09-J4000-65

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Reviewed: 09/11/24

Revised: 10/15/24

Subject: Avacincaptad pegol (Izervay) intravitreal injection

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DESCRIPTION:

Geographic atrophy (GA) is a secondary complication of age-related macular degeneration (AMD) and occurs in the intermediate or advanced stages of AMD. GA is classified as a non-neovascular form of AMD and has an estimated prevalence of 0.81% (in at least one eye) in U.S. patients over 40 years of age, and since aging is the primary risk factor, the prevalence of GA increases to 3.5% in patients 75 years of age and older. More than half of all patients with GA experience significant vision impairment with 20% developing severe vision loss (e.g., visual acuity of 20/200 or worse).

Medications such as vascular endothelial growth factor (VEGF) inhibitors are used to treat neovascular AMD (nAMD) or wet AMD (wAMD); however, these agents are ineffective in the treatment of non-neovascular forms of AMD, including GA. On February 17, 2023, the FDA approved pegcetacoplan intravitreal injection (Syfovre), which was the first therapeutic option for the treatment of GA secondary to AMD. A second therapeutic option, avacincaptad pegol (Izervay), was FDA-approved on August 5, 2023. Avacincaptad pegol (Izervay) is similar to pegcetacoplan (Syfovre) in that it works on the complement cascade; however, avacincaptad pegol (Izervay) binds to and inhibits complement protein C5 rather than C3. By inhibiting C5, avacincaptad pegol (Izervay) prevents its cleavage to C5a and C5b, decreasing membrane attack complex (MAC) formation.

The efficacy and safety of avacincaptad pegol (Izervay) was evaluated in two clinical trials. The first study (GATHER1) was an international, prospective, randomized, double-masked, sham-controlled, phase 2/3 clinical trial. Enrolled patients were 50 years of age or older with best-corrected visual acuity between 20/25 and 20/320 in the study eye. The GA lesion had to be non-center point involving but within 1.5 mm from the foveal center. Additionally, the total GA area had to be between 2.5 and 17.5

mm^2. Patients were excluded if they had macular atrophy secondary to any condition other than AMD (e.g., myopic degeneration, hereditary retinal degeneration), received any prior treatment for AMD or intravitreal treatment for any indication, if any subtype of macular neovascularization was detected, if any ocular condition was present that could progress during the study and impact central vision, or if there was any sign of diabetic retinopathy. The study design consisted of two simultaneous parts. In part 1, patients were randomized 1:1:1 to receive avacincaptad pegol 1 mg, avacincaptad pegol 2 mg, or sham, and in part 2, patients were randomized 1:2:2 to receive avacincaptad pegol 2 mg, avacincaptad pegol 4 mg, or sham. For all patients, intravitreal injections were administered monthly for 18 months. The GA lesion area was measured at baseline, 6 months, 12 months, and 18 months, and the primary efficacy endpoint was the mean change in the GA lesion area at 12 months. Overall, 286 patients (77 patients in part 1 and 209 patients in part 2) were enrolled, and 201 patients completed the study. For the mean rate of change in GA area at 12 months, growth (square root transformed) was reduced by 25.3% (0.097 mm, 95% CI [0.017-0.177]) in the 2-mg treatment group when compared to sham (least squares mean values of 0.287 and 0.384 mm, respectively) and 28% (0.117 mm, 95% CI [0.033-0.202]) in the 4-mg treatment group when compared to sham (least squares mean values of 0.301 and 0.418 mm, respectively). For the mean rate of change in GA area at 18 months, growth (square root transformed) was reduced by 28.1% (0.168 mm, 95% CI [0.066-0.271]) in the 2-mg treatment group when compared to sham (least squares mean values of 0.430 and 0.599 mm, respectively) and 30% (0.167 mm, 95% CI [0.062-0.273]) in the 4-mg treatment group when compared to sham (least squares mean values of 0.391 and 0.559 mm, respectively). Avacincaptad pegol intravitreal injections were generally well tolerated over 18 months, with most ocular adverse events related to the injection procedure. Macular neovascularization (MNV) was more frequent in the 2-mg (11.9%) and 4-mg (15.7%) groups as compared to their respective sham control groups (2.7% and 2.4%).

In the second clinical trial (GATHER2) was an international, prospective, randomized, double-masked, sham-controlled, phase 3 trial. Enrolled patients were 50 years of age or older with non-center point involving GA and best-corrected visual acuity between 20/25 and 20/320 in the study eye. Patients were assigned 1:1 to monthly avacincaptad pegol 2 mg or sham intravitreal injections for the first 12 months. The primary endpoint was GA lesion size measured by fundus autofluorescence at baseline, 6 months, and 12 months. A total of 448 patients (225 patients in the treatment group and 223 patients in the sham group) were enrolled; one patient in the sham group did not receive study treatment and was excluded from analyses. From baseline to 12 months, the mean rate of GA growth (square root transformed) was 0.336 mm/year [standard error (SE): 0.032] with avacincaptad pegol 2 mg and 0.392 mm/year (SE: 0.033) with sham, a difference in growth of 0.056 mm/year (95% CI 0.016-0.096; p=0.0064), representing a 14% difference between the treatment and sham group. Ocular treatment-emergent adverse events occurred in 110 (49%) patients in the treatment group and 83 (37%) in the sham group. There were no endophthalmitis, intraocular inflammation, or ischemic optic neuropathy events over 12 months. At 12 months, macular neovascularization occurred in 15 (7%) patients in the treatment group and 9 (4%) patients in the sham group, with exudative macular neovascularization occurring in 11 (5%) patients in the treatment group and 7 (3%) in the sham group.

