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Refusal of the marketing authorisation for Syfovre (*pegcetacoplan*)

Re-examination confirms refusal

The company that applied for marketing authorisation, Apellis Europe B.V., had requested re-examination of EMA's initial opinion of 27 June 2024 recommending the refusal of the marketing authorisation for Syfovre, a medicine intended for the treatment of geographic atrophy caused by age-related macular degeneration (AMD).

After re-examining its initial opinion, the European Medicines Agency issued its final opinion on 19 September 2024 in which it confirmed its recommendation to refuse marketing authorisation for Syfovre.

What is Syfovre and what was it intended to be used for?

Syfovre was developed as a medicine to treat adults with geographic atrophy, an advanced form of AMD. AMD is a disease that affects the central part of the retina (called the macula) at the back of the eye. In patients with geographic atrophy, lesions (areas of cell death) develop in the retina and macula, leading to loss of vision. Syfovre contains the active substance pegcetacoplan and was to be available as a solution to be injected into the eye.

How does Syfovre work?

The complement system is a set of proteins that is part of the immune system (the body's natural defences). In people with geographic atrophy, the complement system is overactive, causing inflammation and cell death. The active substance in Syfovre, pegcetacoplan, attaches to and blocks the C3 protein of the complement system. By blocking C3, pegcetacoplan prevents activation of the complement system. This slows down the growth of geographic atrophy lesions.

What did the company present to support its application?

The company presented results from two main studies involving a total of 1,258 adults with geographic atrophy caused by AMD. The studies lasted 24 months and compared Syfovre injections into the eye with a sham procedure where no actual injection was given. The main measure of effectiveness was the change in the size of geographic atrophy lesions in the eye after 12 months.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

What were the main reasons for refusing the marketing authorisation?

At the time of the initial evaluation, although the studies showed that Syfovre slowed the growth of geographic atrophy lesions, the Agency considered that this did not lead to clinically meaningful benefits for patients. It was noted that benefits of a treatment should have an impact on patients' everyday functioning, and this was not demonstrated in the studies. In terms of safety, regular injections into the eye carry a significant risk of adverse events, including the development of other forms of AMD or inflammation in the eye, which could further worsen vision.

These concerns did not change after re-examination of the data provided and consideration of information shared by patients and healthcare professional organisations (so-called third-party interventions). Although the Agency recognises the unmet medical need for effective treatment for people with geographic atrophy caused by AMD, its opinion remained that the magnitude of Syfovre's effectiveness did not outweigh the potential risks. The Agency therefore concluded that a positive balance of the medicine's benefits and risks could not be established in the treatment of geographic atrophy caused by AMD.

Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials with Syfovre.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.