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Human Medicines Research and Development Support Division

Summary of the evaluation of the proposed paediatric investigation plan

Chimeric anti-disialoganglioside (GD2) monoclonal antibody (ch14.18/CHO) (APN311)

On 21 March 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for chimeric anti-disialoganglioside (GD2) monoclonal antibody (ch14.18/CHO) (APN311) for the treatment of children with a neuroblastoma.

What is ch14.18/CHO (APN311), and how is it expected to work?

Chimeric anti-disialoganglioside (GD2) monoclonal antibody (ch14.18/CHO) (APN311) is an antibody that is produced in animal cells. About a third of its molecular is similar to antibodies produced by animals, while the structure of other parts is similar to human antibodies. It is not authorised in the European Union. Studies in children are currently on-going. This medicine is expected to bind to neuroblastoma tumour cells and, together with the patient's immune cells and defence substances, destroy these tumour cells.

What was the proposal from the applicant?

For children, the applicant proposed to study the medicine in children from 1 years to less than 18 years old affected by neuroblastoma, in a paediatric investigation plan.* The future indication proposed for children was: treatment of patients with neuroblastoma in combination with two other molecules (aldesleukin and isotretinoin).

The plan includes the development of a pharmaceutical form* to be used in children, for intravenous use. It also includes a proposal to determine the right dose and to show the safety of the medicine in non-clinical and clinical studies.

Is there a need to treat children affected by neuroblastoma?

Neuroblastoma is a life-threatening and, in most patients, difficult to treat cancer. It occurs in all paediatric ages. Based on existing knowledge, and on data submitted by the Applicant, the Paediatric Committee concluded that the PIP should not be limited to the indication proposed by the applicant, because the characteristics of the product likely support testing in younger patients and in patients with only small amounts of neuroblastoma.

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

At present, some treatments are used for the treatment of neuroblastoma in children in the European Union, such as cyclophosphamide, doxorubicin, vincristine and melphalan. Therefore, the Committee considered that new data are required to decide whether the use of this medicine will bring a benefit to the children affected by the condition, and to understand any potential risks.

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

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- Studies are not necessary in children up to 1 month of age, because neuroblastoma in these children would first be treated with other medicines.
- Studies in animals need to be performed, to identify any risk before the medicine is used in young children.
- Determination of the best dose administration schedule should be made with two studies of the medicine's behaviour in the body and of 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 two studies comparing the medicine to results of previous studies with other medicines.
- 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 the nervous system.

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/or in children.

The EMA Decision* on the agreed Paediatric Investigation Plan means that the applicant is bound to perform the studies 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 in the Paediatric Investigation Plan is December 2016.

Trials included in the Paediatric Investigation Plan will be 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 shown in the register within 6 months after they have been 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 reactions 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
Antibody	Large protein used by the body's immune system
Children	All children, from birth to the day before 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).