Oscar Clinical Guideline: Syfovre (pegcetacoplan injection) (PG150, Ver. 1)

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 condition characterized by two major forms: dry (non-neovascular) and wet (neovascular, exudative). The dry form is more prevalent, occurring in about 90% of patients, and is characterized by retinal pigment epithelium abnormalities with focal accumulation of metabolic byproducts called drusen. Geographic atrophy (GA) is an advanced form of dry AMD that is associated with the progressive and irreversible loss of the retinal pigment epithelium, photoreceptors, and underlying choriocapillaris.

Patients with GA may experience difficulty reading, seeing in low-light conditions, and potentially severe vision loss. Until recently, there was no established treatment for dry AMD.

The wet form of AMD is less common, present in about 10% of patients, and can occur alongside GA. This form is characterized by a rapid decrease in central visual acuity due to newly developed leaky vessels and scar tissue growing from the choroid into the subretinal space. Treatments that inhibit

vascular endothelial growth factor (VEGF) have proven effective at reducing vision loss in cases of wet AMD.

Pegcetacoplan (Syfovre – Apellis), a complement C3 inhibitor, is the first FDA-approved drug for the treatment of GA secondary to AMD. This treatment involves a series of monthly or every-other-month intravitreal injections. This approval is a breakthrough, as it is the first treatment available for atrophic dry AMD.

Clinical trials have shown that the progression of GA can be slowed over a 24-month period with either monthly or every-other-month intravitreal injections of pegcetacoplan. The most notable effects were observed in the final six months of the trial. However, while it slowed the progression of GA, pegcetacoplan did not reduce the loss of visual acuity.

A potential downside is that every-other-month injections of pegcetacoplan doubled the risk of conversion to wet AMD, while monthly injections increased the risk fourfold, compared to sham injections. Therefore, while pegcetacoplan offers a new approach for treating GA secondary to AMD, its long-term efficacy in preserving vision remains to be established, and the increased risk of developing wet AMD is a cause for concern.

Definitions

"**Age-related macular degeneration (AMD)**" is a disease that blurs the sharp, central vision you need for activities like reading and driving. Age-related macular degeneration (AMD) is a common eye condition among people age 50 and older. It is a leading cause of vision loss in older adults.

"**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.

Policy Statement on Syfovre (pegcetacoplan injection) Efficacy Information

The FDA approval of pegcetacoplan for the treatment of GA secondary to AMD was grounded in two unpublished, double-masked trials (OAKS and DERBY) of 1258 patients aged 60-100 years with atrophic dry AMD. These trials showed that pegcetacoplan statistically significantly reduced the growth of GA lesions over 24 months compared to sham injections, with the most notable differences observed in the last 6 months of treatment.

However, despite these positive findings, all groups saw continued visual acuity decline, with no significant differences observed between drug-treated and sham-treated patients. This raises questions about the practical benefits of the treatment, as preserving or improving visual acuity is a significant goal in the management of AMD.

Additionally, the use of pegcetacoplan has been linked with an increased risk of converting to the wet form of AMD, with rates of 12% and 7% for monthly and every-other-month administrations respectively, compared to 3% with sham injections. Other adverse reactions included ocular discomfort, vitreous floaters, conjunctival and retinal hemorrhages, keratitis, ocular inflammation, optic nerve injury, and increased intraocular pressure.

Further supporting this, the FILLY trial, a phase II randomized sham-controlled trial, and six subsequent post hoc analyses provided limited published evidence evaluating intravitreal pegcetacoplan for the treatment of GA. While the FILLY trial did meet its primary endpoint, indicating that pegcetacoplan slowed lesion growth, ocular adverse events were noted, and there was a higher incidence of neovascular AMD in pegcetacoplan-treated patients than in those receiving sham injections.

Given this evidence, while pegcetacoplan has demonstrated the ability to slow the progression of GA secondary to AMD, its long-term efficacy in preserving visual acuity remains uncertain, and the increased risk of developing wet AMD is concerning. Further research is needed to more definitively establish the long-term benefits and risks of pegcetacoplan treatment for GA secondary to AMD.

Medical Necessity Criteria for Syfovre (pegcetacoplan injection)

Given the clinical evidence currently available, the Plan has determined that it does not have established medical necessity criteria for coverage of pegcetacoplan (Syfovre) for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

While the clinical trials show that pegcetacoplan can reduce the growth of GA lesions, the drug has not demonstrated the ability to prevent or reverse the decline in visual acuity, a significant factor in the management of AMD. Additionally, the increased risk of conversion from dry AMD to the more severe wet AMD associated with pegcetacoplan treatment is a matter of concern.

Considering these factors, we believe that more extensive clinical data is necessary to establish the long-term efficacy and safety of pegcetacoplan. Until such evidence is available, the Plan cannot establish medical necessity criteria for its coverage.

