To: Retina Specialists
From: Caroline Baumal, MD, CMO <apellismedical@apellis.com>

Subject: **Over 702,000 SYFOVRE® (pegcetacoplan) Injections**

August 14, 2025

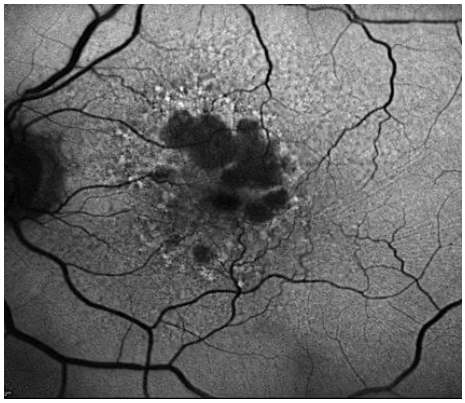
SYFOVRE® (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

SELECT SAFETY INFORMATION
SYFOVRE is contraindicated in patients with ocular or periocular infections, in patients with active intraocular inflammation, and in patients with hypersensitivity to pegcetacoplan or any of the excipients in SYFOVRE. Systemic hypersensitivity reactions (e.g., anaphylaxis, rash, urticaria) have occurred.
Please see additional Important Safety Information below.

Dear Retina Community,

It was great to see many colleagues at ASRS and APRIS 2025. The most recent post-hoc data was presented from OAKS, DERBY and GALE studies, showing continued treatment efficacy of SYFOVRE in GA secondary to AMD compared to sham/projected sham. Highlights from these five podium presentations included:

- 3.16 mm^2 of retinal tissue preserved with SYFOVRE monthly in nonsubfoveal GA (vs. sham/projected sham at 48 months)*
- Earlier SYFOVRE treatment led to more retina tissue preservation compared to the delayed crossover arm (vs. sham/projected sham at 48 months)
- SYFOVRE showed a better treatment response in patients with baseline nonsubfoveal GA vs. subfoveal GA (vs. sham OAKS & DERBY 24 months) when select ocular baseline parameters were compared
- SYFOVRE showed a reduction in ellipsoid zone loss (EZ) vs. sham on OCT using an AI analysis (OAKS & DERBY at 24 months)



Nonsubfoveal, multifocal GA lesion total area measuring 3.634 mm^2

For full presentations, visit Apellis Medical Hub.

*Post-hoc: Retinal tissue preserved is the change from baseline in total area of GA lesion(s) vs. sham/projected sham at month 48 in a post-hoc analysis of study subjects with nonsubfoveal lesions. SYFOVRE every other month preserved 2.7 mm^2 of retinal tissue at month 48 in an identical analysis. Delayed treatment with SYFOVRE (monthly + EOM) in patients with NSF GA [sham observed patients that received no treatment for the first 24 months and then crossed over to active treatment for the second 24 months] preserved 1.11 mm^2 of retinal tissue vs. 3.16 mm^2 in the early treatment group that received 48 months of continuous monthly treatment.

SYFOVRE showed increasing efficacy through 4 years when comparing the first 24 months of SYFOVRE treatment with the second 24 months of SYFOVRE treatment (post-hoc). SYFOVRE offers flexible dosing frequency with as few as 6 injections per year. The recommended dose for SYFOVRE I once every 25 to 60 days. Additionally:

- As of June 30th, 2025,[1,2]
    - **Over 702,000 SYFOVRE intravitreal injections** and **over 118,000 first injections** estimated to have been administered across real world and clinical trials.
    - Retinal vasculitis has been reported following SYFOVRE injection and appears to be a first injection phenomenon with an estimated rate of ~1/4,000 per first injection. Of first injections, the estimated rate of retinal vasculitis resulting in severe vision loss is ~1/8,000.[3]

We remain committed to supporting your treatment decisions with real-world evidence. This body of evidence continues to grow with presentations at major congresses throughout the year. Thank you for your continued collaboration.

ABOUT OAKS AND DERBY

OAKS (n=637) and DERBY (n=621) are Phase 3, multicenter, randomized, double-masked, sham-controlled studies comparing the efficacy and safety of SYFOVRE with sham injections across a broad and heterogenous population of patients with GA secondary to AMD. Treatment with both monthly and every other month SYFOVRE reduced GA lesion growth with increasing treatment effects over time. In all GA patients regardless of lesion location, SYFOVRE reduced GA growth by 18% and 22% monthly, 17% and 18% every other month over 24 months in OAKS and DERBY, respectively. There was no statistically significant difference between SYFOVRE arms and sham pooled on pre-specified visual functional measures at 24 months.

ABOUT GALE

GALE (n=792) is a Phase 3, multicenter, open-label, extension study to evaluate the long-term efficacy and safety of SYFOVRE in patients with GA secondary to AMD. Open-label studies can allow for selection bias. Treatment effect from months 24-48 is compared to a projected sham (rather than an actual sham) that assumes a linear growth rate. This is a prespecified analysis but there is no statistical testing hierarchy. In all GA patients regardless of lesion location, SYFOVRE reduced GA growth by 24% monthly and 23% every other month over 48 months. SYFOVRE reduced GA growth vs. sham by 19% monthly and 18% every other month between months 0 and 24 and reduced GA growth vs. projected sham by 28% monthly and 28% every other month between months 24 and 48 (post-hoc; all $p<0.001$; nominal). SYFOVRE safety evaluated over 4 years with monthly and EOM dosing.

INDICATION

SYFOVRE® (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

SYFOVRE is contraindicated in patients with ocular or periocular infections, in patients with active intraocular inflammation, and in patients with hypersensitivity to pegcetacoplan or any of the excipients in SYFOVRE. Systemic hypersensitivity reactions (e.g., anaphylaxis, rash, urticaria) have occurred.

WARNINGS AND PRECAUTIONS

- **Endophthalmitis and Retinal Detachments**
  - Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
- **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 SYFOVRE. Cases may occur with the first dose of SYFOVRE and may result in severe vision loss. Discontinue treatment with SYFOVRE in patients who develop these events. Patients should be instructed to report any change in vision without delay.
- **Neovascular AMD**
  - In clinical trials, use of 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 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 SYFOVRE administration.
- **Intraocular Inflammation**
  - In clinical trials, use of 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 SYFOVRE.
- **Increased Intraocular Pressure**
  - Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

- Most common adverse reactions (incidence ≥5%) are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage.

Please see full Prescribing Information for more information.

Sincerely,

Caroline Baumal
Chief Medical Officer

1. Data on file as of June 30, 2025, including real world and clinical trial injections.
2. Injections are calculated based on 1) vials distributed to eyecare professional (ECP) practices and 2) estimates of patient numbers extrapolated from licensed data and inventory levels from key accounts, representative of our market.
3. Severe vision loss is defined as ≥ 6 lines lost from baseline. 12 out of 31 eyes with retinal vasculitis resulted in severe vision loss.