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Human Medicines Research and Development Support Division

Summary of the evaluation of the proposed paediatric investigation plan

Potassium citrate monohydrated / potassium hydrogen carbonate for Treatment of cystinuria

On 15 August 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for Potassium citrate monohydrated / potassium hydrogen carbonate for the treatment of cystinuria (EMEA-001535-PIP01-13).

What is Potassium citrate monohydrated / potassium hydrogen carbonate, and how is it expected to work?

Potassium citrate monohydrated / potassium hydrogen carbonate is not authorised in the European Union. Studies in adults and children are currently on-going. This medicine is proposed for the treatment of cystinuria and prevention of cystine lithiasis.

This medicine is expected to increase urinary pH in order to increase cystine solubility. This should facilitate its elimination through urine and avoid the formation of stones.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from 6 months to less than 18 years old affected by cystinuria, in a paediatric investigation plan*. The future indication proposed for children is: treatment of cystinuria. The plan includes the development of a specific pharmaceutical form to be used in children and in adults*, prolonged-release granules. It also includes a proposal to determine the right dose and to show efficacy and safety of the medicine in clinical studies.

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

Is there a need to treat children affected by cystinuria?

Taking into account the proposed indication in adults, the paediatric therapeutic needs and the characteristics of the medicine, the Paediatric Committee considered this medicine of potential use for the treatment of cystinuria. This condition occurs also in children.

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 cystinuria in children in the European Union. Some treatments are available for the treatment of cystinuria in adults in the European Union, such as alkalinizing agents, which are used off-label in children.

Because there is a need for authorised medicines for the treatment of cystinuria in children, and this medicine has a potential interest for children, the Committee considered that clinical studies were necessary and should start without waiting for all the results of studies in adults.

The Committee agreed with the request of the applicant that the completion of one paediatric clinical study should be deferred to avoid a delay in the availability of the medicine.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- Studies are not necessary in children below 6 months of age because the medicine is not expected to bring a significant therapeutic benefit in this age group.
- A pharmaceutical form* adequate for children is being developed by the applicant (prolonged-release granules).
- Determination of the best dose should be made with one trial of the medicine's behaviour in the body.
- It is necessary to study if the medicine is efficacious to treat the disease in children. This will be done in 1 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.

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 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 January 2017.

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).