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Withdrawal of application to change the marketing authorisation for Cervarix (human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed))

GlaxoSmithKline Biologicals SA withdrew its application to use Cervarix in individuals from the age of nine years for the prevention of head and neck cancers that are caused by certain types of human papillomavirus (HPV).

The company withdrew the application on 22 October 2021.

What is Cervarix and what is it used for?

Cervarix is a vaccine that is used from the age of nine years to protect against the following conditions caused by certain types of HPV:

- cancer of the cervix (neck of the womb) or anus;
- precancerous lesions (abnormal cell growth) in the genital area (cervix, vulva, vagina or anus).

It is a suspension for injection that contains proteins for two types of HPV (16 and 18) and is available in vials or prefilled syringes.

Cervarix has been authorised in the EU since September 2007. Further information on Cervarix's current uses can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/cervarix.

What change had the company applied for?

The company applied to extend the use of Cervarix in individuals from the age of nine years to include protection against head and neck cancers that are related to HPV infection. These cancers share important features with HPV-related cancer of the cervix, including onset of disease at a young age and the types of HPV involved.

How does Cervarix work?

Papillomaviruses are viruses that cause warts and abnormal tissue growth. There are more than 100 types of papillomavirus, some of which are associated with genital and anal cancers, as well as head

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and neck cancers, particularly cancers of the mouth and throat. The most common HPV types involved in these cancers are types 16 and 18. All HPV types have a shell or 'capsid', which is made up of distinctive proteins called 'L1 proteins'.

Cervarix contains purified L1 proteins for HPV types 16 and 18. When a person is given the vaccine, the body's immune system makes antibodies against the L1 proteins. If, later on, the person comes into contact with HPV virus, their immune system will recognise it and be ready to defend the body against it. This will help to protect against the diseases caused by these viruses.

In the prevention of head and neck cancer, Cervarix was expected to work in the same way as it does in its existing indication.

What did the company present to support its application?

The company presented the results of a main study which looked at the effectiveness of Cervarix in preventing HPV infection in the mouth and throat. The results were based on 4,871 girls aged between 12 and 15 years who received either Cervarix or a comparator vaccine that is not active against HPV (in this case, a vaccine against hepatitis B virus). Effectiveness was measured by testing saliva samples for DNA (genetic material) of the HPV virus.

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

The application was withdrawn after the European Medicines Agency had evaluated the initial information from the company and had prepared 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 Cervarix could not have been authorised for the prevention of head and neck cancers. In particular, the Agency had concerns about the design of the main study. The Agency noted that the way prevention of persistent HPV infection in the mouth and throat was measured was not adequate as testing was only done once and not repeated over time. In addition, the results were not statistically meaningful.

Therefore, at the time of the withdrawal, the Agency was not able to draw conclusions on the effectiveness of Cervarix in preventing head and neck cancers related to HPV infection and its opinion was that the benefits of Cervarix 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 application, the company stated that the withdrawal is based on the fact that the available data were not considered sufficient to conclude on a positive risk-benefit balance for the proposed indication.

Does this withdrawal affect patients in clinical trials?

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

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