09-J4000-47

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Reviewed: 09/11/24

Revised: 10/15/24

Subject: Pegcetacoplan (Syfovre) intravitreal injection

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Geographic atrophy (GA) is a secondary complication of age-related macular degeneration (AMD) and occurs in the intermediate or advanced stages of AMD. GA is classified as a non-neovascular form of AMD and has an estimated prevalence of 0.81% (in at least one eye) in U.S. patients over 40 years of age, and since aging is the primary risk factor, the prevalence of GA increases to 3.5% in patients 75 years of age and older. More than half of all patients with GA experience significant vision impairment with 20% developing severe vision loss (e.g., visual acuity of 20/200 or worse).

Medications such as vascular endothelial growth factor (VEGF) inhibitors are used to treat neovascular AMD (nAMD) or wet AMD (wAMD); however, these agents are ineffective in the treatment of non-neovascular forms of AMD, including GA. On February 17, 2023, the FDA approved pegcetacoplan intravitreal injection (Syfovre) for the treatment of GA secondary to AMD, which is the first therapeutic option for GA. Pegcetacoplan (Syfovre) binds to complement protein C3 and its activation fragment C3b with high affinity thereby regulating the cleavage of C3 and the generation of downstream effectors of complement activation.

The efficacy and safety of pegcetacoplan (Syfovre) was evaluate in two phase 3, multi-center, randomized, double-masked, sham-controlled studies, OAKS (NCT03525613) and DERBY (NCT03525600), which are ongoing. Enrolled patients were 60 years of age or older with best-corrected visual acuity greater than or equal to 24 letters and a GA area between 2.5 and 17.5 mm^2, including foveal and extrafoveal lesions. Patients were excluded if they had an ocular or periocular infection, active intraocular inflammation, active or history of choroidal neovascularization (CNV), including any evidence of retinal pigment epithelium rips or evidence of neovascularization, intraocular surgery (including lens replacement surgery) within 3 months prior to randomization, history of laser therapy in the macular region, and history of prior intravitreal injection(s). In each study, patients were randomly assigned in a 2:2:1:1 ratio to 1 of 4 dosing regimens: (1) pegcetacoplan (Syfovre) 15 mg/0.1 mL monthly, (2) pegcetacoplan (Syfovre) 15 mg/0.1 mL every other month, (3) sham administered monthly, and (4) sham administered every other month. The primary endpoint for both studies was change in GA lesion size from baseline to Month 12 measured by fundus autofluorescence. The OAKS and DERBY studies enrolled 637 and 621 patients, respectively. The OAKS study demonstrated significant reductions in GA lesion growth with pegcetacoplan (Syfovre) as compared to the sham in the monthly and every other month arms by 22% (p=0.0003) and 16% (p=0.0052), respectively. Additionally, the DERBY study

demonstrated decreased GA lesion growth with pegcetacoplan (Syfovre) as compared to the sham by 12% (p=0.0528) and 11% (p=0.0750) in the monthly and EOM arms, respectively. A prespecified pooled analysis showed reductions were 17% (p<0.0001; nominal) and 14% (p=0.0012; nominal) in the monthly and every other month versus the sham.

The most common adverse reactions (incidence ≥5%) associated with pegcetacoplan (Syfovre) intravitreal injections are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

POSITION STATEMENT:

The administration of pegcetacoplan (Syfovre) intravitreal injection **meets the definition of medical necessity** when **ALL** of the following are met:

1. The member has a diagnosis of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).
2. Ophthalmic test documentation of GA secondary to AMD (e.g., optical coherence tomography, fluorescein angiography, fundus photography) – laboratory or medical record documentation provided
3. The member does not have any ocular or periocular infections or active intraocular inflammation.
4. Not used in combination with other intravitreal complement inhibitor therapies (e.g., Izervay)
5. The dose does not exceed 15 mg per eye every 25 days.

Approval duration: 1 year

Pegcetacoplan (Syfovre) intravitreal injection is considered **experimental or investigational** for any other indications due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcome.

