11 November 2021
EMA/627715/2021
EMEA/H/C/005043

Withdrawal of application for the marketing authorisation of Flynpovi (eflornithine / sulindac)

Cancer Prevention Pharma (Ireland) Limited withdrew its application for a marketing authorisation of Flynpovi for the treatment of familial adenomatous polyposis.

The company withdrew the application on 12 October 2021.

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 (surgical 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.

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.

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

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 the growth of polyp cells 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.

How far into the evaluation was the application when it was withdrawn?

The evaluation had finished and the European Medicines Agency had recommended refusing marketing authorisation. The company had requested a re-examination of the Agency's recommendation, but it withdrew the application before this re-examination had finished.

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had recommended refusing marketing authorisation for Flynpovi for the treatment of familial adenomatous polyposis.

The Agency considered that, 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 Agency 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. Data on the long-term safety of Flynpovi were considered insufficient, 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).

At the time of the withdrawal, while the re-examination was ongoing, the Agency was still of the opinion that the benefits of Flynpovi did not outweigh its risks and it recommended refusing marketing authorisation.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of the application, the company stated that it withdrew its application due to the identification of pre-clinical and clinical issues and the fact that the Agency considered that the data provided did not allow to conclude on a positive benefit-risk balance.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no ongoing clinical trials with Flynpovi.