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Questions and answers

Withdrawal of the marketing authorisation application for Heplisav (hepatitis B (rDNA) vaccine, adjuvanted)

On 10 February 2014, Dynavax International B.V. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Heplisav, for the prevention of hepatitis B infection.

What is Heplisav?

Heplisav is a vaccine which contains hepatitis B surface antigen, a protein from the outer coat of the hepatitis B virus. It was to be available as a solution for injection.

What was Heplisav expected to be used for?

Heplisav was expected to be used to protect against hepatitis B infection in adults.

How is Heplisav expected to work?

Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. Heplisav contains hepatitis B surface antigen (a protein from the outer coat of the hepatitis B virus). When a person is given the vaccine, the immune system recognises the viral protein as 'foreign' and makes antibodies against it. The immune system will then be able to produce antibodies more quickly when it is exposed to the virus again. This may help to protect against disease caused by the hepatitis B virus.

The hepatitis B surface antigen is produced by a method known as 'recombinant DNA technology': it is made by yeast cells into which a gene (DNA) has been introduced that makes them able to produce the protein. The vaccine contains an 'adjuvant' to enhance the immune response.

What did the company present to support its application?

The company presented the results of three main studies involving over 4,000 subjects who had never had hepatitis B or been vaccinated against it; two studies involved healthy subjects and one involved patients with long-term kidney disease. In all three studies, Heplisav was compared with another hepatitis B vaccine, Engerix-B. The main measure of effectiveness was the percentage of patients who produced protective levels of antibodies against the hepatitis B virus after a course of vaccinations.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after that the CHMP had evaluated the documentation provided by the company and formulated lists of questions. The company had not yet responded to the last round of questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

Based on the review of the data, at the time of the withdrawal, the CHMP had had some concerns and was of the provisional opinion that Heplisav could not have been approved for the prevention of hepatitis B.

The Committee considered that the way in which the study in patients with kidney disease had been carried out and documented was not satisfactory. This followed an inspection of some of the sites involved in the study, to ensure proper standards for medicines studies (Good Clinical Practice) had been followed. The nature of the findings from the inspection also raised questions about the other main studies. Therefore, there were serious uncertainties at that point about the reliability of the data submitted in support of the application. Furthermore, the number of patients in whom the safety of the medicine had been tested was insufficient to rule out an unacceptable level of risk for less common but serious side effects.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the medicine could not have been approved based on the data presented by the company.

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 was withdrawing the application since it would not be possible to provide the additional safety data needed within the timetable required by the procedure.

The withdrawal letter is available [here](#).

What consequences does this withdrawal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are no ongoing clinical trials or compassionate use programmes with Heplisav in the EU.