Continuation of pegcetacoplan (Syfovre) intravitreal injection **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization for the requested agent has been previously approved by Florida Blue or another health plan in the past 2 years (if another health plan, documentation of a health plan-paid claim during the 90 days before the authorization request must be submitted), OR the member currently meets all indication-specific initiation criteria.
2. The member has experienced a clinically beneficial response from the pegcetacoplan (Syfovre) intravitreal injections without any significant adverse events requiring discontinuation (e.g., retinal vasculitis, retinal vascular occlusion, endophthalmitis, retinal detachment, neovascular (wet) AMD or choroidal neovascularization, increased intraocular pressure that cannot be adequately treated).
3. The member does not have any ocular or periocular infections or active intraocular inflammation.
4. Not used in combination with other intravitreal complement inhibitor therapies (e.g., Izervay)
5. The dose does not exceed 15 mg per eye every 25 days.

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Pegcetacoplan (Syfovre) intravitreal injection is indicated for the treatment of GA secondary to AMD.
- Prior to the intravitreal injection, patients should be monitored for elevated intraocular pressure (IOP). If necessary, ocular hypotensive medication can be given to lower the IOP.
- The recommended dose is 15 mg/0.1 mL administered by intravitreal injection to each affected eye once every 25 to 60 days. Any excess volume from the single-dose vial should be discarded.

Dose Adjustments

- None

Drug Availability

- Injection: 150 mg/mL in a single-dose vial.
- Store in the original carton to protect from light and under refrigeration between 2°C to 8°C (36°F to 46°F).
- Do not use beyond the expiration date or shake the vial.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Ocular or periocular infections
- Active intraocular inflammation

Precautions/Warnings

- **Endophthalmitis and Retinal Detachments:** Intravitreal injections, including those with pegcetacoplan (Syfovre), may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering pegcetacoplan (Syfovre) in order to minimize the risk of endophthalmitis. Aseptic conditions include the use of surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum topical microbicide to disinfect the periocular skin, eyelid, and ocular surface should be administered prior to the injection. Patients

should be instructed to immediately report any symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) following the injection.

- **Neovascular AMD**: In clinical trials, use of pegcetacoplan (Syfovre) was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving pegcetacoplan (Syfovre) should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from the pegcetacoplan (Syfovre) administration.
- **Intraocular inflammation:** In clinical trials, use of pegcetacoplan (Syfovre) was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves patients may resume treatment with pegcetacoplan (Syfovre).
- **Increased Intraocular Pressure:** Acute increase in IOP may occur within minutes of any intravitreal injection, including with pegcetacoplan (Syfovre). Perfusion of the optic nerve head should be monitored following the injection and managed as needed.
- **Retinal Vasculitis and/or Retinal Vascular Occlusion**: Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of pegcetacoplan (Syfovre). Cases may occur with the first dose and may result in severe vision loss. Discontinue treatment with pegcetacoplan (Syfovre) in patients who develop these events. Patients should be instructed to report any change in vision without delay.

BILLING/CODING INFORMATION:

HCPCS Coding

J2781	Injection, pegcetacoplan, intravitreal, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

H35.3113	Advanced atrophic without subfoveal involvement, right eye
H35.3114	Advanced atrophic with subfoveal involvement, right eye
H35.3123	Advanced atrophic without subfoveal involvement, left eye
H35.3124	Advanced atrophic with subfoveal involvement, left eye
H35.3133	Advanced atrophic without subfoveal involvement, bilateral
H35.3134	Advanced atrophic with subfoveal involvement, bilateral

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination

(LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. URL www.clinicalpharmacilogy-ip.com Accessed 8/29/24.
2. DynaMed [database online]. Ipswich, MA: EBSCO Information Services.; 2023. URL http://www.dynamed.com. Accessed 2/23/23.
3. Micromedex Healthcare Series [Internet Database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed 8/29/24.
4. Syfovre (pegcetacoplan) intravitreal injection [package insert]. Apellis Pharmaceuticals, Inc., Waltham (MA): November 2023.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 9/11/24.

GUIDELINE UPDATE INFORMATION:

04/15/23	New Medical Coverage Guideline – Pegcetacoplan (Syfovre) intravitreal injection for the treatment of GA secondary to AMD.
07/01/23	Revision: Added HCPCS code C9151 and deleted code C9399.
10/01/23	Revision: Added HCPCS code J2781 and deleted codes C9151 and J3490.
10/15/24	Review and revision to the guideline consisting of revising the position statement for submission of ophthalmic test documentation for GA secondary to AMD, extending the initial approval to 1 year, not allowing concomitant therapy with other intravitreal complement inhibitors, and adding the warning for retinal vasculitis and retinal vascular occlusion.