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Public summary of the evaluation of the proposed paediatric investigation plan

Cholera vaccine, live attenuated, oral (strain CVD 103-HgR) for prevention of disease caused by V. cholerae serogroup O1

On 12 September 2014 the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for cholera vaccine, live attenuated, oral (strain CVD 103-HgR) for the prevention of disease caused by V. cholerae serogroup O1 (EMEA-001490-PIP01-13).

What is cholera vaccine, live attenuated, oral (strain CVD 103-HgR), and how is it expected to work?

Cholera vaccine, live attenuated, oral (strain CVD 103-HgR) is not authorised in the European Union. Studies in adults are currently on-going. This medicine is proposed in adults for the prophylaxis of disease caused by V. cholerae serogroup O1.

This medicine is expected to prevent cholera in adults and children from 6 months of age who will be visiting areas where cholera is common.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in healthy children from 2 years to less than 18 years of age in a paediatric investigation plan*. The future indication proposed for children is: active immunisation against disease caused by V. cholerae serogroup O1 in children aged 2 years old or older who will be visiting cholera endemic or epidemic areas. The plan includes the development of a specific pharmaceutical form to be used in children* age-appropriate oral liquid dosage form for children from 6 months to less than 2 years of age. It also includes a proposal to show efficacy and safety of the medicine in clinical studies.

The applicant proposed a deferral* for the development of a specific pharmaceutical form to be used in children and for paediatric clinical studies.

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

Is there a need to prevent disease caused by V. cholerae serogroup O1 in children?

Taking into account the proposed indication in adults, and the characteristics of the medicine, the Paediatric Committee considered this medicine of potential use for the prevention of disease caused by V. cholerae serogroup O1. This condition occurs also in children. The vaccine's rapid onset of protection in 7 days after a single administration makes it beneficial for individuals preparing to travel to areas where cholera is common.

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. However, it was considered that a lower age range, from birth to less than 6 months of age, should be exempt because the Committee concluded that this medicinal product is likely to be not effective in this age group.

At present, some treatments are available for the prevention of disease caused by V. cholerae in children in the European Union, such as Dukoral that is authorised. However, cholera vaccine, live attenuated, oral (strain CVD 103-HgR) has a rapid onset of protection in 7 days after a single administration. Therefore, the Committee considered that new data are required to decide whether the use of this medicine will bring a benefit to healthy children from 6 months to less than 18 years of age who will be visiting areas where cholera is common, and to understand any potential risks.

The Committee considered that there is also a need to develop a specific pharmaceutical form* of this medicine, which would allow to use the medicine safely and accurately in young children, and whose composition* must only include components that are known to be safe in children.

Because there is a need for more medicines for the prevention of disease caused by V. cholerae serogroup O1 in children, and this medicine has a potential interest for children, the Committee considered that clinical studies were necessary.

The Committee considered that it is more prudent to confirm that the medicine is effective and safe in adults, before starting the paediatric studies.

The Committee agreed with the request of the applicant that the development of a specific pharmaceutical form to be used in children and paediatric clinical studies should be deferred to avoid a delay in the availability of the medicine for adults.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- Studies are not necessary in children from birth to less than 6 months of age because this medicinal product is likely to be not effective in this age group.
- A pharmaceutical form* such as age-appropriate oral liquid dosage form is needed for children from 6 months to less than 2 years of age. An age-appropriate oral liquid dosage form will be developed by the applicant.
- It is necessary to study if the medicine is efficacious to prevent the disease in children. This will be done in 2 studies comparing the medicine to historical control*.
- It is necessary to study the potential side effects of the medicine, to prevent them or to reduce the consequences if they occur.

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 and in children.

The Decision* on the agreed Paediatric Investigation Plan means that the applicant is bound to perform the studies and trials with children in the next months or years. In case of difficulties, or a change in current knowledge or availability of new data, the applicant may request changes to the plan at a later stage. This can be done through a modification of the PIP.

The agreed completion of all the studies and trials included in the Paediatric Investigation Plan is March 2017.

Trials in the Paediatric Investigation Plan will be listed in the public EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/) as soon as they have been authorised to be started, and their results will have to be listed in the register within 6 months after they have completed.

The results of the studies conducted in accordance with the agreed Paediatric Investigation Plan will be assessed, and any relevant information will be included in the Product Information (summary of product characteristics, package leaflet). If the medicine proves to be efficacious and safe to use in children, it can be authorised for paediatric use, with appropriate recommendations on the dose and on necessary precautions. The product information will also describe which adverse effects are expected with the medicine, and wherever possible, how to prevent or reduce these effects.

*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).