irreversible loss of vision is greatly increased by the presence of CNV.

Standard Clinical Management

Usual care for neovascular AMD includes intravitreal agents that target vascular endothelial growth factor, including pegaptanib, ranibizumab, bevacizumab, and aflibercept. Photodynamic therapy is an older method that has been largely replaced by anti-vascular endothelial growth factor therapies. The intravitreal therapies may necessitate repeated intravitreal injections. Hence, alternative treatments, such as intraocular radiation, including brachytherapy, proton beam therapy (PBT), and stereotactic radiotherapy, are being investigated.

Intraocular Radiotherapy
The NeoVista Epi-Rad90 Ophthalmic System, a brachytherapy device, treats CNV by delivering focal radiation to a subfoveal choroidal neovascular lesion. Using a standard vitrectomy procedure, the cannula tip of a handheld (pipette-like) surgical device is inserted into the vitreous cavity and positioned under visual guidance over the target lesion. The radiation source (strontium 90) is advanced down the cannula until it reaches the tip, which is then held in place over the lesion for a "prescribed" time to deliver focused radiation. The system is designed to deliver a 1-time peak dose of beta particle energy (24 gray) for a target area 3 mm in depth and up to 5.4 mm in diameter. This dose is believed to be below that toxic to the retina and optic nerve. Radiation exposure outside of the target area is expected to be minimal.

Proton beam therapy (PBT) is a type of external radiotherapy that uses charged atomic particles (protons or helium ions) to target a given area. PBT differs from conventional electromagnetic (photon) radiotherapy in that, with PBT, there is less scatter as the particle beams pass through tissue to deposit ionizing energy at precise depths (Bragg peak). The theoretical advantage of PBT over photon therapy is the ability to deliver higher radiation doses to the target without harm to adjacent normal tissue.

Stereotactic radiotherapy is a nonsurgical procedure performed in an office setting. It uses a robotically controlled device to deliver radiation beams through the inferior sclera to overlap at the macula.

Other Treatments
Other available therapeutic options for AMD not addressed in this policy include photodynamic therapy and vascular endothelial growth factor (VEGF) antagonists or angiostatics.

For those whose visual loss impairs their ability to perform daily tasks, low-vision rehabilitative services offer resources to compensate for deficits.

Regulatory Status

No devices are specifically approved by the U.S. Food and Drug Administration (FDA) for the intraocular radiation. An investigational device exemption (IDE) has been granted by the U.S. Food and Drug Administration (FDA) for a Phase III multicenter trial to of the EPI-RAD90™ (now known as Vidion Anti-Neovascular Epimacular Brachytherapy [EMBT] System; NeoVista), to provide data for application to the Food and Drug Administration. This is a category B procedure.

Medical Policy Statement

Intraocular placement of a radiation source, (brachytherapy), proton beam therapy and stereotactic radiotherapy for the treatment of choroidal neovascularization are considered experimental/investigational. These procedures have not been scientifically shown to be as safe and effective as conventional treatment.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

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.):

67036 67218 67299

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 (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs 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.

Brachytherapy

Clinical Context and Therapy Purpose

The purpose of brachytherapy for individuals who have choroidal neovascularization associated with age-related macular degeneration 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.

Population
The relevant population of interest is individuals with choroidal neovascularization associated with age-related macular degeneration.

Interventions
The treatment being considered is brachytherapy. Brachytherapy treats choroidal neovascularization by delivering focal radiation to a subfoveal choroidal neovascular lesion.

Brachytherapy is performed in a surgical setting. After surgery, patients are hospitalized for 2-4 days during the brachytherapy. Once the brachytherapy is complete, the patient undergoes another operation to remove the protective gold plaque that was placed on the eye during the first operation. At this point the patient may go home.

Comparators
The following practices are currently being used to treat choroidal neovascularization associated with age-related macular degeneration: intravitreal vascular endothelial growth factor and photodynamic therapy.

Outcomes
The general outcomes of interest are change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity.

Follow-up of 1-2 years is 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

Systematic Review
Evans et al (2020) evaluated the efficacy of radiotherapy on neovascular age-related macular degeneration in a Cochrane review.(1) The review included 18 RCTs in which radiotherapy (dosage range: 7.5 to 24 Gy) was compared to another treatment, sham treatment, low dosage irradiation, or no treatment. Of the 18 studies, 3 involved brachytherapy (plaque and epimacular). Two of these 3 studies (discussed below) evaluated epimacular brachytherapy combined with intravitreal vascular endothelial growth factor injections versus intravitreal vascular endothelial growth factor alone. Overall, patients receiving combination radiotherapy/intravitreal vascular endothelial growth factor injections were more likely to lose 3 or more lines of best-corrected visual acuity at 12 months compared with injections alone across the 3 trials (risk ratio, 2.11; 95% confidence interval [CI], 1.40 to 3.17; moderate

certainty). The authors also concluded that visual outcomes with epimacular brachytherapy are likely to be worse, with an increased risk of adverse events, probably related to vitrectomy.

