European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE MARKETING APPLICATION
for
AFLUNOV
Common name: ***Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) (A/VietNam/1194/2004)***

On 13 June 2008, Novartis Vaccines and Diagnostics S.r.l. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Aflunov, for the prophylaxis of H5N1 avian influenza in adults and the elderly.

What is Aflunov?
Aflunov is a vaccine. It consists of a suspension for injection that contains some parts (outer membranes) of the influenza (flu) virus strain called A/VietNam/1194/2004.

What was Aflunov expected to be used for?
Aflunov was expected to be used in adults and the elderly to protect against flu caused by the H5N1 strain (type) of the influenza A virus.
Aflunov is a 'prepandemic' vaccine. This is a special type of vaccine that is intended to protect against a strain of flu that may cause a future pandemic. A flu pandemic happens when a new strain of flu virus appears that can spread easily from person to person because people have no immunity (protection) against it. A pandemic can affect most countries and regions around the world. Health experts are concerned that the next flu pandemic could be caused by the H5N1 strain of the virus. Aflunov was expected to provide protection against this strain, so that it could be used before or during a flu pandemic.

How is Aflunov expected to work?
Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. When a person is given the vaccine, the immune system recognises the parts of the flu virus it contains as 'foreign' and makes antibodies against them. The immune system will be able to produce antibodies more quickly when it is exposed to flu virus of the same strain. This helps to protect against the disease.
Aflunov contains small parts of the H5N1 strain of the flu virus. The virus used in the vaccine was first inactivated (killed) so that it does not cause any disease. Then, the outer membranes that contain the 'surface antigens' (proteins on the outer membrane of the virus that the body recognises as foreign) were extracted and purified before being included in the vaccine. Aflunov also contains an 'adjuvant' (a compound containing oil), which is expected to stimulate a better response.

What documentation did the company present to support its application to the CHMP?
The effects of Aflunov were first tested in experimental models before being studied in humans.
The main clinical study of Aflunov involved over 4,000 adults. It compared Aflunov's safety and its ability to stimulate the production of antibodies ('immunogenicity') with those of a similar vaccine against seasonal flu. The comparator vaccine contained different strains of seasonal flu virus, but the rest of the components were the same as in Aflunov.

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How far into the evaluation was the application when it was withdrawn?
The application was at day 190 when the company withdrew. After the CHMP had assessed the responses from the company to a list of questions, there were still some unresolved issues outstanding. The CHMP normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the CHMP reviews them and may, before giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around two months for the European Commission to grant a licence.

What was the recommendation of the CHMP at that time?
Based on the review of the data and the company's response to the CHMP list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Aflunov could not have been approved for the prophylaxis of H5N1 avian influenza.

What were the main concerns of the CHMP?
The CHMP was concerned over the way the main clinical study was carried out. An inspection of some of the study sites showed that the study had not been conducted in compliance with 'good clinical practice' (GCP). Consequently, the study results could not be considered reliable and could not be used for the evaluation of the vaccine. As a result, the size of the clinical database for the assessment of the vaccine's safety was not sufficient to fulfil the requirements of the EMEA's guidelines on prepandemic vaccines.
Therefore, at the time of the withdrawal, the CHMP could not conclude on the benefit-risk balance of Aflunov.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials with Aflunov?
The company informed the CHMP that there are no consequences for individuals currently included in clinical trials with Aflunov. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.