Medical Drug Clinical Criteria

Subject:	Izervay (avacincaptad pegol)		
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Overview

This document addresses the use of Izervay (avacincaptad pegol), an intravitreal therapy under review by the Food and Drug Administration 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. 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 These individuals were withdrawn from the study.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 phase 3 confirmatory study (GATHER2) has not been published yet. Per the FDA label, the recommended dose is 2 mg (0.1 mL) administered by intravitreal injection to each affected eye once monthly for up to 12 months.

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. 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.

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

J3490	Unclassified drugs when specified as [Izervay] (avacincaptad pegol))
J3590	Unclassified biologics when specified as [Izervay] (avacincaptad pegol))
J9999	Not otherwise classified, antineoplastic drugs when specified as [Izervay] (avacincaptad pegol))
C9399	Unclassified drugs or biologicals when specified as [Izervay] (avacincaptad pegol))

ICD-10 Diagnosis

	All diagnoses pend

Document History

New: 08/18/2023
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- 08/18/2023 – Select Review: Add new clinical criteria document for Izervay (avacincaptad pegol). Added HCPCS codes J3490, J3590, J9999, C9399. All diagnoses pend.

References

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3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. Izervay (avacincaptad pegol) [prescribing information]. 2023.she
5. 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.

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.