Randomized Controlled Studies

Jackson et al (2016) reported the results of a phase III RCT, Epimacular Brachytherapy for Previously Treated Neovascular Age Related Macular Degeneration (Macular Epiretinal Brachytherapy versus Ranibizumab (Lucentis) Only Treatment - MERLOT), comparing epimacular brachytherapy (EMB) plus as-needed ranibizumab (n=224) with as-needed ranibizumab alone (n=119) in patients with neovascular age-related macular degeneration (AMD), already receiving ranibizumab.(2) It was not feasible to mask patients to their surgical group (EMB), but visual acuity testing and macular imaging were evaluated by masked assessors. The trial was powered to test the hypothesis that EMB would reduce the number of antivascular endothelial growth factor (anti-VEGF) treatments, with a noninferior visual outcome (a margin of five letters of visual acuity). Over 12 months of follow-up, the mean number of as needed ranibizumab injections did not differ significantly between the EMB arm (4.8 treatments) and the ranibizumab monotherapy arm (4.1 treatments; p=0.068). From baseline to month 12, the mean change in best-corrected visual acuity was -4.8 letters in the EMB arm compared with -0.9 letters in the ranibizumab monotherapy arm (between-group difference 95% confidence interval [CI], -6.6 to -1.8, which did not demonstrate inferiority at the prespecified 5-letter margin). In contrast to the null hypothesis, ranibizumab monotherapy patients had superior outcomes for visual acuity. Adverse events were more common in the EMB arm. Overall, these results did not support the use of EMB over ranibizumab monotherapy for neovascular AMD.

In 2020, Jackson et al published 24-month efficacy and safety data from the MERLOT trial as epimacular brachytherapy typically takes several months to have an effect, and radiation damage is thought to be more likely in the second year after treatment.3, Results at 24 months of follow-up revealed that the mean number of ranibizumab injections was 9.3 in the brachytherapy group versus 8.3 in the ranibizumab group (p=0.13) and the mean change in best-corrected visual acuity was -11.2 letters in the brachytherapy group versus -1.4 in the ranibizumab group (difference: 9.8; 95% CI: -6.7 to -12.9). Microvascular abnormalities were seen in 20 (9.7%) of 207 eyes in the brachytherapy group versus 1 (1%) of 97 eyes in the ranibizumab group. Overall, the results continued to show that epimacular brachytherapy did not reduce the number of ranibizumab injections and was associated with worse visual acuity than ranibizumab alone.

A phase III multicenter RCT, A Study of Strontium90 B Radiation with Lucentis to Treat Age-Related Macular Degeneration (CABERNET; NCT00454389), enrolled 494 subjects with AMD-related wet CNV from 42 sites.(4,5) The safety and efficacy of EMB combined with 2 loading injections of ranibizumab (Lucentis) were compared with ranibizumab monotherapy (2 loading doses and then quarterly). Patients in both arms of the trial could receive monthly treatment with ranibizumab as needed. At 24 months, 77% of the patients in the EMB group lost fewer than 15 letters compared with 90% in the control group. This result did not meet the prespecified noninferiority margin. EMB treatment also did not meet the superiority end point, which was the proportion of participants gaining more than 15 letters (16% vs 26% for the ranibizumab group). The most common serious adverse event was cataract surgery (known to be associated with vitrectomy), which occurred in 40% of the EMB group compared with 11% of the ranibizumab monotherapy group. Mild radiation retinopathy occurred in 3% of the

patients who received EMB treatment. This trial did not support the use of epiretinal radiotherapy.

Nonrandomized Studies

Twelve- and 24-month results from the multicenter study, A Study of the NeoVista Ophthalmic System for the Treatment of Subfoveal choroidal neovascularization Associated With Wet age-related macular degeneration in Patients That Require Persistent Antivascular Endothelial Growth Factor Therapy (MERITAGE; NCT00809419) were reported in 2012 and 2014.(6-8) MERITAGE was a phase 1/2 study of EMB for the treatment of subfoveal choroidal neovascularization (CNV) associated with wet AMD in patients requiring continued anti-VEGF therapy to maintain an adequate response. Following a single 24-gray (Gy) dose, the 53 patients in the study received retreatment with ranibizumab administered monthly (as needed). In the 12 months before the study, participants received 0.45 injections per month. At the 12-month follow-up, 81% (43/53) of patients maintained stable vision (loss of <15 letters), with a mean of 3.49 anti-VEGF injections (0.29 per month). Over 24 months, the durability of the application diminished, with 68% (32/47) of patients maintaining stable vision at a mean of 8.7 anti-VEGF injections (0.72 per month).

