Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Avacincaptad pegol intravitreal solution (Izervay®)	MP-RX-FP-117-24	☒ MMM MA ☐ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Avacincaptad pegol intravitreal solution (Izervay®), a complement inhibitor approved by the Food and Drug Administration (FDA) for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Background Information

Geographic atrophy (GA) represents an advanced and severe manifestation of dry age-related macular degeneration (AMD). It occurs due to the gradual deterioration of light-sensitive cells in the macula, leading to the formation of irreversible lesions in the retinal pigment epithelium (RPE). As GA progresses, it results in a gradual decline in visual function. Common symptoms include scotomas, difficulty in recognizing faces, reduced reading speed, impaired adaptation to darkness, low luminance deficit (LLD), compromised contrast sensitivity, and challenges with night driving. More than half of GA patients experience significant impairment in everyday vision, and approximately 20% may suffer from severe vision loss, with a visual acuity of 20/200 or worse.

The precise cause of GA remains unknown, although it is believed to stem from a complex interplay of factors. Age and family history are prominent risk factors, with genetics contributing to disease susceptibility. Errors in genes associated with the complement cascade are thought to induce inflammation, rendering the eye more vulnerable to GA. Additional risk factors include smoking and higher body mass index.

Two types of AMD include: dry (aka atrophic AMD) and wet (aka advanced neovascular AMD). Dry AMD is the more common condition of the two, in which the macula gets thinner with age, specifically because of the loss of photoreceptors and retinal pigment epithelium cells which results in atrophy of the retinal tissue. Dry AMD typically has a slow progression. Late-stage dry AMD is referred to as Geographic Atrophy (GA), which is irreversible. GA is characterized by sharply defined atrophy of the outer retinal tissue, retinal pigment epithelium, and choriocapillaris. Wet AMD typically is seen to progress faster than dry AMD. Late-stage wet AMD can lead to GA. Therefore, GA can occur in both dry and wet AMD.

The complement cascade has been linked to the pathophysiology of dry AMD and GA. Within the innate immune system, there are 3 different pathways: classical, alternative, and lectin. Once a pathway (or multiple pathways) is activated, an inflammatory and cytolytic immune response from proteins within the complement system occurs.

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All 3 activation pathways converge at C3 convertase. C3 convertase promotes cleavage of C3 into C3a and C3b subunits. This cleavage results in subsequent generation of complement C5 convertase, which cleaves complement C5 into C5a and C5b. Findings of inflammatory cytokines and chemokines in the retina, along with the overactivity of the complement system and the subsequent formation of drusen, supports the hypothesis that the complement system is a key component for the development and progression of GA.

Izervay (avacincaptad pegol) is a pegylated RNA aptamer and a specific inhibitor of complement C5. Inhibiting the cleavage of C5 prevents formation of C5a and C5b. It is thought that inhibition at C5 within the complement system can reduce or slow down the downstream processes that can lead to continuous retinal atrophy. During the phase 2/3 study (GATHER1), adverse events of choroidal neovascularization or neovascular "wet" AMD were reported. These individuals were withdrawn from the study.

The first 12-months results from the GATHER2 trial were published in September 2023. The GATHER2 trial was a 24-month, multicenter, phase 3 trial aimed to evaluate the efficacy and safety of avacincaptad pegol 2 mg in reducing GA lesion growth. Eligible patients were aged 50 years or older with non-centrepoint-involving GA and best corrected visual acuity between 20/25 and 20/320 in the study eye. Participants were randomly assigned (1:1) to receive monthly avacincaptad pegol 2 mg intravitreal injections or sham treatment for the first 12 months. The primary endpoint was GA lesion size measured by fundus autofluorescence at baseline, month 6, and month 12. The trial included 448 enrolled patients. Results showed that avacincaptad pegol 2 mg significantly reduced the mean rate of GA lesion growth compared to sham treatment over 12 months, with a difference in growth of 0.056 mm/year (95% CI 0.016–0.096; p=0·0064), representing a 14% difference between the groups. Ocular treatment-emergent adverse events were reported in both groups, with no significant differences between avacincaptad pegol 2 mg and sham. The authors concluded that monthly avacincaptad pegol 2 mg demonstrated good tolerability and significantly slower GA growth over 12 months compared to sham treatment.

