Original Effective Date: 06/21/2023
Current Effective Date: 11/29/2024
Last P&T Approval/Version: 10/30/2024
Next Review Due By: 10/2025
Policy Number: C25311-A

Syfovre (pegcetacoplan intravitreal)

PRODUCTS AFFECTED

Syfovre (pegcetacoplan intravitreal)
*Empaveli (pegcetacoplan) – SEE EMPAVELI MHI C21423-A

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. GEOGRAPHIC ATROPHY:
   1. Documentation of diagnosis of geographic atrophy (GA) secondary to age-related macular

degeneration
AND
2. Documentation of baseline visual status and GA lesion area with notation of eye(s) being treated [DOCUMENTATION REQUIRED]
AND
3. Documentation of presence of extrafoveal lesions [2,3]
AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Syfovre (pegcetacoplan injection) include: Ocular or periocular infections and active intraocular inflammation]

CONTINUATION OF THERAPY:

A. GEOGRAPHIC ATROPHY:

1. Reauthorization request is for the same eye(s) as initial authorization
NOTE: The continuation of therapy criteria is only for the same previously treated eye(s). If member has developed condition in an untreated eye, Prescriber must submit new request with Initial Coverage criteria.
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of improvement or stabilization of disease state and visual status or GA lesion area [DOCUMENTATION REQUIRED]
AND
4. Documentation of administration records showing dates and eye(s) administered, along with documentation of member compliance with treatment plan

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified ophthalmologist or retinal specialist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

60 years of age and older

QUANTITY:

15 mg (0.1 mL of 150 mg/mL solution) each affected eye once every 25 to 60 days

PLACE OF ADMINISTRATION:

The recommendation is that intravitreal medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility- based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Intravitreal Injection

DRUG CLASS:

Ophthalmic Complement C3 Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD) that leads to progressive and irreversible vision loss. GA is caused by the gradual breakdown of light-sensitive cells in the macula, resulting in the growth of irreversible lesions in the retinal pigment epithelium (RPE) that can lead to impaired vision or blindness. Progressive GA can eventually affect the fovea, or central part of the macula, which is responsible for high-acuity vision.
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. AMD occurs in progressive stages of severity, which are defined as early, intermediate, or advanced.
GA occurs only in the intermediate or advanced stages of AMD. In the intermediate stage, GA affects the RPE, but the center of the fovea is not involved; in the advanced stage of AMD, GA also affects the foveal center. Choroidal neovascularization (CNV) may also occur during the advanced stage of AMD. AMD with CNV is often referred to as exudative AMD (eAMD), neovascular AMD (nAMD), or wet AMD (wAMD).

Syfovre (pegcetacoplan) is a complement inhibitor that binds to components C3 and C3b to control excessive complement activation, which is associated with lesion growth in GA. Pegcetacoplan is already FDA-approved as a subcutaneous infusion formulation for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) under the brand name Empaveli; Syfovre is formulated as an intravitreal injection and is indicated for the treatment of GA secondary to AMD.

Syfovre was evaluated in the Phase 2 FILLY study (NCT02503332) and two Phase 3 studies, DERBY (NCT03525600) and OAKS (NCT03525613), for the treatment of GA due to AMD. The FDA approval of Syfovre was based on the Phase 3 studies.

In the Phase 2 FILLY study Patients with GA were assigned randomly in a 2:2:1:1 ratio to receive intravitreal injections of 15 mg pegcetacoplan monthly or every other month (EOM) or sham intravitreal injections monthly or EOM for 12 months with follow-up at months 15 and 18. Area and growth of GA were measured using fundus autofluorescence imaging. The primary efficacy end point was mean change in square root GA lesion area from baseline to month 12. Secondary outcome measures included mean change from baseline in GA lesion area without the square root transformation, distance of GA lesion from the fovea, best-corrected visual acuity (BCVA), low-luminance BCVA, and low-luminance visual acuity deficit. The primary safety end point was the number and severity of treatment-emergent adverse events. In patients receiving pegcetacoplan monthly or EOM, the GA growth rate was reduced by 29% (95% confidence interval [CI], 9-49; P = 0.008) and 20% (95% CI, 0-40; P = 0.067) compared with the sham treatment group. Post hoc analysis showed that the effect was greater in the second 6 months of treatment, with observed reductions of 45% (P = 0.0004) and 33% (P = 0.009) for pegcetacoplan monthly

