Clinical Guideline

Oscar Clinical Guideline: Syfovre (pegcetacoplan injection) (PG150, Ver. 3)

Syfovre (pegcetacoplan injection)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Age-related macular degeneration (AMD) is a common eye condition and a leading cause of vision loss among people aged 50 and older. The disease blurs the sharp, central vision needed for activities like reading and driving. AMD occurs in two forms: dry (non-neovascular) and wet (neovascular or exudative). The dry form is more prevalent, affecting about 90% of patients, and is characterized by the accumulation of drusen (yellow deposits) under the retina and alterations in the retinal pigment epithelium.

Geographic atrophy (GA) represents an advanced stage of dry AMD. It involves the progressive and irreversible loss of retinal pigment epithelium, photoreceptors, and underlying choriocapillaris, leading to visual function impairment. Patients with GA may experience difficulty reading, seeing in low-light conditions, and may eventually suffer severe vision loss.

Until recently, there were limited treatment options for GA secondary to AMD. Syfovre (pegcetacoplan injection) is the first FDA-approved therapy for GA secondary to AMD. Pegcetacoplan is a complement C3 inhibitor that regulates the cleavage of complement protein C3 and the generation of downstream effectors of complement activation, which are involved in the pathogenesis of AMD.

Clinical trials, including the phase 3 OAKS and DERBY studies, have demonstrated that Syfovre reduces the rate of GA lesion growth compared to sham injections over 24 months. The treatment is administered via intravitreal injection either monthly or every other month. While Syfovre slows the progression of GA, it does not restore lost vision or completely halt disease progression. Common adverse reactions observed with Syfovre include ocular discomfort, neovascular (wet) AMD, vitreous floaters, and conjunctival hemorrhage.

Definitions

"**Age-related macular degeneration (AMD)**" is a common eye condition among people age 50 and older that leads to deterioration of the macula and central vision loss.

"**Complement C3 inhibitor**" is a type of drug that blocks the action of a protein in the immune system (known as C3) that can cause inflammation and damage in various body tissues. Pegcetacoplan is an example of a Complement C3 inhibitor.

"**Drusen**" are yellow deposits under the retina, often found in people over age 60. The presence of drusen is usually the first sign of age-related macular degeneration.

"**Dry form of AMD**" is the more common form of AMD. It affects the majority of people who have AMD. It occurs when parts of the macula get thinner with age and tiny clumps of protein called drusen grow.

"**Geographic Atrophy (GA)**" is an advanced form of dry AMD. It involves the slow progressive degeneration of the retinal cells causing atrophy and leading to a loss of vision.

"**Intravitreal Injections**" are injections into the eye's vitreous, a jelly-like substance in the middle of the eye. It is used to provide treatment directly to the retina.

"**Vascular Endothelial Growth Factor (VEGF)**" is a protein that promotes the growth of new blood vessels. In wet AMD, VEGF is responsible for the growth of new, abnormal blood vessels.

"**Neovascular AMD**" is another term for wet AMD, referring to the growth of new blood vessels in an area, such as the macula, where they are not supposed to be.

"**Wet form of AMD**" is the more serious form of AMD. It occurs when abnormal blood vessels grow from the choroid under and into the macular portion of the retina. These new blood vessels leak fluid or blood, distorting or destroying the central vision.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Syfovre (pegcetacoplan injection)** medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with an ophthalmologist or retinal specialist; ***AND***
2. The member is 18 years of age or older; ***AND***
3. The member has a diagnosis of geographic atrophy secondary to age-related macular degeneration supported by clinical documentation (e.g., fundus autofluorescence (FAF) imaging, optical coherence tomography (OCT), Fluorescein Angiography (FA)); ***AND***
4. The member does NOT have any of the following contraindications:
    a. Active ocular or periocular infections; ***or***
    b. Active intraocular inflammation; ***AND***
5. Syfovre is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication
    ➢ *15 mg (0.1 mL of 150 mg/mL solution) administered by intravitreal injection to each affected eye once every 25 to 60 days (i.e., monthly or every other month).*

