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

Subject: Apellis Update to MDs | Over 420,000 SYFOVRE® (pegcetacoplan) injections administered!

November 5, 2024

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

SELECT SAFETY INFORMATION

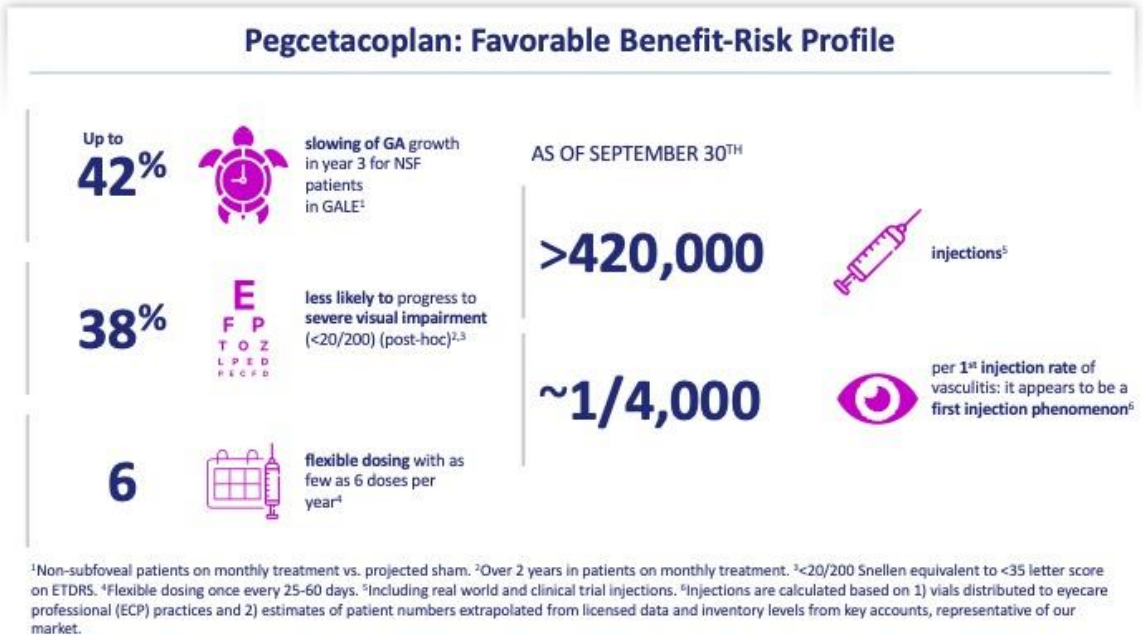
SYFOVRE is contraindicated in patients with ocular or periocular infections, and in patients with active intraocular inflammation.

Please see additional Important Safety Information below.

Dear Retina Community,

It was great to see many of you at the American Academy of Ophthalmology (AAO) Annual Meeting. We hope you had the opportunity to attend our oral presentations, including a late-breaking abstract highlighting SYFOVRE's long-term efficacy. SYFOVRE is the only GA treatment to show increasing efficacy through 3 years with as few as 6 injections per year. Additionally:

- SYFOVRE demonstrated anatomical and functional benefits in the phase 3 GA clinical program.
- SYFOVRE is the only approved GA treatment to include subfoveal and non-subfoveal GA patients in its clinical studies.
- SYFOVRE allows for flexible dosing and preserved ~1 optic disc of tissue in non-subfoveal lesions in a post hoc analysis at Year 3 in GALE.



- As of September 30, 2024,
    - **Over 420,000 SYFOVRE injections** and **over 90,000 first injections** estimated to have been administered across real-world and clinical trials.[1,2]
    - Retinal vasculitis has been reported following SYFOVRE injection and appears to be a first injection phenomenon with a rate of ~1/4,000 per first injection.

We remain committed to supporting your treatment decisions with real-world evidence. This body of evidence continues to grow with data most recently presented at The Retina Society Annual Scientific Meeting. 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 geographic atrophy (GA). 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 21% monthly and 17% every other month over 24 months. There was no statistically significant difference between SYFOVRE arms and sham pooled on pre-specified visual functional measures at 24 months.

A post-hoc time-to-event analysis was conducted for the persistent drop of visual acuity in treated or sham eyes to less than 35 letters (equivalent to 20/200). There was a delay in those events compared with sham in eyes treated with pegcetacoplan monthly (risk reduction of 38% over 2 years vs sham) and in those treated with pegcetacoplan every other month (risk reduction of 12% vs sham).

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 geographic atrophy (GA). Open-label studies can allow for selection bias. Treatment effect from months 24-36 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 25% monthly and 20% every other month over 36 months. The safety profile in the first 12 months of GALE is consistent with OAKS and DERBY.

Patients in the sham crossover group completed sham treatment from Months 0-24 in the Phase 3 OAKS study and received SYFOVRE from Months 24-36. Microperimetry was a key secondary endpoint measured only in the OAKS study, and therefore, patients who crossed over from the OAKS study were included in this analysis.

In a post hoc analysis at Month 36, the mean area of retinal tissue preserved in patients with NSF GA was 2.44 mm^2 with PM and 1.94 mm^2 with PEOM. The 50^{th} percentile for area of the optic disc is 1.95 mm^2.[3]

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, and in patients with active intraocular inflammation

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

Adam Townsend
Chief Operating Officer

1. Data on file as of September 30, 2024, 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. Marta Gonzalez-Hernandez, Daniel Gonzalez-Hernandez, Daniel Perez-Barbudo, Manuel Gonzalez de la Rosa - Optic disc area frequency distribution in a large sample of retinographic images: BMJ Open Ophthalmology 2022;7:e000972.