August 22, 2023

To the Retina Community,

As part of our commitment to keep you informed, we are writing to provide two important updates.

Recommended actions related to the filter needle included in certain injection kits

As part of our comprehensive investigation into the real-world safety events, internal structural variations were identified in the specific 19-gauge x 1½ inch filter needle included in certain injection kits supplied by Apellis. A causal relationship has not been established between the structural variations in this 19-gauge filter needle and the rare events of retinal vasculitis in the real world.

Out of an abundance of caution, we are taking the following voluntary actions:

- We recommend that practitioners immediately discontinue use of, remove from inventory, and dispose of any remaining injection kits that contain the 19-gauge filter needle (specific lot numbers listed at the end of this letter).
- We recommend that practitioners use injection kits with the 18-gauge filter needle, which are already in distribution.
- Apellis is now exclusively distributing injection kits with the 18-gauge filter needle.
- If you do not have an injection kit with the 18-gauge filter needle, you may request a new kit at no cost by emailing info@apellis.com or contacting your Apellis Territory Business Manager.

We have communicated this course of action to the FDA.

Update on rare events of retinal vasculitis

We wanted to provide an update on the rare events of retinal vasculitis with real world use of SYFOVRE® (pegcetacoplan injection). The estimated rate of retinal vasculitis has remained consistent at approximately 0.01% per injection with SYFOVRE in the real-world based on the number of vials distributed for commercial use and for administration in clinical trials.

- Over 100,000 SYFOVRE vials have been distributed in the real-world and for administration in clinical trials. This includes:
    - Over 78,000 vials distributed since launch, including commercial vials shipped and sample vials distributed to physician practices. Over 26,000 vials distributed in the third quarter to date
    - Approximately 24,000 SYFOVRE injections administered in clinical trials to date.
- In total, eight events of retinal vasculitis (five occlusive, three non-occlusive) have been confirmed. The last confirmed event of retinal vasculitis occurred on June 20, based on a review of adverse events reported to the Company.
    - This includes one additional event of occlusive vasculitis, which occurred in May, and was reported after our last communication on July 29.
    - Two of the patients had their SYFOVRE injection in April, three in May, and three in June.

- All events of retinal vasculitis were observed after the first injection of SYFOVRE.
- One patient remained stable at baseline vision, two patients have recovered vision nearly back to baseline, two patients have severe vision impairment which is unlikely to be resolved, and three patients' outcomes are still pending.

- There are two events of suspected retinal vasculitis. As previously disclosed, there was one event that occurred in May and the patient's vision has returned to baseline. The other event occurred in August and the patient's outcome is pending. Neither event has been confirmed.

All post-marketing adverse events reported to the company, including events of retinal vasculitis, are reviewed by Apellis' Medical and Safety Committee. Any suspected events of vasculitis are also evaluated by external retina/uveitis specialists for adjudication.

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.

Best,

Caroline Baumal, MD	Tuan Dong Si
Chief Medical Officer	Senior Vice President, Global Drug Safety & Pharmacovigilance

Lot numbers of injection kits with a 19-gauge x 1½ filter needle

223186	**230036**	**230056**	**230236**	**230316**
230326	**230336**	**230406**	**231926**	**231946**
231956	**231986**			

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.