14 December 2015
EMA/556214/2015
Human Medicines Research and Development Support Division

Public summary of the evaluation of a proposed paediatric investigation plan

Adenovirus associated viral vector serotype 2 containing the human RPE65 gene for the treatment of genetic congenital retinal disorders

On 14 August 2015, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for adenovirus associated viral vector serotype 2 containing the human RPE65 gene for the treatment of genetic congenital retinal disorders (EMEA-001684-PIP01-14).

What is adenovirus associated viral vector serotype 2 containing the human RPE65 gene and how is it expected to work?

Adenovirus associated viral vector serotype 2 containing the human RPE65 gene is not authorised in the European Union. Studies in adults and children have recently been completed. This medicine is proposed in adults for the treatment for inherited retinal degeneration due to autosomal-recessive RPE65 gene mutations.

This medicine is expected to overcome the defects associated with the impaired function of the RPE65 protein in the eye (whose normal activity is required for vision) by inserting in cells wild-type copies of the gene encoding this protein, which will in turn produce a normal RPE65 protein, able to support vision.

What was the proposal from the applicant?

For children, the applicant proposed:

Studies already ongoing in children from 3 years to less than 18 years of age affected by Leber's congenital amaurosis type 2, in a paediatric investigation plan*. The future indication proposed for children is: Treatment for inherited retinal degeneration due to autosomal-recessive RPE65 gene mutations.

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 treat children affected by Leber's congenital amaurosis type 2?

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 treatment of genetic congenital retinal disorders. This condition is symptomatic at birth or within the first few months of life and progressively deteriorates.

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

At present, no treatment is authorised for the treatment of genetic congenital retinal disorders in children in the European Union. Therefore, the Committee considered that new data are required to decide whether the use of this medicine will bring a benefit to children from 3 years to less than 18 years of age affected by the condition, and to understand any potential risks.

Because there is a need for more medicines for the treatment of genetic congenital retinal disorders in children, and this medicine has a potential interest for children, the Committee considered that clinical studies were necessary.

The Committee considered that the condition is serious enough in children, and that there are no treatments available for children yet. Consequently, studies with children should be completed without waiting for all the results of studies in 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 3 years of age because clinical studies are not feasible in this population, since the risks associated with the administration of the medicine to this population overweight the possible benefits.
- It is necessary to study if the medicine is effective to treat the disease in children. This will be done in one study using the medicine in one eye and comparing its effect to no treatment of the other eye.
- It is necessary to study the potential side effects of the medicine, to prevent them or to reduce the consequences if they occur. The main concern identified by the PDCO is the potential toxicity of the medicine, which could result in pieces of DNA inserted randomly in the genome of certain cells.

What happens next?

The applicant has now received the EMA Decision (P/0221/2015)* 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 April 2015.

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).