Approved Indications

Izervay® is approved by the FDA for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

Other Uses

None

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J2782	Injection, avacincaptad pegol, 0.1 mg (Izervay)

ICD-10	Description
H35.3113	Advanced atrophic without subfoveal involvement-RT EYE
H35.3123	Advanced atrophic without subfoveal involvement-LT EYE
H35.3133	Advanced atrophic without subfoveal involvement-Bilateral
H35.3114	Advanced atrophic with subfoveal involvement-RT EYE
H35.3124	Advanced atrophic with subfoveal involvement-LT EYE
H35.3134	Advanced atrophic with subfoveal involvement-Bilateral

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Avacincaptad pegol intravitreal solution (Izervay®)

A. Criteria For Initial Approval (*Provider must submit documentation (such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information) supporting the patient's diagnosis for the drug and confirming that the patient has met approval criteria)*

i. Individual has a diagnosis of geographic atrophy of the macula secondary to age-related macular degeneration; **AND**

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ii. Diagnosis has been verified by geographic atrophy secondary to age-related macular degeneration sensitive tests (including but not limited to optical coherence tomography, fluorescein angiography, fundus photography).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Avacincaptad pegol intravitreal solution (Izervay®) therapy medically necessary in members requesting reauthorization when the maximum duration of therapy has not been exceeded, and the following information is provided for reauthorization:

A. Documented evidence of disease response; **AND**

B. Documentation that additional dosses are clinically necessary; **AND**

C. Documentation that there are no physical findings of toxicity (Included but not limited to elevated intraocular pressure, signs of neovascular age-related macular degeneration, active intraocular inflammation)

C. Authorization Duration

i. Initial Approval Duration: Up to 12 months

ii. Reauthorization Approval Duration: Up to 12 months

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Drug	Recommended Dosing Schedule
Avacincaptad pegol intravitreal solution (Izervay®)	2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately 28 ± 7 days). Izervay is available as an intravitreal injection solution of 20 mg/mL in a single dose vial. Approvals will be limited to two (2)- 20mg/mL single dose vial every 28 days.
Exceptions	
• According to manufacturer, each single-dose vial should only be used for the treatment of a single eye.	

Reference Information

- Khanani, A. M., Patel, S. S., Staurenghi, G., Tadayoni, R., Danzig, C. J., Eichenbaum, D. A., … GATHER2 trial investigators, . (2023). Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial. *Lancet*, *402*(10411), 1449–1458. https://doi.org/10.1016/S0140-6736(23)01583-0
- DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
- DrugPoints¬Æ System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
- Lexi-Comp ONLINE,Ñ¢ with AHFS,Ñ¢, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
- Izervay (avacincaptad pegol) [prescribing information]. 2023.
- Jaffe GJ, Westby K, Csaky KG, et al. C5 Inhibitor Avacincaptad Pegol for Geographic Atrophy Due to Age-Related Macular Degeneration: A Randomized Pivotal Phase 2/3 Trial. Ophthalmology. 2021 Apr;128(4):576-586. doi: 10.1016/j.ophtha.2020.08.027.
- DailyMed - izervay- AVACINCAPTAD Pegol Injection (no date) U.S. National Library of Medicine. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=1642fe6a-dc26-4d20-ae6e-654af744e3bd (Accessed: 24 March 2025).

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 03/24/2025	Efficacy-Labeling Change with Clinical Data (02/12/2025)-Indication no longer states restriction of use up to 12 months. Addition of continuation criteria since the drug's new clinical findings do not limit the use to 12 months. Addition of reauthorization approval duration: up to 12 months	4/16/2025	5/6/2025
Select Review	Coding Reviewed: No changes. Effective 4/1/2024 Added HCPCS J2782. Added ICD-10-CM H35.3113, H35.3123, H35.3133, H35.3114, H35.3124, H35.3134. Removed HCPCS J3490, J3590, J9999, C9162.	N/A	N/A
Policy Inception 6/28/2024	Elevance Health's Medical Policy adoption	N/A	6/28/2024