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Update as of 22 July 2021:

The applicant for Flynpovi has requested a re-examination of EMA's June 2021 opinion. Upon receipt of the grounds of the request, the Agency will re-examine its opinion and issue a final recommendation.

25 June 2021

Refusal of the marketing authorisation for Flynpovi (eflornithine / sulindac)

The European Medicines Agency has recommended the refusal of the marketing authorisation for Flynpovi, a medicine intended for the treatment of familial adenomatous polyposis.

The Agency issued its opinion on 24 June. The company that applied for authorisation, Cancer Prevention Pharma (Ireland) Limited, may ask for re-examination of the opinion within 15 days of receiving the opinion.

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

Flynpovi was developed as a medicine to treat adults with familial adenomatous polyposis (FAP), a hereditary disease in which numerous polyps (growths) form in the gut, first in the large intestine and later in the small intestine. It was to be used in addition to standard of care, including regular endoscopy checks, to delay major surgery in patients who have an intact colon or rectum (lower parts of the gut), or an ileo-anal pouch (connection between the final section of the small intestine, the ileum, and the anus).

Flynpovi contains the active substances eflornithine and sulindac and was to be available as tablets.

Flynpovi was designated an 'orphan medicine' (a medicine used in rare diseases) on 24 January 2013 for the treatment of FAP. Further information on the orphan designation can be found on the Agency's website: ema.europa.eu/medicines/human/orphan-designations/eu3121086.

How does Flynpovi work?

Flynpovi is made up of two substances, eflornithine and sulindac.

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Eflornithine works by blocking the action of an enzyme called ornithine decarboxylase, which is involved in the production of substances called polyamines that are required for cells to grow. In patients with FAP, ornithine decarboxylase is overactivated, leading to an overproduction of polyamines which has been linked with the rapid growth of polyp cells. By blocking the enzyme, eflornithine was expected to slow down the polyps' growth.

Sulindac works by activating an enzyme called SSAT that expels polyamines from intestinal cells. This was expected to reduce the levels of polyamine in the intestine, thereby reducing polyp cells' growth and improving the symptoms of the disease.

The combination of the two substances was expected to have an additive effect, slowing down the growth of the polyps more than either substance alone.

What did the company present to support its application?

The company provided results from a main study in 171 patients with FAP who received either Flynpovi or one of its active substances, eflornithine or sulindac, on their own. The main measure of effectiveness was the time before the first occurrence of any FAP-related event, such as need for surgery, progression to more advanced polyps, development of cancer or death.

What were the main reasons for refusing the marketing authorisation?

In terms of effectiveness, the study failed to show that Flynpovi delays the occurrence of a first FAP-related event compared to each of Flynpovi's active substances (eflornithine and sulindac) when used on their own. The CHMP noted that Flynpovi was not compared to standard of care or placebo (a dummy treatment) and that neither eflornithine nor sulindac alone have previously shown clear benefits in treating this condition. The CHMP also considered that no sufficient data were provided on the long-term safety of Flynpovi, given that the medicine is intended as a life-long treatment. In addition, the company did not provide sufficient data to demonstrate that Flynpovi is not genotoxic (meaning it cannot damage the genetic materials in the cells).

Therefore, the Agency's opinion was that the benefits of Flynpovi did not outweigh its risks 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 Flynpovi.