Pharmacy Management Drug Policy

SUBJECT: Geographic Atrophy
POLICY NUMBER: PHARMACY-104
EFFECTIVE DATE: 07/2024
LAST REVIEW DATE: 11/19/2025

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Age-related macular degeneration (AMD) is a common eye condition and a leading cause of vision loss among people 60 years of age and older. AMD is classified as either dry (nonexudative or non-neovascular AMD) or wet (exudative or neovascular AMD). Dry AMD is the more common form affecting approximately 75 percent of patients.[1] In the early stages, yellow waste deposits, called drusen, build up under the retina, and cells of the macula may slowly break down as a result. Geographic Atrophy (GA) is an advanced stage of dry AMD affecting approximately 1 million people in the United States. Geographic atrophy is caused by the gradual breakdown of light-sensitive cells in the macula, resulting in growth of irreversible lesions in the retinal pigment epithelium (RPE) that can lead to impaired vision or blindness.

The progression rate of GA varies but is relatively slow and progresses over years. Initially, the GA lesions appear in the perifoveal macula, but as the disease progresses, lesions expand to include the fovea. Perifoveal atrophy affects visual performance, whereas foveal involvement impacts central visual acuity; once the fovea is involved, patients experience a relatively rapid loss of visual function. The median time from non-foveal to foveal GA is estimated to be approximately 2.5 years. More than half of all patients with GA experience significant impairment of everyday vision, and about 20% of patients develop severe vision loss with visual acuity of 20/200 or worse. GA formation in one eye highly suggests that GA will, at some point, affect the other eye.[9] Geographic atrophy results in progressive and eventually permanent vision loss.

Contributing factors to GA include genetics, environment, and age. Age is the most significant factor associated with any AMD diagnosis.[3] GA is generally not common in individuals under age 50 years and, compared to individuals between ages 65 and 74, the risk of GA development increases more than threefold for those over the age of 75 years.[4] Positive family history of AMD in a first-degree relative is also a non-modifiable risk. Smoking is considered the most modifiable risk factor for AMD, with a two-fold risk of developing the disease for individuals who smoke at least 25 cigarettes per day. Obesity is another potentially modifiable risk factor associated with late AMD and progression from early to advanced stages.[7,8] There are no guidelines specific to the treatment of geographic atrophy. Lifestyle modifications to slow or prevent disease progression have been the mainstays of dry AMD treatment.

On February 17, 2023, the FDA approved Syfovre (pegcetacoplan injection) for the treatment of geographic atrophy secondary to age-related macular edema. Izervay (avacincaptad pegol intravitreal solution), the second treatment for GA, was FDA approved on August 4, 2024. Both medications are complement inhibitors. It is thought that the complement system plays a role in the pathogenesis and progression of GA as it is involved in maintenance of cellular integrity, tissue homeostasis, and adaptive immune responses.

SYFOVRE (pegcetacoplan injection)

The efficacy of Syfovre (pegcetacoplan injection) was evaluated in two pivotal, multicenter, randomized, double-masked, sham-controlled, Phase III studies, OAKS, and DERBY. Patients 60 years of age or older with GA secondary to AMD and best-corrected visual acuity (BCVA) of 24 or better (approximately 20/320 Snellen equivalent) were eligible to enroll. Lesions with or without subfoveal involvement were allowed and the GA lesion area size had to be between 2.5 and 17.5 mm^2. For multifocal GA lesions, at least one focal lesion had to be at least 1.25 mm^2.

In OAKS and DERBY, patients were randomized 2:2:1:1 to receive pegcetocoplan 15 mg intravitreal injection monthly or every other month, or sham monthly or every other month. The primary endpoint was the change from baseline to month 12 in the total area of geographic atrophy lesions in the study eye based on fundus autofluorescence (FAF) imaging. Key secondary endpoints (measured at 24 months) were change in monocular maximum reading speed of the study eye, change from baseline in mean functional reading independence score, change from baseline in normal luminescence best-corrected visual acuity (BCVA) score, and change from baseline in the mean threshold sensitivity of all points in the study by mesopic microperimetry (OAKS only).[6]

Results

The OAKS trial met the primary endpoint at 12 months, with pegcetocoplan monthly showing a statistically significant -21% difference in total area of GA lesion growth compared to sham and a -16% difference in GA lesion growth with pegcetocoplan every other month compared to sham. At 24 months, pegcetocoplan monthly and every other month slowed the growth of the GA lesions by 22% and 18% compared to sham. In DERBY, the 12-month primary endpoint was not met as the lesion growth differences of -12% for pegcetocoplan monthly and -11% for every other month were not significant compared to sham treatment. However, at 24 months, pegcetocoplan monthly and every other month slowed the growth of the GA lesions by 19% and 16% compared to sham, demonstrating a statistically significant difference.

