BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 01/15/24**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE:**
	CURRENT EFFECTIVE DATE: 01/15/24
	LAST CRITERIA REVISION DATE:
NEXT ANNUAL REVIEW DATE: 4TH QTR 2024	**ARCHIVE DATE:**

IZERVAY (avacincaptad pegol)
SYFOVRE (pegcetacoplan)

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Izervay (avacincaptad pegol) and Syfovre (pegcetacoplan) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is an ophthalmologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) confirmed by age-related macular degeneration sensitive tests (e.g., optical coherence tomography [OCT], fundus autofluorescence [FAF] imaging)

  4. There are **NO** contraindications including:

     - Ocular or periocular infections
     - Active intraocular inflammation

  5. Individual does **NOT** have geographic atrophy secondary to any conditions other than age-related macular degeneration (e.g., Stargardt disease, cone rod dystrophy, toxic maculopathies, drug-induced)

  Initial approval duration: 6 months
  - Izervay: every month (28±7 days)
  - Syfovre: every 25-60 days

- **Criteria for continuation of coverage (renewal request):** Izervay (avacincaptad pegol) and Syfovre (pegcetacoplan) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by an ophthalmologist

  2. Individual's condition has responded while on therapy with response defined as stabilization or reduction in the rate of disease progression while on therapy compared to pretreatment baseline measured by **ONE** of the following:

     - Best corrected visual acuity (BCVA)
     - Fundus autofluorescence (FAF)
     - Optical coherence tomography (OTC)

  3. Individual has been adherent with the medication

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4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use, including but not limited to:

    - Ocular or periocular infections
    - Active intraocular inflammation
    - Endophthalmitis and retinal detachments
    - Neovascular AMD
    - Intraocular inflammation
    - Increased intraocular pressure

5. Individual does NOT have geographic atrophy secondary to any other conditions other than age-related macular degeneration (e.g., Stargardt disease, cone rod dystrophy, toxic maculopathies, drug-induced)

Renewal duration:
- Izervay: 6-12 months (maximum 12 month total duration)
    - Dosing every month (28±7 days)
- Syfovre: 12 months
    - Dosing every 25-60 days

➢ Izervay (avacincaptad pegol) and Syfovre (pegcetacoplan) for all other indications not previously listed are considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Description:

Geographic atrophy (GA) secondary to age-related macular degeneration (AMD) is a leading cause of severe vision loss worldwide with approximately 1 million patients in the US alone. It is characterized by progressive and irreversible atrophy of the retinal cells. Patients with geographic atrophy secondary to

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AMD experience a profound decrease in quality of life; they have difficulty reading, recognizing faces and experience a loss of independence. The goal of treatment is to preserve the retina cells such as retinal pigment epithelium (RPE), photoreceptors and choriocapillaris.

Izervay (avacincaptad pegol) and Syfovre (pegcetacoplan) are both indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Avacincaptad pegol is an RNA aptamer, a PEGylated oligonucleotide that binds to and inhibits complement protein C5. Although it inhibits C5 activation, it does not inhibit cleavage of C3 to C3a and C3b. By inhibiting C5 it may prevent the cleavage to C5a and C5b which decreases the formation of the membrane attack complex (MAC), it is thought to slow progression of GA secondary to AMD while preserving the retinal architecture.

Pegcetacoplan binds to complement protein C3 and its activation fragment C3b regulating the cleavage of C3 and the generation of downstream effectors of complement activation. Pegcetacoplan acts proximally in the complement cascade controlling both the C3b-mediated extravascular hemolysis and terminal complement-mediated intravascular hemolysis.

Definitions:

Age-Related macular degeneration (AMD):
Degenerative disease of photoreceptors in the central portion of the retina (the macula) and the supporting retinal pigment epithelium (RPE). This disease is characterized by a loss of central vision, presence of lipid rich extracellular deposits under the RPE called drusen, and retinal pigmentary and atrophic changes.

Geographic atrophy (GA):
Geographic atrophy is considered an advanced form of disease that effects 15% of AMD patients and is responsible for most of the severe vision loss experienced in AMD. It is characterized by a loss of photoreceptors, retinal pigment epithelium (RPE) and choriocapillaris.

Best corrected visual acuity (BCVA):
Measurement of the possible ability to distinguish shapes and details of objects at a given distance with the use of corrective lenses.

Fundus autofluorescence (FAF):
Non-invasive imaging technique used to detect naturally occurring molecules called fluorophores. This imaging can provide information about the health and function of the central retina. It allows for functional evaluation of geographic atrophy making it possible to assess and monitor therapy response as well as disease progression.

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Optical coherence tomography (OTC):
Non-invasive imaging test that uses light waves to take a cross-section picture of the retina. This allows for mapping and measurement of the distinct retina layers to help with diagnosis and treatment of eye diseases.

History:	Date:	Activity:
Pharmacy and Therapeutics Committee	11/16/23	Approved guideline (effective 01/15/24)
Clinical Pharmacist	10/26/23	Development

Coding:

HCPCS: C9399, J2781, J3490

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Resources:

Literature reviewed 11/16/23. We do not include marketing materials, poster boards and non-published literature in our review.

1. American Academy of Ophthalmology. Age-Related Macular Degeneration Preferred Pratice Pattern. September 2019. Accessed October 24, 2023. https://www.aao.org/education/preferred-practice-pattern/age-related-macular-degeneration-ppp

2. Izervay (avacincaptad pegol intravitreal solution) prescribing information, revised by IVERIC bio, Inc. 08/2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed September 21, 2023.

3. Syfovre (pegcetacoplan injection) prescribing information, revised by Apellis Pharmaceuticals, Inc. 02/2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 13, 2023.

4. Vavvas DG. Age-related macular degeneration. Gardiner MF, Schmader KE, Givens J (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Topic last updated October 13, 2023. Accessed October 24, 2023.

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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html