Medical Drug Clinical Criteria

Subject:	Syfovre (pegcetacoplan)		
Document #:	CC-0234	**Publish Date:**	12/23/2024
Status:	Reviewed	**Last Review Date:**	11/15/2024

Table of Contents

Overview

This document addresses the use of Syfovre (pegcetacoplan), an FDA- approved intravitreal therapy 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. 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. During the phase 2 study (FILLY trial), adverse events of choroidal neovascularization or neovascular “wet” AMD were reported. The FDA advises that individuals who receive this drug will need to be monitored for signs of neovascular AMD. The phase 3 clinical studies (OAKS and DERBY) primary endpoint was the anatomical measurement of the geographic atrophy lesion growth. While the OAKS trial met the primary endpoint, DERBY did not. However, all study groups had an increase in the GA lesion growth over time. At the end of 24 months, there was no statistical difference regarding change in visual acuity.

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.

Syfovre (pegcetacoplan)

Requests for 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 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 pegcetacoplan 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. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Syfovre (pegcetacoplan) Quantity Limits

Drug	Limit
Syfovre (pegcetacoplan) 150 mg/mL vial	0.1 mL (or 15 mg) per eye; each eye may be treated as frequently as every 25 to 60 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

J2781	Injection, pegcetacoplan, intravitreal, 1 mg

ICD-10 Diagnosis

H35.30	Unspecified macular degeneration
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
H35.3210-H35.3293	Exudative age-related macular degeneration, right eye
H35.351-H35.359	Cystoid macular degeneration

Document History

Reviewed: 11/15/2024
Document History:

- 11/15/2024 – Annual Review: No changes. Coding Reviewed: Add ICD-10-CM H35.30, H35.3210-H35.3293, H35.351-H35.359.
- 11/17/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 02/24/2023 – Select Review: Add new clinical criteria document for Syfovre. Coding Reviewed: Added HCPCS J3490, C9399. All diagnoses pend. Effective 7/1/2023 Added HCPCS C9151. Removed HCPCS C9399. Effective 10/1/2023 Removed HCPCS C9151, Removed J3490. Added HCPCS J2781. Added ICD-10-CM H35.3113, H35.3123, H35.3133, H35.3114, H35.3124, H35.3134.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. 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.
5. 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.
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, randomised, double-masked, sham-controlled, phase 3 trials. *Lancet*. 2023;402(10411):1434-1448. doi:10.1016/S0140-6736(23)01520-9.

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.