

Utilization Management and Clinical Medical Policy

Policy Name: Syfovre® (pegcetacoplan)	Policy Number: MP-RX-FP-86-23	Scope: <input checked="" type="checkbox"/> MMM MA <input checked="" type="checkbox"/> MMM MultiHealth	Origination Date: 11/30/2023 Last Review Date: 2/22/2026	Effective Date: 2/22/2026 Frequently Revision: 2/22/2027
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Service Category:

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| <input type="checkbox"/> Anesthesia | <input type="checkbox"/> Medicine Services and Procedures |
| <input type="checkbox"/> Surgery | <input type="checkbox"/> Evaluation and Management Services |
| <input type="checkbox"/> Radiology Procedures | <input type="checkbox"/> DME/Prosthetics or Supplies |
| <input type="checkbox"/> Pathology and Laboratory Procedures | <input checked="" type="checkbox"/> Part B DRUG |

Service Description:

This document addresses the use of **Syfovre® (pegcetacoplan)**, an intravitreal therapy approved by the Food and Drug Administration (FDA) for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Background Information:

AMD is a leading cause of severe, irreversible vision loss in adults. 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. 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.

Syfovre (pegcetacoplan) is a pegylated complement C3 inhibitor peptide. It is thought that inhibition at C3 within the complement system can reduce the downstream processes that can lead to continuous retinal atrophy. In the phase 2 FILLY (NCT02503332) trial, pegcetacoplan demonstrated slowed GA lesion growth but was associated with an increased risk of choroidal neovascularization (conversion to wet AMD), prompting recommendations for ongoing retinal monitoring. In the phase 3 OAKS (NCT03525613) and DERBY (NCT03525600) trials, the primary endpoint was reduction in GA lesion growth. While OAKS met this endpoint and DERBY did not, both studies confirmed a dose-dependent slowing of atrophy expansion. Over 24 months,

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however, there was no statistically significant improvement in visual acuity, highlighting the challenge of translating structural benefits into functional vision gains.

The 2025 study by Wykoff and colleagues reported 36-month results from the GALE (NCT04770545) open-label extension of the pivotal OAKS and DERBY trials, evaluating pegcetacoplan, a complement C3 inhibitor, for geographic atrophy (GA) secondary to age-related macular degeneration. Patients received monthly or every-other-month intravitreal pegcetacoplan, with about 92% retention at 36 months. Treatment slowed GA lesion growth by up to 32% overall and 42% in nonsubfoveal lesions, and reduced new scotomatous points by 18% on microperimetry, suggesting preserved retinal sensitivity. The safety profile was consistent with prior studies. 4.5% developed exudative AMD, 1.9% had intraocular inflammation, and no retinal vasculitis occurred.

Although the results confirm that pegcetacoplan provides durable slowing of GA progression, the open-label design and lack of sham control limit interpretability, and visual acuity gains remained minimal. The modest risk of neovascular conversion highlights the need for ongoing OCT monitoring. Overall, pegcetacoplan demonstrates a sustained, disease-modifying effect with manageable safety, most beneficial for patients with extrafoveal GA where slowing atrophy may help maintain visual function.

Approved Indications

- A. Geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

Other Uses

- A. N/A

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J2781	Injection, pegcetacoplan, intravitreal, 1 mg

ICD-10	Description
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H35.3113	Advanced atrophic without subfoveal involvement-RT EYE
H35.3123	Advanced atrophic without subfoveal involvement-LT EYE
H35.3133	Advanced atrophic without subfoveal involvement-Bilateral
H35.3114	Advanced atrophic with subfoveal involvement-RT EYE
H35.3124	Advanced atrophic with subfoveal involvement-LT EYE
H35.3134	Advanced atrophic with subfoveal involvement-Bilateral

Medical Necessity Guidelines:

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.