The most common adverse reactions outlined in the prescribing information include conjunctival hemorrhage (13%), increased intraocular pressure (9%), blurred vision (8%) and neovascular age-related macular degeneration (7%).

POSITION STATEMENT:

The administration of avacincaptad pegol (Izervay) intravitreal injection **meets the definition of medical necessity** when **ALL** of the following are met:

1. The member has a diagnosis of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).
2. Ophthalmic test documentation of GA secondary to AMD (e.g., optical coherence tomography, fluorescein angiography, fundus photography) – laboratory or medical record documentation provided.
3. The member does not have any ocular or periocular infections or active intraocular inflammation.
4. Not used in combination with other intravitreal complement inhibitor therapies (e.g., Syfovre).
5. The dose does not exceed 2 mg per eye every 28 days (but no more frequently than 21 days).

Approval duration: 1 year

Avacincaptad pegol (Izervay) intravitreal injection is considered **experimental or investigational** for any other indications due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcome.

Continuation of avacincaptad pegol (Izervay) intravitreal injection **meets the definition of medical necessity** when **ALL** the following criteria are met:

1. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years (if another health plan, documentation of a health plan-paid claim during the 90 days before the authorization request must be submitted), OR the member currently meets all indication-specific initiation criteria.
2. The member has experienced a clinically beneficial response from the avacincaptad pegol (Izervay) intravitreal injections without any significant adverse events requiring discontinuation (e.g., endophthalmitis, retinal detachment, neovascular (wet) AMD or choroidal neovascularization, increased intraocular pressure that cannot be adequately treated).
3. The member does not have any ocular or periocular infections or active intraocular inflammation.
4. Not used in combination with other intravitreal complement inhibitor therapies (e.g., Syfovre).
5. The dose does not exceed 2 mg per eye every 28 days (but no more frequently than 21 days).

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Avacincaptad pegol (Izervay) intravitreal injection is indicated for the treatment of GA secondary to AMD.
- Prior to the intravitreal injection, patients should be monitored for elevated intraocular pressure (IOP). If necessary, ocular hypotensive medication can be given to lower the IOP.
- The recommended dose is 2 mg/0.1 mL administered by intravitreal injection to each affected eye once monthly (approximately 28 ± 7 days) for up to 12 months. Any excess volume from the single-dose vial should be discarded.

Dose Adjustments

None

Drug Availability

- Avacincaptad pegol (Izervay) intravitreal solution is supplied as a sterile, clear to slightly opalescent, colorless to slightly yellowish 20 mg/mL solution in a single-dose glass vial.
- Each avacincaptad pegol (Izervay) carton (NDC 82829-002-01) contains one glass vial, one sterile 5-micron transfer filter needle (19-gauge x 1½ inch, 1.1 mm x 40 mm), and one sterile 1 mL Luer lock syringe.
- Store in the original carton to protect from light and under refrigeration between 2°C to 8°C (36°F to 46°F) but do not freeze.
- Prior to use, allow the vial to reach room temperature, 20^{o}C to 25^{o}C (68^{o}F to 77^{o}F). The vial may be kept at room temperature for up to 24 hours.
- Do not use beyond the expiration date or shake the vial.

PRECAUTIONS:

Boxed Warning

None

Contraindications

- Ocular or periocular infections
- Active intraocular inflammation

Precautions/Warnings

- **Endophthalmitis and Retinal Detachments**: Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering avacincaptad pegol (Izervay) in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.

- **Neovascular AMD**: In clinical trials, use of avacincaptad pegol (Izervay) was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving avacincaptad pegol (Izervay) should be monitored for signs of neovascular AMD.
- **Increase in Intraocular Pressure**: Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with avacincaptad pegol (Izervay). Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

BILLING/CODING INFORMATION:

HCPCS Coding

J2782	Injection, avacincaptad pegol, 0.1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

H35.3113	Advanced atrophic without subfoveal involvement, right eye
H35.3114	Advanced atrophic with subfoveal involvement, right eye
H35.3123	Advanced atrophic without subfoveal involvement, left eye
H35.3124	Advanced atrophic with subfoveal involvement, left eye
H35.3133	Advanced atrophic without subfoveal involvement, bilateral
H35.3134	Advanced atrophic with subfoveal involvement, bilateral

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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7. Patel SS, Lally DR, Hsu J, et al. Correction: Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the GATHER1 trial [published online ahead of print, 2023 May 26]. Eye (Lond). 2023;10.1038/s41433-023-02548-2. doi:10.1038/s41433-023-02548-2.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 9/11/24.

GUIDELINE UPDATE INFORMATION:

11/15/23	New Medical Coverage Guideline – Avacincaptad pegol (Izervay) intravitreal injection for the treatment of GA secondary to AMD.
01/01/24	Revision: Added HCPCS code C9162 and deleted code C9399.
04/01/24	Revision: Added HCPCS code J2782 and deleted codes C9162 and J3490.
10/15/24	Review and revision to the guideline consisting of revising the position statement for submission of ophthalmic test documentation for GA secondary to AMD, extending the initial approval to 1 year, and not allowing concomitant therapy with other intravitreal complement inhibitors.