11 November 2014
EMA/691347/2014
Human Medicines Research and Development Support Division

Public summary of the evaluation of the proposed paediatric investigation plan

Nanobody directed towards the fusion protein of human respiratory syncytial virus (ALX-0171) for treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV)

On 15 August 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for Nanobody directed towards the fusion protein of human respiratory syncytial virus (ALX-0171) for the treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV) (EMEA-001553-PIP01-13).

What is nanobody directed towards the fusion protein of human respiratory syncytial virus (ALX-0171), and how is it expected to work?

Nanobody directed towards the fusion protein of human respiratory syncytial virus (ALX-0171) is not authorised in the European Union. Studies in children are currently on-going. This medicine is proposed in children for the treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV).

This medicine is expected to protect the lungs from severe infection from RSV by interfering with the penetration of the virus into respiratory epithelial cells.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from birth to 3 years old affected by severe lower respiratory tract disease (e.g. pneumonia or bronchiolitis), which occurs predominantly in infants and young children, in a paediatric investigation plan*. The future indication proposed for children is: treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV). The plan includes the development of a nebuliser solution to be used in children*. It also includes a proposal to determine the right dose and to show efficacy and safety of the medicine in non-clinical and clinical studies and to extrapolate data from studies in infants and young children to older children with a compromised immune system, who also may be affected by severe RSV infection.

The applicant proposed a deferral* for the clinical studies in older immunocompromised children.

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Is there a need to treat children affected by RSV infection ?

Taking into account the characteristics of the medicine, the Paediatric Committee considered this medicine of potential use for the treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV). This condition predominantly occurs in young children and affects in particular neonates, infants and toddlers.

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

Because there is a need for more medicines for the treatment of lower respiratory tract disease caused by human respiratory syncytial virus (RSV), and this medicine has a potential interest for children, the Committee considered that non-clinical and clinical studies were necessary.

The Committee agreed with the request of the applicant that the clinical studies in older immunocompromised children should be deferred to avoid a delay in the availability of the medicine for infants and young children with severe lower respiratory tract RSV infections.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- Studies are not necessary in older children and adolescents with normal immune system in whom RSV infection is associated with only mild cold-like symptoms, not requiring specific treatment.
- As severe lower respiratory tract RSV infection affects neonates, infants, and young children, nine clinical studies including children from birth to less than 3 years of age will be performed to obtain the necessary data.
- Studies in animals need to be performed, to identify any risk before the medicine is used in infants and neonates / young children.
- Studies in models of the disease need to be performed, to inform how to best study / use the medicine in children.
- Determination of the best dose should be made with 4 trials of the medicine's behaviour in the body and the body's reactions to it.
- It is necessary to study if the medicine is efficacious to treat the disease in children. This will be done in three studies comparing the medicine to placebo.
- While partial extrapolation of efficacy/safety is possible in the development of this product, between infants/young children and older children with compromised immune system in whom RSV infections may cause severe lower respiratory tract disease, the appropriate dose for this patient population will need to be determined.

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 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 09/2021.

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.
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).