and EOM, respectively. Two cases of culture-positive endophthalmitis and 1 case of culture-negative endophthalmitis occurred in the pegcetacoplan monthly group. New-onset investigator-determined exudative AMD was reported more frequently in pegcetacoplan-treated eyes (18/86 eyes [20.9%] and 7/79 eyes [8.9%] in monthly and EOM groups, respectively) than in sham-treated eyes (1/81 eyes [1.2%])

Overall, results from this study showed that participants who received pegcetacoplan had slower growth of GA lesions than participants who received the sham injection. After the participants had stopped receiving pegcetacoplan, the effect of the treatment seemed to be reduced. Pegcetacoplan did not change how well the participants could see during their vision tests in this trial.

The FDA approval was based on data from the phase 3 DERBY (ClinicalTrials.gov Identifier: NCT03525600) and OAKS (ClinicalTrials.gov Identifier: NCT03525613) studies, which evaluated the efficacy and safety of intravitreal pegcetacoplan in 1258 patients with GA secondary to AMD for 24 months. Patients were randomly assigned 2:2:1:1 to receive either pegcetacoplan 15mg/0.1mL once monthly, pegcetacoplan 15mg/0.1mL every other month, sham once monthly or sham every other month. The primary endpoint for both studies was the change in the total area of GA lesions from baseline as measured by fundus autofluorescence at 12 months.

In DERBY, treatment with pegcetacoplan monthly and every other month injections reduced the rate of GA lesion growth by 18.1% and 17.4%, respectively, from baseline to month 24. In OAKS, treatment with pegcetacoplan monthly and every other month injections reduced the rate of GA lesion growth by 21.9% and 18.1%, respectively, from baseline to month 24.

At 24 months, there was no statistically significant difference in measures of visual function, including normal luminance best-corrected visual acuity (BCVA), maximum reading speed, Functional Reading Independence Index, and microperimetry: mean threshold sensitivity (OAKS only), between either treatment group (monthly or EOM) and the sham group. BCVA in the treatment groups continued to decline at a rate similar to the sham group.

The most common adverse reactions reported with pegcetacoplan included ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage. The treatment is contraindicated for use in patients with ocular or periocular infections and patients with active intraocular inflammation.

At 24 months, Apellis noted 16 cases of intraocular inflammation (IOI) in the pooled data for patients treated monthly in DERBY and OAKS (N = 419), and nine cases of IOI in the pooled EOM group (N = 420). There was one IOI case in the pooled sham group (N = 417). Four of these events occurred in 2018 and were related to a drug impurity. Four cases of infectious endophthalmitis occurred through 24 months: two each in the monthly and EOM groups.

There is potential for accelerated development of nAMD in the clinical trials; nAMD occurred in 12% of patients in the Syfovre monthly arms of the DERBY and OAKS trials (pooled), 7% of patients in the Syfovre EOM arms, and 3% of patients in the sham groups. Previous results from the FILLY trial indicated that patients with CNV in the fellow (untreated) eye were more likely to develop nAMD in the study eye. In pooled results from the DERBY and OAKS trials, this correlation was not as pronounced.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Syfovre (pegcetacoplan injection) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Syfovre (pegcetacoplan injection) include ocular or periocular infections and active intraocular inflammation.

OTHER SPECIAL CONSIDERATIONS:

Syfovre (pegcetacoplan injection) must be administered by a qualified physician.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
J2781	Injection, pegcetacoplan, intravitreal, 1 mg

AVAILABLE DOSAGE FORMS:

Syfovre SOLN 15MG/0.1ML

REFERENCES

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Coding/Billing Information Template Update	Q4 2024
REVISION- Notable revisions: Products Affected Required Medical Information Background Coding/Billing Information	Q4 2023
NEW CRITERIA	Q2 2023