In the combined studies, differences between treatment groups and sham in visual function endpoints of BCVA, functional reading independence scores, monocular maximum reading speed, and mean threshold sensitivity as assessed by mesopic microperimetry were not significant.[6]

IZERVAY (avacincaptad pegol)

The efficacy of Izervay (avacincaptad pegol) was evaluated in two randomized, double-masked, sham-controlled, multicenter pivotal studies. GATHER1 was a Phase II/III 18-month study; GATHER2 was a Phase III study with 12 months of data. Patients 50 years of age or older with GA secondary to AMD and best-corrected visual acuity (BCVA) between 20/25 and 20/320 were eligible to participate in the studies.[17] In addition, patients had to have nonfoveal GA, in part within 1.5 mm from the foveal center, and total GA area had to be between 2.5 and 17.5 mm^2, as determined by fundus autofluorescence (FAF) images. For multifocal GA lesions, at least one focal lesion had to be at least 1.25 mm^2.

GATHER1 consisted of two simultaneous parts. In Part 1, patients were randomized 1:1:1 to receive avacincaptad pegol (ACP) 1mg, ACP 2mg, or sham. In part 2, patients were randomized 1:2:2 to receive ACP 2 mg (one 100 µl injection + 1 sham administration), ACP 4 mg (two 2mg injections, total volume 200 µl), or sham (2 sham administrations). Investigators administered monthly intravitreal injections of ACP or sham for a duration of 18 months. The primary endpoint was the mean change from baseline in GA lesion area as measure by FAF over 12 months (measured at baseline, Month 6 and Month 12). Secondary endpoints included the mean change in best-corrected visual acuity (BCVA) as well as low luminance best-corrected visual acuity (LL-BCVA) from baseline to month 12.

In GATHER2, patients were randomly assigned 1:1 to monthly avacincaptad pegol 2 mg or sham. At month 12, randomization was repeated for patients receiving ACP 2 mg, with these patients randomly assigned 1:1 to either continue receiving monthly ACP 2 mg or to receive ACP 2 mg every other month through to month 23. All patients receiving sham on day 1 continued to receive sham throughout the study. The primary endpoint was GA lesion size as measure by FAF for at least three timepoints (measured at baseline, Month 6 and Month 12). Secondary endpoints included the change in best-corrected visual acuity (BCVA) as well as low luminance best-corrected visual acuity (LL-BCVA) from baseline to month 12.

Results

In both GATHER1 and GATHER2, compared with sham, Izervay significantly reduced the rate of GA growth (0.10 mm/year in GATHER1 [P<0.01] and 0.05 mm/year in GATHER2 [P<0.01] {with square root transformed data}).[12] However, secondary endpoints were not met in either of the GATHER trials. In GATHER1, ACP 2 mg or 4 mg did not have an impact on the mean change in BCVA or low luminance BCVA from baseline to month 12, compared to the corresponding sham groups. In GATHER2 at 12 months, there were no substantial differences in mean changes in BCVA or LL-BCVA between the treatment groups.

SAFETY

Syfovre Safety

In the clinical trials, the administration of Syfovre was found to be associated with higher rates of macular or choroidal neovascularization. Specifically, the incidence of neovascular AMD was 12% in the monthly administration group and 7% in every other month versus 3% in the sham group by month 24.[14] Retinal hemorrhages and vitreous detachments were observed at rates of 5% and 6% in the every other month treatment group, compared to 4% in the monthly administration group and 3% in the sham group for both occurrences.[16] Ocular inflammation was reported in 4% of patients receiving Syfovre monthly, 2% of those treated every other month, and less than 1% of the sham group. Throughout the OAKS and DERBY trials, no instances of retinitis or occlusive/nonocclusive vasculitis were reported. However, following the launch of Syfovre in February 2023 until July 2023, confirmed cases of occlusive (4 cases) and non-occlusive (3 cases) retinal vasculitis emerged.[15] In November 2023, a warning regarding retinal vasculitis and/or retinal vascular occlusion was added to the FDA-approved prescribing information from the manufacturer. In addition, data from the FDA Adverse Event Reporting System Public Dashboard revealed an additional 10 cases of retinal occlusive vasculitis through March 31, 2024.[18]

Izervay Safety

Avacincaptad pegol was generally well tolerated in both clinical trials. The most common ocular adverse effects occurring across both trials were conjunctival hemorrhage (13% in the Izervay group vs 9% in the sham), increased intraocular pressure (9% in Izervay vs 1% sham), and choroidal neovascularization (7% in the Izervay group vs 4% in the sham group). There are currently no reports of retinal vasculitis with Izervay to date.

