Medical Drug Clinical Criteria

Subject:	Izervay (avacincaptad pegol)		
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Status:	~~Reviewed~~Revised	**Last Review Date:**	~~11/15/2024~~03/20/2025

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Overview

This document addresses the use of Izervay (avacincaptad pegol), an FDA-approved intravitreal therapy for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). AMD is a leading cause of severe, irreversible vision impairment. 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. 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. The GATHER2 study evaluated Izervay or sham administered monthly in individuals with GA due to AMD. At Month 12, the difference in the mean rate of change from baseline in the geographic atrophy area by square root transformation for Izervay 2 mg (2.991) as compared to sham (3.112) was 0.056. This demonstrates a statistically significant reduction of 14.25% in the mean rate of GA growth compared to sham. The most frequent adverse reactions that occurred within the Izervay 2 mg group was conjunctival hemorrhage, increased intraocular pressure, blurred vision, choroidal neovascularization, and eye pain. All of which occurred at a higher rate within the Izervay 2 mg group compared to the sham group. Per the FDA label, the recommended dose is 2 mg (0.1 mL) administered by intravitreal injection to each affected eye every 28 days, +/- 7 days.

Clinical Criteria

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.

Izervay (avacincaptad pegol)

Requests for Izervay (avacincaptad pegol) may be approved if the following criteria are met:

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

Requests for Izervay (avacincaptad pegol) may not be approved for the following:

I. Geographic atrophy that is secondary to a condition other than age-related macular degeneration (including but not limited to Stargardt disease, cone rod dystrophy or toxic maculopathies); **OR**
II. Individual has a history of or active choroidal neovascularization or wet age-related macular degeneration; **OR**
III. Individual has an ocular or periocular infection(s); **OR**
IV. Individual has active intraocular inflammation; **OR**
~~V. Individual has utilized Izervay (avacincaptad pegol) for a total duration of 12 months or more; **OR**~~
~~VI.~~V. May not be approved when the above criteria are not met and for all other indications.

Approval Duration: 1 year ~~(12 months max of drug therapy)~~

Quantity Limits

Izervay (avacincaptad pegol) Quantity Limits

Drug	Limit
Izervay (avacincaptad pegol) 20 mg/mL vial	0.1 mL (or 2 mg) per eye; each eye may be treated as frequently as every 28 days~~.~~ +/- 7 days.

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.

HCPCS

J2782	Injection, avacincaptad pegol, 0.1 mg [Izervay]

ICD-10 Diagnosis

H35.30	Unspecified macular degeneration
H35.3113	Nonexudative age-related macular degeneration, right eye, advanced atrophic without subfoveal involvement~~Advanced atrophic without subfoveal involvement RT EYE~~
H35.3123	Nonexudative age-related macular degeneration, right eye, advanced atrophic with subfoveal involvement~~Advanced atrophic without subfoveal involvement LT EYE~~
H35.3133	Nonexudative age-related macular degeneration, left eye, advanced atrophic without subfoveal involvement~~Advanced atrophic without subfoveal involvement Bilateral~~
H35.3114	Nonexudative age-related macular degeneration, left eye, advanced atrophic with subfoveal involvement~~Advanced atrophic with subfoveal involvement RT EYE~~
H35.3124	Nonexudative age-related macular degeneration, bilateral, advanced atrophic without subfoveal involvement~~Advanced atrophic with subfoveal involvement LT EYE~~

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H35.3134	Nonexudative age-related macular degeneration, bilateral, advanced atrophic with subfoveal involvement~~Advanced atrophic with subfoveal involvement - Bilateral~~
H35.3210-H35.3293	Exudative age-related macular degeneration, right eye
H35.351-H35.359	Cystoid macular degeneration

Document History

Revised: 03/10/2025
Document History:

- 03/10/2025 – Select Review: Removed limit of 12 months of use per label. Clarified dosing every 28 days +/- 7 days. Coding Reviewed: Updated descriptions for ICD-10-CM H35.3113, H35.3114, H35.3123, H35.3124, H35.3133, H35.3134, H35.3210-H35.3293.
- 11/15/2024 – Annual Review: No changes. Coding Reviewed: Add ICD-10-CM H35.30, H35.3210-H35.3293, H35.351-H35.359.
- 11/17/2023 – Annual Review: No changes. 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.
- 08/18/2023 – Select Review: Add new clinical criteria document for Izervay (avacincaptad pegol). Added HCPCS codes J3490, J3590, J9999, C9399. All diagnoses pend. Effective 1/1/2024 Added HCPCS C9162. Added ICD-10-CM H35.210-H35.3233. Removed HCPCS C9399.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. 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.
5. Khanani AM, Patel SS, Staurenghi G, et al. Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial. *Lancet*. 2023;402(10411):1449-1458. doi:10.1016/S0140-6736(23)01583-0