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October 10, 2023

To the Retina Community,

As part of our commitment to keep you informed, we are writing to provide a SYFOVRE update on long-term and real-world safety and how cases are evaluated and reported.

On October 5, we announced that more than 100,000 commercial and sample vials have been shipped to physician practices since FDA approval, with approximately 37,000 commercial vials and 10,000 samples distributed in the third quarter.

Long-term and real-world safety

- In the GALE study at 30 Months, the safety profile of SYFOVRE continued to be consistent with previously reported Phase 3 data. There were no cases of vasculitis identified in any of the SYFOVRE clinical trials, representing more than 24,000 injections to date.

- The estimated real-world rate of retinal vasculitis remains rare, at 0.01% per injection.
    - In total, there have been 10 confirmed events of retinal vasculitis (seven occlusive, three non-occlusive) and two suspected events.
    - Since the last update on August 22, 2023, there was one new confirmed event that occurred in early August and two new suspected events, one that occurred in mid-August and one in September. Of the two events that were previously classified as suspected, one event has been confirmed and the other was adjudicated to not be retinal vasculitis.
    - Of the confirmed retinal vasculitis events, six patients have recovered vision either fully or partially, three patients have severe vision impairment that is unlikely to be resolved, and one patient's outcome is pending. Visual outcomes in both suspected events are pending.

How are cases evaluated and reported

As shared with Retina Today, Drug Safety and Pharmacovigilance is an integral part of Apellis' process and culture, safeguarding patient safety at all times. Apellis' Safety & Medical Team reviews all post-market events reported with SYFOVRE. Any new suspected events of IOI, including retinal vasculitis, are systematically assessed and adjudicated based on all available information. Where information is missing, targeted follow-up (i.e., specific questionnaire, collection of imaging) is performed by internal Apellis team members. Requested data includes baseline patient characteristics, imaging (angiography,

OCT, fundus photography) and long-term visual outcomes. All suspected retinal vasculitis cases are also independently evaluated and adjudicated by two external sources: a panel of four retina and uveitis experts, and an independent reading center, Digital Angiography Reading Center (DARC).

Apellis submits all reported adverse events to the FDA and other applicable Regulatory Agencies consistent with reporting guidelines and regulations for drug manufacturers. Apellis and the American Society of Retina Specialists (ASRS) Research and Safety in Therapeutics (ReST) Committee are in close communication regarding reported cases of retinal vasculitis following SYFOVRE treatment. While the adjudication of vasculitis may differ between ASRS and Apellis, the visual outcomes are most important, and are monitored closely by both parties.

Patient safety is our top priority. We are committed to making a meaningful difference in the lives of people impacted by geographic atrophy and will continue to provide you with the information you need to make the best treatment decisions for patients.

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.

Best,

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