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Withdrawal of application for the marketing authorisation of Neffy (adrenaline)

ARS Pharmaceuticals IRL, Limited withdrew its application for a marketing authorisation of Neffy for the emergency treatment of allergic reactions, including anaphylaxis.

The company withdrew the application on 4 April 2022.

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

Neffy was developed as a medicine to be taken intranasally (through the nose) for the emergency treatment of allergic reactions, including anaphylactic reactions (a sudden, severe allergic reaction with breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating and loss of consciousness).

Neffy contains the active substance adrenaline and was to be available as a nasal spray.

How does Neffy work?

When given intranasally, the active substance in Neffy, adrenaline, is absorbed by the nasal mucosa (the moist lining of the nose) and distributed through the body. Adrenaline then binds to different receptors (targets) in the body to decrease the anaphylactic reaction. Binding to these receptors lessens the widening of blood vessels to improve blood flow and relaxes the smooth muscles in the lungs to make it easier to breathe. Adrenaline also binds to receptors on cells of the immune system to stop the release of histamine (a substance in the body that causes allergic symptoms).

What did the company present to support its application?

For both ethical and practical reasons, it was considered infeasible to conduct studies on Neffy's effectiveness in people experiencing a severe allergic reaction, but there is extensive information available about the use of adrenaline to treat severe allergy and it is currently the standard treatment for anaphylaxis. The company therefore provided results of four clinical studies that compared Neffy with products where the active substance was injected, which looked at pharmacokinetics (how a medicine is absorbed, modified and removed from the body), as well as blood pressure and heart rate as indicators of the medicine's effectiveness in almost 700 healthy people aged 18 to 55 years.

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How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and prepared the first list of questions for the company. The company had not responded to the questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the available information, at the time of the withdrawal, the Agency had concerns and its provisional opinion was that without additional studies Neffy could not have been authorised for the emergency treatment of allergic reactions, including anaphylaxis.

The Agency considered that the company had not provided sufficient evidence that the medicine absorption in the nasal mucosa of patients with acute anaphylaxis is comparable with that seen in healthy volunteers and that the proposed dose could achieve the expected clinical outcome. In addition, the Agency was concerned about the inclusion of antimicrobial preservatives and antioxidants in the medicine and considered that it should be reformulated to remove these substances.

Therefore, at the time of the withdrawal, the Agency was not able to draw conclusions on the effectiveness of Neffy in treating allergic reactions and its opinion was that the benefits of Neffy in this use did not outweigh its risks.

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 they withdrew their application following EMA's request for additional information and data. The company has indicated an intent to submit a new application that addresses the requests.

Does this withdrawal affect patients in clinical trials?

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

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