Three publications from 2 studies have been reported by Avila et al on EMB using the EPI-RAD90 system.(9-11) One report (2009) described 12-month safety and visual acuity results of a feasibility study in 34 treatment-naive patients from Turkey, Mexico, and Brazil recruited between 2005 and 2006.(9) The second report (2009) described 12-month safety and visual acuity results from 24-Gy EMB combined with bevacizumab in 34 treatment-naive patients enrolled between 2006 and 2007.(10) Adverse events related to the device or procedure included subretinal hemorrhage (n=1), retinal tear (n=1), subretinal fibrosis (n=2), epiretinal membrane (n=1), and cataract (n=6/24; 24 patients were phakic at baseline). All occurrences of cataracts were deemed to be related to the vitrectomy procedure. Two- and 3-year results from this trial were published in 2012.(11) All 34 subjects were followed for 24 months; one site that enrolled 19 patients agreed to re-consent and follow patients for three years. On average, the cohort followed for 36 months received 3.0 bevacizumab injections. Twelve (50%) of the 24 phakic patients developed cataracts, and four had phacoemulsification with intraocular lens implantation. Mean change in visual acuity at 36 months was +3.9 letters. Seven (54%) of 13 phakic patients developed cataracts, and 4 had phacoemulsification with intraocular lens implantation. One case of nonproliferative radiation retinopathy was observed at 36 months.

Section Summary: Brachytherapy

At least 2 RCTs, which have been supported by additional nonrandomized studies and a Cochrane review, have found that epimacular brachytherapy (EMB) is inferior to local treatment with ranibizumab for the treatment of wet age-related macular degeneration.

Proton Beam Therapy

Clinical Context and Therapy Purpose

The purpose of proton beam therapy for individuals who have choroidal neovascularization associated with age-related macular degeneration 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 of interest is individuals with choroidal neovascularization associated with age-related macular degeneration.

Interventions
The treatment being considered is proton beam therapy. Proton beam therapy is external therapy that uses charged atomic particles to target a given area with less scatter of particle beams than conventional electromagnetic (photon) radiotherapy. Multiple treatments are required.

Comparators
The following practices are currently being used to treat choroidal neovascularization associated with age-related macular degeneration: intravitreal vascular endothelial growth factor and photodynamic therapy. These treatments are generally administered by an ophthalmologist or other eye specialist in an outpatient clinical setting.

Outcomes
The general outcomes of interest are change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity.

Follow-up of 1 to 3 years is desirable to assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the principles described in the first indication.

Review of Evidence

Pilot Study
Park et al (2012) reported 12- to 36-month follow-up of a pilot study of ranibizumab combined with proton beam therapy (PBT) for AMD.(12) Six eyes (6 patients) were treated with 4 monthly ranibizumab plus 24-Gy proton-beam treatments, followed by ranibizumab treatment if needed. No radiation retinopathy was observed at follow-up.

Randomized Controlled Trial
Ciulla et al (2002) reported results from a randomized, prospective, sham-controlled, double-masked treatment trial that examined the effect of proton beam radiation on subfoveal choroidal neovascular membranes associated with AMD.(13) Thirty-seven subjects were randomized to 16-Gy proton irradiation delivered in 2 fractions 24 hours apart or to sham control treatment. Recruitment was halted at 37 subjects for ethical reasons related to randomization to sham treatment when U.S. Food and Drug Administration approval of verteporfin (Visudyne; a light-activated drug used with photodynamic therapy) was anticipated. PBT was associated with a trend toward stabilization of visual acuity, but this association was not statistically significant.

Section Summary: Proton Beam Therapy
There is currently no available clinical trial evidence suggesting that PBT is noninferior to available treatment alternatives for AMD.

Stereotactic Radiotherapy

Clinical Context and Therapy Purpose
The purpose of stereotactic radiotherapy for individuals who have choroidal neovascularization associated with age-related macular degeneration 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 of interest is individuals with choroidal neovascularization associated with age-related macular degeneration.

Interventions
The treatment being considered is stereotactic radiotherapy. Stereotactic radiotherapy is a nonsurgical procedure using a robotically controlled device to deliver radiation beams through the inferior sclera to overlap at the macula.

