05 December 2014
EMA/502465/2014
Human Medicines Research and Development Support Division

Public summary of the evaluation of the proposed product-specific waiver

Purified adenylate cyclase recombinant protein carrying subfragments of the early protein E7 antigen from human papillomavirus strain 16 (recombinant CyaA-HPV16E7) / purified adenylate cyclase recombinant protein carrying subfragments of the early protein E7 antigen from human papillomavirus strain 18 (recombinant CyaA-HPV18E7)

On 10 October 2014, the Paediatric Committee of the European Medicines Agency agreed a product-specific waiver* for recombinant CyaA-HPV18E7 / recombinant CyaA-HPV16E7 for the treatment of human papillomavirus (HPV) 16 and/or 18 infection (EMEA-001651-PIP01-14).

What is recombinant CyaA-HPV18E7 / recombinant CyaA-HPV16E7, and how is it expected to work?

Recombinant CyaA-HPV18E7 / recombinant CyaA-HPV16E7 is not authorised in the European Union. Studies in adults are currently on-going. This medicine is proposed in adults for the treatment of HPV 16 and/or 18 infection in adult women with no high-grade cervical lesion, co-administered with imiquimod cream.

Human 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 cancers - HPV types 16 and 18 cause approximately 70% of cervical cancers.

Recombinant CyaA-HPV18E7 / recombinant CyaA-HPV16E7 is an immune stimulator (a “therapeutic vaccine”) containing fragments of a protein produced by HPV16 and HPV18 in infected cells. “Vaccination” with recombinant CyaA-HPV18E7 / recombinant CyaA-HPV16E7 is expected to enhance a woman’s immune response to HPV16 and/or HPV18-infected cells. This may result in the woman clearing an existing HPV16 and/or HPV18-infection and thereby prevent the progression of a persistent HPV infection to cervical cancer, which may occur in some HPV-infected women over the years.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

What was the proposal from the applicant?

For children, the applicant proposed:

Not to do any study in children (from birth to less than 18 years of age), because in children and adolescents most HPV16 and/or HPV18 infections are asymptomatic and clear on their own, and because therefore diagnosis of HPV infection is not routinely performed in women below their mid-twenties/early-thirties. Therefore, the applicant requested an exemption (waiver*) from the obligation to study the medicine in any children, in the condition(s) Treatment of HPV 16 and/or 18 infection.

Is there a need to treat children affected by HPV16 and/or HPV18 infection?

Taking into account the proposed indication in adults, and the characteristics of the medicine, the Paediatric Committee considered that this medicine is not of potential use in the paediatric population for the treatment of HPV16 and/or HPV18 infection. In childhood/adolescence HPV16 and/or HPV18 infections are asymptomatic, most clear on their own and are of little long-term clinical significance. Hence, in childhood/adolescence these infections are generally not screened for and do not require treatment.

What did the Paediatric Committee conclude on the potential use of this medicine in children?

The Committee agreed with the request of the applicant to be exempt from performing studies in children from birth to less than 18 years of age, because the medicinal product does not seem to have a potential significant benefit for the treatment of HPV16 and HPV18 infection in childhood/adolescence.

What happens next?

The applicant has now received the EMA Decision* on this medicine. The Decision itself is necessary for the applicant to request in the future a marketing authorisation* for this medicine in adults.

The PDCO emphasises that the granting of a waiver for the condition mentioned above should not prevent the applicant from considering a development in the paediatric population in indications where there is a paediatric need.

*Definitions:

Applicant	The pharmaceutical company or person proposing the Paediatric Investigation Plan or requesting the Product-Specific Waiver
Children	All children, from birth to the day of the 18th birthday.
Paediatric investigation plan (PIP)	Set of studies and measures, usually including clinical studies in children, to evaluate the benefits and the risks of the use of a medicine in children, for a given disease or condition. A PIP may include "partial" waivers (for example, for younger children) and/or a deferral (see below).
Waiver	An exemption from conducting studies in children, for a given disease or condition. This can be granted for all children (product-specific waiver), or in specific subsets (partial waiver): for example, in boys or in children below a given age.
Deferral	The possibility to request marketing authorisation for the use of the medicine in adults, before completing one or more of the studies /measures included in a PIP. The Paediatric Committee may grant a deferral to avoid a delay in the availability of the medicine for adults.
Opinion	The result of the evaluation by the Paediatric Committee of the European Medicines Agency. The opinion may grant a product-specific waiver, or agree a PIP.
Decision	The legal act issued by the European Medicines Agency, which puts into effect the Opinion of the Paediatric Committee.
Pharmaceutical form	The physical aspect of the medicine (the form in which it is presented), for example: a tablet, capsule, powder, solution for injection, etc. A medicine can have more than one pharmaceutical form.
Placebo	A substance that has no therapeutic effect, used as a control in testing new drugs.
Active control	A medicine with therapeutic effect, used as a control in testing new drugs.
Historical control	A group of patients with the same disease, treated in the past and used in a comparison with the patients treated with the new drug.
Route of administration	How a medicine is given to the patient. For example: for oral use, for intramuscular use, for intravenous use, etc. The same medicine, or the same pharmaceutical form, may be given through more than one route of administration.
Patent	A form of protection of intellectual property rights. If a medicinal product is protected by a patent, the patent holder has the sole right to make, use, and sell the product, for a limited period. In certain circumstances, a patent for a medicinal product may be extended for a variable period by a Supplementary Protection Certificate.
Marketing Authorisation	When a Marketing Authorisation is granted, the pharmaceutical company may start selling the medicine in the relevant country (in the whole European Union, if the procedure was a centralised one).