RATIONALE:

Syyovre and Izervay both met their primary endpoints from the clinical trials, demonstrating a reduction in the rate of growth of the GA lesion compared to sham treatment. However, both drugs failed to meet the secondary endpoints, indicating patients treated with either Syfovre or Izervay continued to have decline in visual function similar to patients on sham treatment. In other words, results from the clinical trials failed to show any functional improvement in the treated patients. In regard to safety, both Syfovre and Izervay increased the risk of macular neovascularization compared to sham in the clinical trials. Conjunctival hemorrhages, vitreous detachment and increased ocular pressure also occurred with both drugs in the trials. In addition, Syfovre also carries a warning regarding the risk of retinal vasculitis with or without occlusion, which was added to the FDA approved label based on postmarking reports.

POLICY:

Izervay (avacincaptad pegol) - Medical

Izervay coverage varies by line of business as below:

Commercial/Essential/Child Health Plus:

1. Based upon our criteria and assessment of the peer-reviewed evidence, the use of Izervay (avacincaptad pegol) has not been medically proven to be effective and, therefore, is considered **experimental/investigational** for the treatment of geographic atrophy.

   The justification for Izervay (avacincaptad pegol) to be considered investigational is as follows:
   a. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug has a definite positive effect on health outcomes.
   b. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug, over time, leads to improvement in health outcomes (e.g., the beneficial effects of the service outweigh any harmful effects).
   c. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug provides improvement in health outcomes in standard conditions of medical practice, outside the clinical investigatory settings.

   Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Medicare Advantage/Medicaid/HARP:

1. The patient must be 50 years of age or older **AND**
2. Izervay must be prescribed by an ophthalmologist **AND**
3. The patient must have a diagnosis of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)
   a. GA must be confirmed by an appropriate imaging test (such as fundus autofluorescence [FAF], retinal fundus photography, optical coherence tomography [OCT]) **AND**

4. The patient must have best-corrected visual acuity (BCVA) of 20/320 or better using the Snellen Eye Chart
5. **For New Starts Only**: Must have serious side effects or treatment failure to Syfovre
6. Initial and recertification approvals will be for 1 year.
   a. Recertifications will require provider attestation that the patient has not experienced severe vision loss (to the level of hand motion [HM] or worse range) or unacceptable toxicity to the drug.
7. The approved dose is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly. Izervay will not be approved for use at intervals less than 21 days.
8. Documentation must be submitted confirming which eye (left or right), if no both, is being treated.

HCPCS: J2782

Syfovre – pegcetacoplan injection (Medical)

Syfovre coverage varies by line of business as below:

Commercial/ Essential/Child Health Plus:

1. Based upon our criteria and assessment of the peer-reviewed evidence, the use of Syfovre (pegcetacoplan) has not been medically proven to be effective and, therefore, is considered **experimental/investigational** for the treatment of geographic atrophy.

   The justification for Syfovre (pegcetacoplan) to be considered investigational is as follows:
   a. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug has a definite positive effect on health outcomes.
   b. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug, over time, leads to improvement in health outcomes (e.g., the beneficial effects of the service outweigh any harmful effects).
   c. Based upon our assessment of the peer-reviewed medical literature, there is inconclusive evidence that the drug provides improvement in health outcomes in standard conditions of medical practice, outside the clinical investigatory settings.

   Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Medicare Advantage/Medicaid/HARP:

1. The patient must be 50 years of age or older **AND**
2. Syfovre must be prescribed by an ophthalmologist **AND**
3. The patient must have a diagnosis of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)
   a. GA must be confirmed by an appropriate imaging test (such as fundus autofluorescence [FAF], retinal fundus photography, optical coherence tomography [OCT]) **AND**
4. The patient must have best-corrected visual acuity (BCVA) of 20/320 or better using the Snellen Eye Chart
5. Initial and recertification approvals will be for 1 year
   a. Recertifications will require provider attestation that the patient has not experienced severe vision loss (to the level of hand motion [HM] or worse range) or unacceptable toxicity to the drug
6. Documentation must be submitted confirming which eye (left or right), if not both, is being treated
7. See Prescribing Information for approved dosing