Comparators
The following practices are currently being used to treat choroidal neovascularization associated with age-related macular degeneration: intravitreal vascular endothelial growth factor and photodynamic therapy.

Outcomes
The general outcomes of interest are change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity.

Follow-up of 1-2 years is desirable to assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the principles described in the first indication.

Review of Evidence

Randomized Controlled Trials
The study reported by Jackson et al (2013), IRay in Conjunction with antivascular endothelial growth factor (Anti-VEGF) Treatment for Patients with Wet Age-related Macular Degeneration (INTREPID) was a randomized, sham-controlled, double-masked trial with 230 patients that assessed the efficacy and safety of stereotactic radiotherapy (SRT) to treat neovascular AMD.(14) The primary outcome measure was the number of ranibizumab injections needed over 52 weeks. Both SRT and sham control patients received ranibizumab as needed. After one year, treatment with 16- or 24-Gy SRT reduced the number of ranibizumab treatments (median, 2 vs 3.5 for sham controls) with no significant differences from controls in changes in visual acuity over the one-year follow-up. No safety concerns were identified in the first 12 months.

In 2015, year 2 safety and efficacy results from the INTREPID trial were published.(15) Participants received 16- or 24-Gy SRT plus ranibizumab or sham SRT plus ranibizumab for

12 months, with bevacizumab or ranibizumab thereafter as needed. At year two, the 16- and 24-Gy arms received fewer as needed bevacizumab (mean, 4.5; p=0.008) or ranibizumab (mean, 5.4; p=0.09) treatments compared with sham (mean, 6.6). Changes in mean best-corrected visual acuity were -10.0, -7.5, and -6.7 letters, respectively, with 68%, 75%, and 79% losing fewer than 15 letters, respectively. Differences for visual acuity were not statistically significant. Microvascular abnormalities were detected in 6 control eyes and 29 SRT eyes, of which 18 were attributed to radiotherapy, with only 2 possibly affecting vision. The authors concluded that a single dose of SRT significantly reduced intravitreal injections over 2 years, and that, although radiotherapy can induce microvascular changes, only in 1% of eyes did this seem to affect vision.

Observational Study
Ranjbar et al (2016) reported results from an observational study of 32 patients (32 eyes) with neovascular AMD who met criteria for best responders in the INTREPID trial and were treated with SRT (16 Gy) along with aflibercept or ranibizumab.(16) For the study's primary outcome (the number of anti-VEGF treatments in the 12 months after SRT), significantly fewer intravitreal injections were given (3.47) compared with the year preceding SRT (6.81; p<0.001). No ocular or systemic adverse events occurred.

Section Summary: Stereotactic Radiotherapy
Evidence from a double-blind, randomized trial comparing SRT with ranibizumab for neovascular AMD has suggested that SRT can reduce the number or ranibizumab injections but was associated with radiation retinopathy leading to microvascular changes.

SUMMARY OF EVIDENCE
For individuals who have CNV due to AMD who receive brachytherapy, the evidence includes data form a Cochrane review, 2 RCTs comparing brachytherapy plus vascular endothelial growth factor with vascular endothelial growth factor monotherapy as well as phase 1/2 trials and case series on the use of brachytherapy. Relevant outcomes are change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. Both RCTs showed that brachytherapy did not attain noninferiority for visual acuity outcomes and was associated with a higher proportion of adverse events. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have CNV due to AMD who receive PBT, the evidence includes a randomized, prospective, sham-controlled trial and a pilot study. Relevant outcomes are change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. Recruitment into the RCT was halted for ethical concerns, and available results did not show statistically significant stabilization of visual acuity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have CNV due to AMD who receive stereotactic radiotherapy, the evidence includes an RCT with sham control. Relevant outcomes are change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. The RCT showed a reduction in the number of vascular endothelial growth factor treatments at 12- and 24-month intervals, but no significant differences vs controls for

changes in visual acuity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Academy of Ophthalmology

The American Academy of Ophthalmology (2015) updated its evidenced-based preferred practice pattern on age-related macular degeneration.(17) For extrafoveal choroidal neovascularization, radiotherapy was not recommended (SIGN grade: III; GRADE assessment: moderate level of evidence, strong recommendation).

In their 2019 Preferred Practice Pattern for age-related macular degeneration, the Academy states that current data is insufficient “to demonstrate clinical efficacy” of radiation therapy for extrafoveal choroidal neovascularization.(18)

National Institute for Health and Care Excellence

The 2011 guidance from the National Institute for Health and Clinical Excellence stated that current evidence on the efficacy of epiretinal brachytherapy, for wet age-related macular degeneration , is “inadequate and limited to a small number of patients.”(19) For safety, “vitrectomy has well-recognized complications, and there is a possibility of subsequent radiation retinopathy.” The Institute concluded that wet age-related macular degeneration should only be used for “research.”

