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.

July 29, 2023

To the Retina Community,

Thank you for being our valued partner as we bring SYFOVRE® (pegcetacoplan injection) 15mg/0.1mL – the first FDA-approved treatment for geographic atrophy (GA) – to patients.

We are writing to share an update on our review of rare events of retinal vasculitis in real-world treatment with SYFOVRE, which we communicated to you last week following our notification to the ASRS Research and Safety in Therapeutics (ReST) Committee. Apellis has been conducting a thorough evaluation following these reported events, including a review of the SYFOVRE manufacturing process and drug product quality and of the safety data from our Phase 3 clinical trials of SYFOVRE. There were no changes in the formulation of the product between Phase 3 clinical trials and commercial supply.

Based on this review, there are no indications of drug product or manufacturing issues that may have contributed to these events, and there were no new safety findings in the clinical trials upon secondary review. Specifically:

- No manufacturing-related issues impacting product quality were identified;
- No quality issues and no contaminants (e.g., endotoxins) were discovered;
- No single manufacturing lot was implicated;
- No indication of drug-related immunogenicity was observed in the clinical trial data;
- Zero events of retinal vasculitis were reported by investigators or identified by an independent reading center in the Phase 3 clinical trials; in addition:
    - Apellis re-reviewed all IOI cases and confirmed no vasculitis events;
    - External retina/uveitis specialists re-reviewed all severe intraocular inflammation (IOI) cases and further confirmed no vasculitis events.

In an update to our communication to you last week, Apellis has confirmed seven total events of retinal vasculitis (4 occlusive and 3 non-occlusive) since launch. Two of these events followed injections in April, two in May, and three in June. Apellis is also evaluating one reported event of retinal vasculitis which the company has not confirmed. The estimated rate of Apellis-confirmed retinal vasculitis events is approximately 0.01% per injection based on clinical trial injections and estimated number of real-world injections derived from the number of vials distributed since launch.

We can only review and confirm cases that have been reported directly to Apellis, and we will continue to submit all reported adverse events to the U.S. Food and Drug Administration (FDA) consistent with reporting guidelines for drug manufacturers. To report suspected adverse reactions, contact Apellis Pharmaceuticals, Inc. at 1-833-866-3346 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

More than 68,000 vials of SYFOVRE have been distributed since approval, including commercial and sample vials delivered to practices. In addition, more than 23,000 SYFOVRE injections have been administered in clinical trials to date.

Patients are central to everything we do and we are committed to ensuring that you and your patients have the information you need to make informed treatment decisions. We look forward to seeing many of

you at the ASRS Annual Meeting, and are happy to connect should you have any questions. At ASRS, we also look forward to sharing seven presentations on SYFOVRE and GA. Including the new 30-month safety and efficacy data of SYFOVRE in patients with GA from the GALE long-term extension study.

We believe that SYFOVRE is an important product for the 1 million patients in the US that are impacted by geographic atrophy, a leading cause of irreversible vision loss.

Thank you again for your partnership as we work to support patients with GA.

Sincerely,

Cedric Francois, MD, PhD
Co-Founder & Chief Executive Officer/President

Caroline Baumal, MD
Chief Medical Officer

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.
- **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.