If the above prior authorization criteria are met, Syfovre (pegcetacoplan injection) will be approved for 12-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12-months will be granted if clinical chart documentation is provided showing the member meets **ALL** of the following:

1. Prescribed by or in consultation with an ophthalmologist or retinal specialist; ***AND***
2. Clinical documentation is provided showing:
    a. Stabilization or slowing in the growth rate of geographic atrophy lesions, as evidenced by imaging studies (e.g., FAF, OCT); ***and***

b. No evidence of unacceptable toxicity or adverse events, such as endophthalmitis, retinal detachment, intraocular inflammation, increased intraocular pressure, or conversion to neovascular (wet) AMD; ***AND***

3. Continued need for therapy to slow the progression of GA secondary to AMD.

Experimental or Investigational / Not Medically Necessary

Syfovre (pegcetacoplan injection) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- neovascular (wet) age-related macular degeneration.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
Healthcare Common Procedure Coding System (HCPCS) code	
J2781	Injection, pegcetacoplan, intravitreal, 1 mg
Current Procedural Terminology (CPT) codes for imaging	
92134	Optical coherence tomography
92235	Fluorescein angiography (FA)
92250	Fundus photography (Fundus autofluorescence)
92240	Indocyanine green angiography (ICG)
92242	FA and ICG
CPT code for injections	
67028	Intravitreal injection of a pharmacologic agent (separate procedure)

Site modifier *To specify which eye(s) received the injection, append the appropriate modifier to the end of the CPT code 67028. For example, if the injection was given in the left eye, the code would be 67028-LT.*	
LT	Indicates the procedure was performed on the left eye.
RT	Indicates the procedure was performed on the right eye.
50	Indicates the procedure was done on both eyes.
Evaluation and management (E/M) codes	
99203	New Patient Level 3 E/M
99213	Established Patient Level 3 E/M
99204	New Patient Level 4 E/M
99214	Established Patient Level 4 E/M
Office visit modifier	
25	Significant, separately identifiable evaluation and management service by the same physician or other qualified healthcare professional on the same day of the procedure or other services.
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
H35.3113	Nonexudative age-related macular degeneration, right eye, advanced atrophic without subfoveal involvement
H35.3123	Nonexudative age-related macular degeneration, left eye, advanced atrophic without subfoveal involvement
H35.3133	Nonexudative age-related macular degeneration, bilateral, advanced atrophic without subfoveal involvement
H35.3114	Nonexudative age-related macular degeneration, right eye, advanced atrophic with subfoveal involvement
H35.3124	Nonexudative age-related macular degeneration, left eye, advanced atrophic with subfoveal involvement
H35.3134	Nonexudative age-related macular degeneration, bilateral, advanced atrophic with subfoveal involvement