Syfovre® (pegcetacoplan)

A. Criteria For Initial Approval

Initial requests for Syfovre® (pegcetacoplan) 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 confirmed by geographic atrophy secondary to age-related macular degeneration sensitive tests (including but not limited to optical coherence tomography, fluorescein angiography, fundus photography).

B. Criteria For Continuation of Therapy

- a. MMM considers continuation of Syfovre (pegcetacoplan) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) if the following information is provided:
 - i. Documentation of patient response
 - ii. Documentation that the patient did not develop any of the following reactions with previous treatments:
 - A. Endophthalmitis and Retinal Detachments
 - B. Retinal Vasculitis and/or Retinal Vascular Occlusion
 - C. Neovascular AMD
 - D. Intraocular inflammation
 - E. Increased Intraocular Pressure

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C. Authorization Duration

- a. Initial Approval Duration: 6 months
- b. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

- a. Syfovre (pegcetacoplan) may not be approved when the above criteria are not met and for all other indications:
 - 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. May not be approved when the above criteria are not met and for all other indications.

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

- i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Drug	Limit
Syfovre (pegcetacoplan) 150 mg/mL single-dose vial	0.1 mL (or 15 mg) by intravitreal injection per eye; each eye may be treated as frequently as every 25 to 60 days.

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Reference Information:

1. Apellis Pharmaceuticals. A Study to Compare the Efficacy and Safety of Intravitreal APL-2 Therapy With Sham Injections in Patients With Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration. NCT03525613. Clinicaltrials.gov. Available at: <https://clinicaltrials.gov/ct2/show/NCT03525613?term=pegcetacoplan&type=Intr&cond=Geographic+Atrophy&phase=2&draw=2&rank=3> Accessed January 20, 2023.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
5. Fu DJ, Bagga P, Naik G, et al. Pegcetacoplan Treatment and Consensus Features of Geographic Atrophy Over 24 Months. JAMA Ophthalmol. 2024;142(6):548-558. doi:10.1001/jamaophthalmol.2024.1269.
6. Liao DS, Grossi FV, El Mehdi D, et al. Complement C3 Inhibitor Pegcetacoplan for Geographic Atrophy Secondary to Age-Related Macular Degeneration: A Randomized Phase 2 Trial. Ophthalmology. 2020 Feb;127(2):186-195.
7. 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, randomised, double-masked, sham-controlled, phase 3 trials. Lancet. 2023;402(10411):1434-1448. doi:10.1016/S0140-6736(23)01520-9.
8. Wykoff CC, Holz FG, Chiang A, et al. Pegcetacoplan Treatment for Geographic Atrophy in Age-Related Macular Degeneration Over 36 Months: Data From OAKS, DERBY, and GALE. Am J Ophthalmol. 2025;276:350-364. doi:10.1016/j.ajo.2025.04.016.
9. Apellis Pharmaceuticals. (n.d.). SYFOVRE (pegcetacoplan) Prescribing Information. Retrieved January 14, 2026, from https://pi.apellis.com/files/PI_SYFOVRE.pdf
10. Vavvas DG. Age-related macular degeneration. UpToDate. Published Nov 10, 2025. Accessed January 14, 2026. https://www.uptodate.com/contents/age-related-macular-degeneration?search=syfovre&source=search_result&selectedTitle=4~14&usage_type=default&display_rank=3#H732827882

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Added additional clinical trial information to the Background Information section. Added Approved Indication and Other Uses sections. Moved Applicable Codes below the Service Description. Coding reviewed: removed C9151, J3490, and C9399; added ICD-10-CM codes H35.3113, H35.3123, H35.3133, H35.3114, H35.3124, and H35.3134. Added sections for Criteria for Continuation of Therapy, Conditions Not Covered, Duration of Therapy, and Therapeutic Alternatives. Updated the reference list. Wording and formatting changes.	02/13/2026	2/22/2026
Annual Review	Validation of information to ensure is up to date. No changes applied.	4/16/2025	5/6/2025
Policy Inception	Elevance Health’s Medical Policy adoption.	N/A	11/30/2023