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Avacincaptad pegol

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated, and coverage is not required for non-formulary drugs.

Coverage

Avacincaptad pegol (Izervay™) **may be considered medically necessary** when the following criteria are met:

- Individual has a diagnosis of geographic atrophy secondary to age-related macular degeneration (AMD); AND
- Diagnosis has been confirmed by geographic atrophy secondary to AMD-sensitive tests (e.g., fluorescein angiography, fundus photography); AND
- Macular atrophy is not secondary to any conditions other than AMD (e.g., Stargardt disease, cone rod dystrophy, toxic maculopathies).

Avacincaptad pegol (Izervay™) **is considered experimental, investigational and/or unproven** for all other non-U.S. Food and Drug Administration approved indications.

Policy Guidelines

Individuals receiving Izervay should be monitored for signs of neovascular age-related macular degeneration (AMD).

Izervay should be prescribed by or in consultation with an ophthalmologist experienced in treatment of retinal diseases.

Dosing is in accordance with the United States Food and Drug Administration approved labeling.

Authorization is for no more than 12 months.

Description

Background

Geographic Atrophy

Geographic atrophy (GA) is an advanced form of dry age-related macular degeneration (AMD), characterized by atrophic lesions that first start in the outer retina and progressively expand to cover the macula, leading to irreversible loss of vision over time. Researchers have reported about 1 million reported cases of GA in the United States, with about 160,000 cases occurring each year. Primary risk factors for GA include increasing age and family history. (1)

The underlying pathophysiology of GA is complex and thought to involve chronic inflammation due to overactivation of the complement system that leads to the loss of photoreceptors, retinal pigment epithelium (RPE), and the underlying choriocapillaris. The disappearance of these structures appears as atrophic lesions. Over time, these lesions may progressively grow to involve the fovea, severely impairing central vision. (1)

Avacincaptad pegol

Avacincaptad pegol is a complement C5 protein inhibitor that blocks the activity of the complement protein C5. By reducing the activity of the complement cascade that damages the retina, avacincaptad pegol has the potential to slow down the progression of GA. (2)

Regulatory Status

Izervay™ (avacincaptad pegol) was approved by the U.S. Food and Drug Administration (FDA) on August 5, 2023, for the treatment of geographic atrophy secondary to age-related macular degeneration. (3, 4)

Dosage and Administration

The recommended dose for Izervay is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately 28 ± 7 days) for up to 12 months. (4)

Rationale

This policy is based on the U.S. Food and Drug Administration labeled indication for Izervay (avacincaptad pegol).

Izervay (avacincaptad pegol) (4)

The safety and efficacy of Izervay were demonstrated in two randomized, multi-center, double-masked, sham-controlled, 18- and 24-month studies (GATHER1-NCT02686658 and GATHER2-NCT04435366, respectively) in patients with geographic atrophy (GA) due to age-related macular degeneration (AMD). Patient ages ranged from 51 to 97 years with a mean of 77 years. In total, 292 patients were treated with avacincaptad pegol 2 mg, and 332 patients received sham.

In GATHER1, patients were treated with either Izervay or sham monthly for 18 months. In the primary analysis for GATHER1, the mean rate of GA growth (slope) from baseline to Month 12, measured by Fundus Autofluorescence (FAF), was evaluated at 3 time points: baseline, Month 6, and Month 12. Over a 12-month period, there was a statistically significant reduction of the rate of GA growth (0.10 mm/year; $p<0.01$ with square root transformed data) in patients treated with Izervay compared to sham. The observed results are shown in Table 1 below.

In the 24-month GATHER2 study, patients were treated with Izervay or sham monthly for the first 12 months. Patients receiving monthly Izervay were re-randomized at Month 12 to receive

either Izervay monthly (EM) or every other month (EOM). Patients treated with sham in the first 12 months continued monthly sham treatment. At any time during the GATHER2 study, patients that developed choroidal neovascularization were concomitantly treated with anti-VEGF therapy.