References

1. Chakravarthy, U., et al. (2018). Characterizing disease burden and progression of geographic atrophy secondary to age-related macular degeneration. Ophthalmology, 125, 842. doi:10.1016/j.ophtha.2017.11.036.
2. Charters, Lynda. Comparing the Efficacy of Pegcetacoplan and Avacincaptad Pegol in Patients with GA. Dec. 2023. www.ophthalmologytimes.com, https://www.ophthalmologytimes.com/view/comparing-the-effifficacy-of-pegcetacoplan-and-avacincaptad-pegol-in-patients-with-ga.
3. Desai, D., & Dugel, P. U. (2022). Complement cascade inhibition in geographic atrophy: a review. Eye (Lond), 36, 294. doi:10.1038/s41433-021-01765-x.
4. Flaxel CJ, Adelman RA, Bailey ST, Fawzi A, Lim JI, Vemulakonda GA, Ying GS. Age-Related Macular Degeneration Preferred Practice Pattern®. Ophthalmology. 2020 Jan;127(1):P1-P65. doi: 10.1016/j.ophtha.2019.09.024. Epub 2019 Sep 25. Erratum in: Ophthalmology. 2020 Sep;127(9):1279. doi: 10.1016/j.ophtha.2020.06.048. PMID: 31757502.
5. Freund KB, Toth C, Zarbin M. Best Clinical Practice for Age-Related Macular Degeneration Imaging. Journal of VitreoRetinal Diseases. 2019;3(3):167-171. doi:10.1177/2474126419834702.
6. Fu DJ, Bagga P, Naik G, Glinton S, Faes L, Liefers B, Lima R, Wignall G, Keane PA, Ioannidou E, Ribeiro Reis AP, McKeown A, Scheibler L, Patel PJ, Moghul I, Pontikos N, Balaskas K. Pegcetacoplan Treatment and Consensus Features of Geographic Atrophy Over 24 Months. JAMA Ophthalmol. 2024 Jun 1;142(6):548-558. doi: 10.1001/jamaophthalmol.2024.1269. PMID: 38722644; PMCID: PMC11082756.
7. Kim, B. J., Mastellos, D. C., Li, Y., Dunaief, J. L., & Lambris, J. D. (2021). Targeting complement components C3 and C5 for the retina: key concepts and lingering questions. Prog Retin Eye Res, 83, 100936. doi:10.1016/j.preteyeres.2020.100936.
8. Liao, D. S., Grossi, F. V., El Mehdi, D., et al. (2020). Complement C3 inhibitor pegcetacoplan for geographic atrophy secondary to age-related macular degeneration: a randomized phase 2 trial. Ophthalmology, 127(2), 186-195. doi:10.1016/j.ophtha.2019.07.011.
9. Mai, J., Riedl, S., Reiter, G. S., et al. (2022). Comparison of fundus autofluorescence versus optical coherence tomography-based evaluation of the therapeutic response to pegcetacoplan in geographic atrophy. Am J Ophthalmol, 244, 175-182. doi:10.1016/j.ajo.2022.06.023.
10. Nittala, M. G., Metlapally, R., Ip, M., et al. (2022). Association of pegcetacoplan with progression of incomplete retinal pigment epithelium and outer retinal atrophy in age-related macular degeneration: a post hoc analysis of the FILLY randomized clinical trial. JAMA Ophthalmol, 140(3), 243-249. doi:10.1001/jamaophthalmol.2021.6067.
11. Riedl, S., Vogl, W. D., Mai, J., et al. (2022). The effect of pegcetacoplan treatment on photoreceptor maintenance in geographic atrophy monitored by artificial intelligence-based oct analysis. Ophthalmol Retina, 6(11), 1009-1018. doi:10.1016/j.oret.2022.05.030.
12. Steinle, N. C., Pearce, I., Monés, J., et al. (2021). Impact of baseline characteristics on geographic atrophy progression in the FILLY trial evaluating the complement C3 inhibitor pegcetacoplan. Am J Ophthalmol, 227, 116-124. doi:10.1016/j.ajo.2021.02.031
13. Syfovre (pegcetacoplan) [prescribing information]. (December 2023). Waltham, MA: Apellis Pharmaceuticals Inc.

14. Vogl, W. D., Riedl, S., Mai, J., et al. (2023). Predicting topographic disease progression and treatment response of pegcetacoplan in geographic atrophy quantified by deep learning. Ophthalmol Retina, 7(1), 4-13. doi:10.1016/j.oret.2022.08.003.
15. Wykoff, C. C., Rosenfeld, P. J., Waheed, N. K., et al. (2021). Characterizing new-onset exudation in the randomized phase 2 FILLY trial of complement inhibitor pegcetacoplan for geographic atrophy. Ophthalmology, 128(9), 1325-1336. doi:10.1016/j.ophtha.2021.02.025.

Clinical Guideline Revision / History Information

Original Date: 06/29/2023

Reviewed/Revised: 10/27/2023, 12/19/2024