24 February 2022
EMA/120074/2022EMA/120074/2022
EMEA/H/C/005433

Refusal of the marketing authorisation for Ipique (bevacizumab)

Re-examination confirms refusal

After re-examining its initial opinion, the European Medicines Agency has confirmed its recommendation to refuse marketing authorisation for the medicine Ipique. The medicine was intended for the treatment of neovascular (wet) age-related macular degeneration (AMD).

The Agency issued its opinion after re-examination on 24 February 2022. The Agency had issued its initial opinion on 11 November 2021. The company that applied for authorisation of Ipique is Rotterdam Biologics B.V.

What is Ipique and what was it intended for?

Ipique was intended for use in adults to treat the 'wet' form of AMD, a disease which affects the central part of the retina (called the macula) at the back of the eye. The wet form of AMD is caused by choroidal neovascularisation (abnormal growth of blood vessels under the macula), which may leak fluid and blood and cause swelling.

Ipique contains the active substance bevacizumab and was to be available as a solution for intravitreal injection (injection into the vitreous humour, the jelly-like fluid inside the eye).

Bevacizumab is already authorised in the EU for the treatment of certain types of cancer in adults; it has also been used off-label to treat AMD.

How does Ipique work?

The active substance in Ipique, bevacizumab, is a monoclonal antibody (a type of protein) that has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, bevacizumab was expected to block its activity and slow down the growth of blood vessels in the eye, reducing fluid leakage and swelling.

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What did the company present to support its application?

As authorised bevacizumab medicines have been used off-label to treat the condition, the company presented data from a recent literature analysis of 10 studies involving 3,224 patients with AMD. The studies compared intravitreal injection (injection into the eye) of other medicines containing bevacizumab with either ranibizumab (a medicine to treat AMD), other standard treatment for AMD or placebo (a dummy treatment). The main measure of effectiveness was the proportion of people in whom vision improved (defined as gaining at least 15 letters in a standard eye test) after the first year of treatment.

What were the main reasons for refusing the marketing authorisation?

At the time of the initial evaluation, the Agency was concerned that the literature review was only based on data obtained with other bevacizumab-containing medicines and that no evidence had been submitted comparing Ipique with another bevacizumab medicine when used intravitreally. Therefore, the Agency was not able to draw conclusions on whether known or unknown differences between Ipique and these medicines might affect the effectiveness and safety of Ipique when used to treat AMD.

These concerns did not change after re-examination of the data provided, and the Agency's opinion therefore remained that the safety and effectiveness of Ipique had not been properly demonstrated. The Agency therefore considered that the risks of Ipique outweighed its benefits and it recommended refusing marketing authorisation.

Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no ongoing clinical trials with Ipique in the EU.