Ongoing and Unpublished Clinical Trials

Some currently ongoing 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
Ongoing			
NCT02988895	A Prospective Study of Episcleral Brachytherapy for the Treatment of Neovascular Age-related Macular Degeneration (NEAMES)	12	Dec 2022
NCT04268836	Vision Improvement for Patients With Age-Related Macular Degeneration	200	May 2025
NCT02243878	Stereo Tactic Radiotherapy for Wet Age-Related Macular Degeneration (STAR): A Randomised, Double-masked, Sham-controlled, Clinical Trial Comparing Low-voltage Irradiation With as Needed Ranibizumab, to as Needed Ranibizumab Monotherapy	411	Jun 2024

NCT: national clinical trial.

Government Regulations
National/Local:

No Medicare determination is available regarding intraocular radiation for age-related macular degeneration.

(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

- Charged Particle (Proton or Helium Ion) Radiation Therapy
- Photodynamic Therapy for Choroidal Neovascularization
- Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

References

1. Evans JR, Igwe C, Jackson TL, et al. Radiotherapy for neovascular age-related macular degeneration. Cochrane Database Syst Rev. Aug 26 2020; 8: CD004004. PMID 32844399
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10. Avila MP, Farah ME, Santos A et al. Twelve-month short-term safety and visual-acuity results from a multicentre prospective study of epiretinal strontium-90 brachytherapy with bevacizumab for the treatment of subfoveal choroidal neovascularisation secondary to age-related macular degeneration. Br J Ophthalmol 2009; 93(3):305-9. PMID 19019935
11. Avila MP, Farah ME, Santos A et al. Three-year safety and visual acuity results of epimacular 90strontium/90yttrium brachytherapy with bevacizumab for the treatment of

subfoveal choroidal neovascularization secondary to age-related macular degeneration. Retina Jan 2012; 32(1):10-18. PMD 21817963
12. Park SS, Daftari I, Phillips T et al. Three-year follow-up of a pilot study of ranibizumab combined with proton beam irradiation as treatment for exudative age-related macular degeneration. Retina May 2012; 32(5):956-66.
13. Ciulla TA, Danis RP, Klein SB, et al. Proton therapy for exudative age-related macular degeneration: a randomized, sham-controlled clinical trial. Am J Ophthalmol. Dec 2002;134(6):905-906. PMID 12470761
14. Jackson TL, Chakravarthy U, Kaiser PK, et al. Stereotactic radiotherapy for neovascular age-related macular degeneration: 52-week safety and efficacy results of the INTREPID study. Ophthalmology. Sep 2013;120(9):1893-1900. PMID 23490327
15. Jackson TL, Chakravarthy U, Slakter JS, et al. Stereotactic radiotherapy for neovascular age-related macular degeneration: year 2 results of the INTREPID study. Ophthalmology. Jan 2015;122(1):138-145. PMID 25208859
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18. American Academy of Ophthalmology. Age-related macular degeneration preferred practice pattern. October 2019. https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp. Accessed June 23, 2023
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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 6/23/23, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
1/1/09	12/1/08	10/13/08	Joint policy established
7/1/11	4/19/11	5/3/11	Routine maintenance
11/1/12	8/21/12	8/21/12	Routine maintenance
3/1/14	12/10/13	1/6/14	Routine maintenance Replaced “Epiretinal” with “Intraocular” in the policy title; updated rationale and references; added proton beam therapy for the treatment of choroidal neovascularization as experimental/ investigational.
7/1/15	4/24/15	5/8/15	Routine maintenance Added stereotactic radiotherapy to the policy as experimental/ investigational.
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
9/1/18	6/19/18	6/19/18	Routine maintenance
11/1/19	8/20/19		0190T deleted; report using 67299
11/1/20	8/18/20		Routine maintenance
11/1/21	8/17/21		Routine maintenance
11/1/22	8/16/22		Routine maintenance
11/1/23	8/15/23		Routine maintenance (slp) Vendor managed: N/A

Next Review Date: 3rd Qtr, 2024

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: N/A	Revised: N/A

BCBSM: N/A	Revised: N/A

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: INTRAOCULAR RADIATION THERAPY FOR AGE-RELATED MACULAR DEGENERATION

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered.
BCNA (Medicare Advantage)	See Medicare guidelines in the Government 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.