In GATHER2 analysis, the mean rate of GA growth (slope) measured by FAF was evaluated at 5 time points: baseline, Month 6, Month 12, Month 18, and Month 24. Over a 12-month period, there was a statistically significant reduction of the rate of GA growth (0.05 mm/year; $p<0.01$ with square root transformed data) in patients treated with Izervay EM compared to sham. The annualized rate of GA growth over 24 months in the monthly arm was 2.23 mm2/year, resulting in treatment difference versus sham of 0.36 mm^2/year ($p = 0.0165$). In the treatment arm that included patients who received Izervay EM treatment for one year and EOM treatment for the second year, the annualized rate of GA growth was 2.10 mm^2/year. The observed results for EM dosing are shown in Table 1.

In both studies, treatment effects in all pre-specified subgroups (e.g., age, gender, baseline GA disc area) were consistent with the results in the overall population.

Table 1. Efficacy Outcomes of Izervay Monthly Dosing Compared to Sham in GATHER1 and GATHER2

Primary Efficacy Endpoint (MMRM Analysis)	**Month 12**				**Month 24**	
	GATHER1		**GATHER2**		**GATHER2**	
	Izervay N=67	**Sham N=110**	**Izervay N=225**	**Sham N=222**	**Izervay[c] N=96**	**Sham N=203**
GA Rate of Growth (mm^2/year) (observed)[a]	1.22	1.89	1.75	2.12	2.23	2.59
Difference (95% CI) (mm^2/year)	0.67 (0.21-1.13)		0.38 (0.12-0.63)		.036 (0.07-0.66)	
Difference %[b]	35%		18%		14%	
p value	<0.01		<0.01		0.0165	

[a] non-transformed GA growth slope analysis

[b] % difference is calculated by 100*(difference)/(least squares mean from Sham)

[c] Izervay EM (Izervay monthly in both year 1 and year 2)

CI: confidence interval; GA: geographic atrophy; mm: millimeter; MMRM= Mixed Models for Repeated Measures

Summary of Evidence

Based on the clinical studies provided to the U.S. Food and Drug Administration (FDA), Izervay™ (avacincaptad pegol) may be considered medically necessary for the treatment of geographic atrophy secondary to age-related macular degeneration. There is a lack of published peer reviewed scientific literature for the use of Izervay™ (avacincaptad pegol) outside of the FDA approved labeled indication.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	67028
HCPCS Codes	J2782

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

1. U.S. Food and Drug Administration, Drugs @ FDA. Highlights of Prescribing Information: Izervay (avacincaptad pegol) (revised Feb 2025). Available at: <https://www.accessdata.fda.gov> (accessed October 13, 2025).

Other:

2. Bakri SJ, Bektas M, Sharp D, et al. Geographic atrophy: Mechanism of disease, pathophysiology, and role of the complement system. J Manag Care Spec Pharm. May 2023; 29(5-a Suppl):S2-S11. PMID 37125931
3. Izervay. (Mar 19 2025). Available at: <https://www.drugs.com> (accessed October 13, 2025).
4. Izervay FDA Approval History. Available at: <https://www.drugs.com> (accessed October 13, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
11/15/2025	Document updated. The following changes were made to Coverage: Moved the following statements to Policy Guidelines: Izervay should be prescribed

	by or in consultation with an ophthalmologist experienced in treatment of retinal diseases. Dosing is in accordance with the United States Food and Drug Administration approved labeling. Authorization is for no more than 12 months. References updated. No new references added.
07/15/2024	New medical document. Avacincaptad pegol (Izervay) may be considered medically necessary when the following criteria are met: Individual has a diagnosis of geographic atrophy secondary to age-related macular degeneration (AMD); AND Diagnosis has been confirmed by geographic atrophy secondary to AMD-sensitive tests (e.g., fluorescein angiography, fundus photography); AND Macular atrophy is not secondary to any conditions other than AMD (e.g., Stargardt disease, cone rod dystrophy, toxic maculopathies); AND Prescribed by or in consultation with an ophthalmologist experienced in treatment of retinal diseases; AND Dosing is in accordance with the United States Food and Drug Administration approved labeling; AND Authorization is for no more than 12 months. Avacincaptad pegol (Izervay) is considered experimental, investigational and/or unproven for all other indications.