EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Research and Development Support Division

Public summary of the evaluation of the proposed paediatric investigation plan

Ranibizumab for treatment of retinopathy of prematurity

On 20 June 2014 the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for ranibizumab for the treatment of retinopathy of prematurity (EMEA-000527-PIP04-13).

What is Lucentis (ranibizumab), and how is it expected to work?

Lucentis (ranibizumab) is a medicine currently authorised in adults for the treatment of neovascular (wet) age-related macular degeneration, for the treatment of visual impairment due to diabetic macular oedema, for the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion, and for the treatment of visual impairment due to choroidal neovascularisation secondary to pathologic myopia. Its safety and efficacy have not yet been studied in children.

This medicine is expected to prevent oedema of the retina (light-sensitive membrane lining the inner eyeball) and the development of new blood vessels (neovascularisation) in the choroidea (thin vascular layer between the sclera and the retina). Choroidal neovascularisation and retinal / macular oedema (swelling of macula, a special area in the centre of retina) can lead to vision loss.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in preterm infants affected by retinopathy of prematurity in a paediatric investigation plan*. The future indication proposed for children is treatment of patients with retinopathy of prematurity.

The plan includes the development of a specific device (low volume syringe) to ensure accurate dosing of the solution for injection in children. It also includes a proposal to determine the right dose and to show efficacy and safety of the medicine in clinical studies.

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Is there a need to treat children affected by retinopathy of prematurity?

Taking into account the characteristics of the medicine, the Paediatric Committee considered this medicine of potential use for the treatment of retinopathy of prematurity. This condition only occurs in prematurely born babies.

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

At present, no medicine is authorised for the treatment of retinopathy of prematurity 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 premature babies affected by the condition, and to understand any potential risks.

The Committee considered that there is also a need to develop a low volume syringe which would allow using the medicine safely and accurately in premature babies.

Because there is a need for more medicines for the treatment of retinopathy of prematurity and this medicine has a potential interest for premature babies, the Committee considered that clinical studies were necessary.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- As retinopathy of prematurity affects neonates, 1 clinical study in preterm babies comparing the medicine to active control* (laser therapy) will be performed to determine the best dose and to study if the medicine is efficacious and safe to treat the disease.

What happens next?

The applicant has now received the EMA Decision* on this medicine. The Decision itself is necessary for the applicant to request a new indication for this medicine in premature babies, as this medicine is already authorised and protected by a patent*.

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 December 2018.

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.
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).