HCPCS: J2781

POLICY GUIDELINES:

1. Prior authorization is contract dependent.
2. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
3. Unless otherwise indicated within drug specific criteria, the drugs listed in this policy are administered by a healthcare professional and therefore are covered under the medical benefit.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
5. For members with Medicare Advantage, medication with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Heath Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, and imaging.
7. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
8. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
9. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

EXCLUSIVE CRITERIA:

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

Codes may not be covered under all circumstances. Please read the policy and guidelines statements carefully.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

HCPCS:

Drug Name	J-Code (if assigned)	NDC
Izervay (avacincaptad pegol)	J2782	82829-0002-01
Syfovre (pegcetacoplan injection)	J2781	73606-0020-01 73606-0020-02

UPDATES:

Date	Revision
11/19/2025	Revised
11/01/2025	Revised
04/22/2025	Revised
03/06/2025	Revised
02/21/2025	Revised
02/06/2025	P&T Committee Review & Approval
12/19/2024	Revised
08/16/2024	Revised
07/01/2024	Created and Implemented
02/08/2024	P&T Committee Review & Approval

REFERENCES:

1. Vavvas DG. “Age-related macular degeneration.” *UpToDate*, 10 January 2024. Age-related macular degeneration - UpToDate
2. Spaide RF, Vavvas DG. COMPLEMENT INHIBITION FOR GEOGRAPHIC ATROPHY: Review of Salient Functional Outcomes and Perspective. Retina 2023; 43:1064
3. Antonio-Aguirre, B., Arevalo, J.F. Treating patients with geographic atrophy: are we there yet?. *Int J Retin Vitr* **9**, 72 (2023). https://doi.org/10.1186/s40942-023-00493-6
4. Desai D, Dugel PU. Complement cascade inhibition in geographic atrophy: a review. *Eye* (2022) 36:294-302
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; 402:1449.
6. Heier JS, Lad EM, Holz FG, et al. Pegcetacoplan for the treatment of geographic atrophy secondary to age-related macular degeneration (OAKS and DERBY): two multicentre, randomized, double-masked, sham-controlled, phase 3 trials. *Lancet* 2023; 402:1434
7. Zhang Q-Y, Tie L-J, Wu S-S, Lv P-L, Huang H-W, Wang W-Q, et al. Overweight, obesity, and risk of age-related macular degeneration. Invest Ophthalmol Vis Sci. 2016;57(3):1276–83.
8. Seddon JM, Cote J, Davis N, Rosner B. Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio. Arch Ophthalmol. 2003;121(6):785–92.
9. Fleckenstein M, Mitchell P, Freund KB, Sadda SV, Holz FG, Brittain C, et al. The progression of geographic atrophy secondary to age-related macular degeneration. Ophthalmology. 2018;125:369-90.

10. Patel SS, Lally DR, Hsu J, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the GATHER1 trial. *Eye (Lond)*. 2023 Mar 24. [Online ahead of print]. Available at: https://www.nature.com/articles/s41433-023-02497-w#citeas. Accessed on February 1, 2024
11. Khan H, Aziz AA, Sulahria H, et al. Emerging treatment options for geographic atrophy (GA) secondary to age-related macular degeneration. Clin Ophthamol. 2023;17:321-327.
12. Izervay™ intravitreal injection [prescribing information]. Parsippany, NJ: Iveric; August 2023.
13. Syfovre™ intravitreal injection [prescribing information]. Waltham MA: Apellis; February 2023.
14. Antonio-Aguirre B, Arevalo JF. Treating pateintes with geographic atrophy: are we there yet? *International Journal of Retina and Vitreous* 2023 9:72
15. Apellis Provides Update on Review of Rare Safety Events with SYFOVRE® (pegcetacoplan injection) for Geographic Atrophy Apellis2023 https://investors. apellis.com/news-releases/ news-release-details/apellis-provides-update-review-rare-safety-events-syfovrer.
16. Apellis. SYFOVRE™ (pegcetacoplan injection) safety: Apellis Pharmaceuticals, Inc.; 2023 https://syfovreecp.com/safety.
17. 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;128:576-586.
18. FDA Adverse Events Reporting System (FEARS) Pubic Dashboard for Syfovre. FDA Adverse Events Reporting System (FAERS) Public Dashboard - FDA Adverse Events Reporting System (FAERS) Public Dashboard | Sheet - Qlik Sense Accessed June 12,2024.