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Human Medicines Research and Development Support Division

Public summary of the evaluation of a proposed paediatric investigation plan

Humanised anti-IL-6 receptor (IL-6R) monoclonal antibody for treatment of neuromyelitis optica

On 22 May 2015 the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for humanised anti-IL-6 receptor (IL-6R) monoclonal antibody for the treatment of neuromyelitis optica (EMEA-001625-PIP01-14).

What is humanised anti-IL-6 receptor (IL-6R) monoclonal antibody, and how is it expected to work?

Humanised anti-IL-6 receptor (IL-6R) monoclonal antibody is a type of protein designed to recognise and target a specific structures found in certain cells. More precisely the medicine targets IL-6 receptors found on the surface of plasmablasts, which produce the disease-causing anti-aquaporin 4 (AQP4) autoantibody in neuromyelitis optica (NMO) and NMO spectrum disorders. Inhibition of IL-6 signalling is expected to reduce disease relapse rate, disability and pain.

Humanised anti-IL-6 receptor (IL-6R) monoclonal antibody is proposed in adults for the treatment of neuromyelitis optica (NMO) and NMO spectrum disorders and is currently not authorised in the European Union. Studies in adults and children are on-going.

What was the proposal from the applicant?

The future indication proposed for children is: treatment of neuromyelitis optica (NMO) and NMO spectrum disorders. For children, the applicant proposed to study the medicine in children from 2 years to less than 18 years of age affected by neuromyelitis optica, in a paediatric investigation plan*.

The plan includes the development of a specific pharmaceutical form to be used in the paediatric population from 2 years of age. 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 older children and adults.

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

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Is there a need to treat children affected by neuromyelitis optica?

Since this condition occurs also in children and affects in particular adolescents and 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 neuromyelitis optica.

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

At present, no treatment is authorised for neuromyelitis optica in children in the European Union, but some treatments are available for the treatment of neuromyelitis optica, such as prednisolone, azathioprine or mycophenolate mofetil that are used off-label in children. Therefore, the Committee considered that new data are required to decide whether the use of this medicine will bring a benefit to children from 2 to less than 18 years of age affected by neuromyelitis optica, and to understand any potential risks and, therefore, that non-clinical and clinical studies were necessary.

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.

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 considered not feasible in children from birth to less than 2 years of age because humanised anti-IL-6 receptor (IL-6R) monoclonal antibody and will not be requested.
- A pharmaceutical form* such as solution for injection for subcutaneous use appropriate for the paediatric population is needed for children aged from 2 years of age to less than 12 years of age. A new form will be developed by the applicant.
- Studies in animals need to be performed, to identify any risk before the medicine is used in young children.
- It is necessary to study if the medicine is effective to treat the disease in children. This will be done in 1 study comparing the medicine to placebo* and in 1 uncontrolled study.
- 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 for bone marrow and the effect on immunity.
- Partial extrapolation of efficacy is possible in the development of this product, between adults/adolescents) and children from 2 to less than 12 years of age, because of similarity of disease in children and adults.

What happens next?

The applicant has now received the EMA Decision (P/0154/2015)* 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 June 2020.

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).