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Human Medicines Research and Development Support Division

Summary of the evaluation of the proposed paediatric investigation plan

Apremilast for treatment of Behcet disease

On 18 July 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for apremilast for the treatment of Behcet disease (EMEA-000715-PIP05-13).

What is apremilast, and how is it expected to work?

Apremilast is not authorised in the European Union, but has been authorised in the United States for treatment of psoriatic arthritis. Studies in adults and children are currently on-going. This medicine is proposed in adults for the treatment of Behcet disease.

Apremilast is expected to work by blocking the production of various messenger molecules, including interleukins and tumour necrosis factors. These messengers are involved in causing inflammation and are found at high levels in patients with Behçet's disease. By blocking their production, apremilast reduces the symptoms of Behçet's disease, such as the sores in the mouth.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from 2 to 18 age years old affected by Behcet disease in a paediatric investigation plan*. The future indication proposed for children is: Treatment of active oral ulcers (with or without concurrent genital ulcers) associated with Behçet's disease in patients, who are candidates for systemic therapy. The plan includes the development of an oral suspension to be used in children*. It also includes a proposal to show efficacy and safety of the medicine in clinical studies.

Is there a need to treat children affected by Behcet disease?

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 Behcet disease. This condition occurs also in children.

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

At present, some treatments are available for the treatment of Behcet disease in children in the European Union, such as azathioprine or systemic corticosteroids. 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.

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 (oral suspension), and whose composition* must only include components that are known to be safe in children.

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

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- Studies are not necessary in children below 2 years of age because this medicinal product is likely to be not safe in this age group.
- A pharmaceutical form* such as oral suspension was needed for children. An oral suspension will be developed by the applicant.
- It is necessary to study if the medicine is efficacious to treat the disease in children. This will be done in a study comparing the medicine to placebo.
- 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 effects on the immune system.
- Partial extrapolation of efficacy is possible in the development of this product, between adults and adolescents/younger children, because the product is expected to act in the same way.

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 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 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 July 2023.

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).