Beneficiaries are encouraged to discuss alternative treatment options with their healthcare providers. The Plan remains committed to providing coverage for a wide range of clinically proven and cost-effective treatments for AMD and will continue to monitor the evolving evidence regarding the use of pegcetacoplan for the treatment of GA secondary to AMD.

We will reassess our coverage policy as new evidence emerges and ensure that our beneficiaries have access to the most effective and safe treatments for AMD. As always, individual clinical circumstances may warrant exceptions to our general policy position. Such requests for coverage of pegcetacoplan will be reviewed on a case-by-case basis.

Experimental or Investigational / Not Medically Necessary

Syfovre (pegcetacoplan injection) for any indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. The Plan has reviewed the current clinical evidence and has concluded that Syfovre (pegcetacoplan injection) for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) is not considered medically necessary at this time due to the following reasons:

1. While clinical trials have demonstrated that Syfovre (pegcetacoplan injection) can slow the growth of GA lesions, they have not shown a significant impact on preventing or reversing the decline in visual acuity. This is a critical limitation, as maintaining or improving visual acuity is a primary goal in the management of AMD.
2. Syfovre (pegcetacoplan injection) treatment has been linked to an increased risk of progression to the more severe form of the disease - wet AMD. This risk is not present with other treatment options, and wet AMD is typically associated with a faster rate of vision loss than the dry form.
3. Clinical trials have shown that Syfovre (pegcetacoplan injection) is associated with a number of ocular adverse events including, but not limited to, ocular discomfort, vitreous floaters, conjunctival and retinal hemorrhages, keratitis, ocular inflammation, optic nerve injury, and increased intraocular pressure. The benefit-risk balance needs further clarification.
4. While Syfovre (pegcetacoplan injection) has demonstrated the potential to slow the progression of GA in clinical trials, the long-term efficacy of this treatment in terms of preserving vision is yet to be definitively established.

Given these concerns, the Plan has concluded that Syfovre (pegcetacoplan injection) does not meet the criteria of medical necessity for the treatment of GA secondary to AMD at this time. The Plan remains committed to providing coverage for a wide range of treatments that have demonstrated both safety and effectiveness based on robust clinical evidence. We will continue to monitor the evolving clinical evidence regarding pegcetacoplan and will reassess our position as more information becomes available. Until then, we encourage our members to explore alternative treatment options with their healthcare providers.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered NOT medically necessary:	
Code	*Description*
67028	Intravitreal injection of a pharmacologic agent (separate procedure)
C9399	Unclassified drugs or biologicals
J3490	Unclassified drug
ICD-10 codes considered NOT medically necessary:	
Code	*Description*
H35.31	Nonexudative age-related macular degeneration
H35.311	Nonexudative age-related macular degeneration, right eye
H35.3110	Nonexudative age-related macular degeneration, right eye, stage unspecified
H35.3111	Nonexudative age-related macular degeneration, right eye, early dry stage
H35.3112	Nonexudative age-related macular degeneration, right eye, intermediate dry stage
H35.3113	Nonexudative age-related macular degeneration, right eye, advanced atrophic without subfoveal involvement
H35.3114	Nonexudative age-related macular degeneration, right eye, advanced atrophic with subfoveal involvement
H35.312	Nonexudative age-related macular degeneration, left eye
H35.3120	Nonexudative age-related macular degeneration, left eye, stage unspecified
H35.3121	Nonexudative age-related macular degeneration, left eye, early dry stage
H35.3122	Nonexudative age-related macular degeneration, left eye, intermediate dry stage
H35.3123	Nonexudative age-related macular degeneration, left eye, advanced atrophic without subfoveal involvement
H35.3124	Nonexudative age-related macular degeneration, left eye, advanced atrophic with subfoveal involvement
H35.313	Nonexudative age-related macular degeneration, bilateral
H35.3130	Nonexudative age-related macular degeneration, bilateral, stage unspecified

H35.3131	Nonexudative age-related macular degeneration, bilateral, early dry stage
H35.3132	Nonexudative age-related macular degeneration, bilateral, intermediate dry stage
H35.3133	Nonexudative age-related macular degeneration, bilateral, advanced atrophic without subfoveal involvement
H35.3134	Nonexudative age-related macular degeneration, bilateral, advanced atrophic with subfoveal involvement
H35.319	Nonexudative age-related macular degeneration, unspecified eye
H35.3190	Nonexudative age-related macular degeneration, unspecified eye, stage unspecified
H35.3191	Nonexudative age-related macular degeneration, unspecified eye, early dry stage
H35.3192	Nonexudative age-related macular degeneration, unspecified eye, intermediate dry stage
H35.3193	Nonexudative age-related macular degeneration, unspecified eye, advanced atrophic without subfoveal involvement
H35.3194	Nonexudative age-related macular degeneration, unspecified eye, advanced atrophic with subfoveal involvement

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