02 July 2015
EMA/318226/2015
Human Medicines Research and Development Support Division

Public summary of the evaluation of a proposed paediatric investigation plan

Canakinumab for treatment of tumour necrosis factor (TNF) receptor associated periodic syndrome

On 13 February 2015, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for canakinumab for the treatment of tumour necrosis factor (TNF)receptor associated periodic syndrome (EMEA-000060-PIP05-14).

What is Ilaris (canakinumab) and how is it expected to work?

Ilaris (canakinumab) is a medicine currently authorised for the indications:

- treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults, adolescents and children aged 2 years and older with body weight of 7.5 kg or above;
- treatment of active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal antiinflammatory drugs (NSAIDs) and systemic corticosteroids;
- symptomatic treatment of adult patients with frequent gouty arthritis attacks.

This medicine is proposed in adults for the treatment of TNF receptor associated periodic syndrome.

This medicine is monoclonal antibody (a type of protein) designed to attach to interleukin-1 beta, a substance which is produced in high levels in patients with TNF receptor associated periodic syndrome, causing inflammation. By attaching to interleukin-1 beta, canakinumab blocks its activity, helping to relieve the symptoms of the diseases.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from 2 years to less than 18 years of age affected by Treatment of TNF receptor associated periodic syndrome, in a paediatric investigation plan*.

The future indication proposed for children was: treatment of TNF receptor associated periodic syndrome.

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

The plan included a proposal to show efficacy and safety of the medicine in clinical studies.

The applicant proposed a deferral* for the completion of the paediatric clinical studies.

Is there a need to treat children affected by tumour necrosis factor (TNF) receptor associated periodic syndrome?

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 TNF receptor associated periodic syndrome (TRAPS).

TRAPS occurs also in children, and the median age at which symptoms appear is 4 years of age, but in a small percentage of patients symptoms may present after 30 years of age .

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 TRAPS in children in the European Union. Some treatments are available, such as NSAIDs that is known that are known to bring relief of symptoms. Therefore, the Committee considered that new data are required to decide whether the use of this medicine will bring a benefit to children from 28 days to less than 18 years affected by the condition, and to understand any potential risks.

Because there is a need for more medicines for the treatment of TNF receptor associated periodic syndrome in children, and this medicine has a potential use, the Committee considered that studies in the paediatric population were necessary.

The Committee considered that the condition is serious enough in children, and that there are no treatments available yet. Consequently, studies with children should start without waiting for all the results of studies in adults.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- It is necessary to investigate whether the medicine is effective to treat the disease in children. This will be done in one study comparing the medicine to placebo*. In the study will be included also adult patients with TNF receptor associated periodic syndrome. This study includes also paediatric and adult patients with familial Mediterranean fever and hyperimmunoglobulin D syndrome (i.e. it is the same study proposed in PIP EMEA-000060-PIP04-14).
- Studies are not necessary in neonates (newborn infants from birth to less than 28 days) with TNF receptor associated periodic syndrome because canakinumab does not represent a significant therapeutic benefit in this paediatric age subset as clinical studies are not feasible.

What happens next?

The applicant has now received the EMA Decision (P/0058/2015)* on this medicine. The Decision itself is necessary for the applicant to request a new indication, a new route of administration* or a new pharmaceutical form*, 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 March 2016.

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).