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Update as of 11 July 2024:

The company for Syfovre has requested a re-examination of EMA's June 2024 opinion. Upon receipt of the grounds of this request, the Agency will re-examine its opinion and issue a final recommendation.

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

The European Medicines Agency has recommended the refusal of the marketing authorisation for Syfovre, a medicine intended for the treatment of geographic atrophy caused by age-related macular degeneration (AMD). AMD is a disease that affects the central part of the retina (called the macula) at the back of the eye. Geographic atrophy is an advanced form of AMD in which lesions (areas of cell death) form in the retina and macula, leading to loss of vision.

The Agency issued its opinion on 27 June 2024. The company that applied for authorisation, Apellis Europe B.V., may ask for re-examination of the opinion within 15 days of receiving the opinion.

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. 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

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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.

What were the main reasons for refusing the marketing authorisation?

Although the studies showed that Syfovre slowed the growth of geographic atrophy lesions, this did not lead to clinically meaningful benefits for patients. It was noted that benefits of a treatment should impact 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, that could further worsen vision. Therefore, the Agency's opinion was that a positive balance of benefits and risks of Syfovre in the treatment of geographic atrophy caused by AMD could not be established and it recommended refusing marketing authorisation.

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.