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Public summary of the evaluation of a proposed paediatric investigation plan

Norovirus GI.1 and GII.4 virus-like particle antigens for the prevention of acute norovirus gastroenteritis

On 17 April 2015, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for norovirus GI.1 virus-like particle antigen / norovirus GII.4 virus-like particle antigen [hereafter abbreviated as norovirus vaccine] for the prevention of acute norovirus gastroenteritis (EMEA-001609-PIP01-14).

What is Norovirus vaccine, and how is it expected to work?

Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against a disease. All noroviruses have a shell called 'capsid'. Norovirus vaccine contains purified capsid proteins from norovirus genotypes GI.1 and GII.4. The proteins are assembled in 'virus-like particles' (structures that look like norovirus, so that the body can recognise them easily, but that do not contain live norovirus and are not infectious).

When a patient is given the vaccine, the immune system recognises the virus-like particles as 'foreign' and makes antibodies against them. In vaccinated people, the immune system is able to produce antibodies more quickly when it is exposed to norovirus. This is expected to help protect against the disease caused by this virus.

Norovirus vaccine is not authorised in the European Union. Studies in adults are currently on-going. This medicine is proposed for the active immunisation to prevent norovirus gastroenteritis.

What was the proposal from the applicant?

The applicant proposed to study the medicine in children from 6 weeks to less than 18 years of age in a paediatric investigation plan*. The future indication proposed for children is: active immunisation to prevent norovirus gastroenteritis. The plan includes the development of a specific strength/composition of the pharmaceutical form (suspension for injection) to be used in children*.

It also includes a proposal to demonstrate safety, immunogenicity (the ability of the vaccine to induce a response from the immune system) and efficacy (the ability of the vaccine to protect from the disease) of the vaccine in non-clinical and clinical studies.

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The applicant proposed a deferral* for the clinical studies in children below 9 years of age.

Is there a need to prevent Norovirus gastroenteritis in children?

Taking into account the proposed indication in adults, and the characteristics of the medicine, the PDCO considered that this medicine could be of potential use for the prevention of acute norovirus gastroenteritis in children.

Noroviruses affect all age groups, with young children amongst those most at risk of severe disease.

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

At present, no vaccine for the prevention of norovirus gastroenteritis is authorised in the European Union. Therefore, the Committee considered that data were required to decide whether the use of this medicine will bring a benefit to children from 6 weeks to 18 years of age, and to understand any potential risks.

The Committee agreed with the applicant that there may also be a need to develop a paediatric-specific strength/composition of this medicine, which would allow to use the medicine safely and accurately in infants, toddlers and young children.

The Committee agreed with the request of the applicant that the development of the paediatric-specific strength/composition of the pharmaceutical form to be used in infants, toddlers and younger children and the conduction paediatric clinical studies in children less than 9 years of age should be deferred, as an initial authorisation will be sought in adults, older children and adolescents.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- studies are not necessary in neonates and infants below 6 weeks of age. Severe norovirus gastroenteritis is rare in neonates and infants, who are likely protected through antibodies passed on from their mother during pregnancy.
- A paediatric-specific strength/composition of the pharmaceutical form* (suspension for injection) may be needed for children aged from 6 weeks to less than 9 years of age. This will be developed by the applicant and its safety and immunogenicity will be confirmed in a paediatric clinical study.
- It is necessary to show immunogenicity of the Norovirus vaccine. This will be done in 9 studies in children from 6 weeks to less than 18 years of age, including studies in which Norovirus vaccine is given together with other authorised vaccines.
- It is necessary to show vaccine efficacy to prevent Norovirus gastroenteritis. This is being done in an efficacy study.
- 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 (P/0125/2015)* 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/or 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 August 2026.

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 effective 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).