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Public summary of the evaluation of the proposed paediatric investigation plan

Human autologous bone marrow-derived osteoblastic cells for treatment of non-traumatic osteonecrosis

On 25 April 2014, the Paediatric Committee of the European Medicines Agency agreed a Paediatric Investigation Plan* (PIP) for human autologous bone marrow-derived osteoblastic cells for the treatment of non-traumatic osteonecrosis (EMEA-001329-PIP02-13).

What are human autologous bone marrow-derived osteoblastic cells, and how are they expected to work?

Human autologous bone marrow-derived osteoblastic cells are not authorised in the European Union. Studies in adults are currently on-going. This medicine is proposed in adults for the treatment of non-traumatic osteonecrosis.

This medicine is composed of bone marrow cells extracted from the individual to be cured, expanded in vitro and re-implanted inside the diseased bone. The medicine is expected to act in two ways: by replacing the missing or defective bone cells at the bone defect site and by re-establishing a healthy bone environment.

What was the proposal from the applicant?

For children, the applicant proposed:

To study the medicine in children from 10 years to less than 18 years of age affected by osteonecrosis developed after treatment for acute lymphoblastic leukaemia, in a paediatric investigation plan*. The future indication proposed for children is: treatment of non-traumatic osteonecrosis. The plan includes a proposal to show efficacy and safety of the medicine in non-clinical and clinical studies.

The applicant proposed a deferral* for the non-clinical and paediatric clinical studies.

Is there a need to treat children affected by a similar 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 non-traumatic osteonecrosis. This condition occurs also in children.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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

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

Studies with children will be done between 2017 and 2021.

The Committee agreed with the request of the applicant that the non-clinical and paediatric clinical study should be deferred to avoid a delay in the availability of the medicine for adults.

What is the content of the Plan after evaluation?

The Paediatric Committee considered that:

- Studies are not necessary in some groups of children because the medicinal product does not represent a significant therapeutic benefit over existing treatments for those paediatric patients.
- It is necessary to show efficacy to treat the disease in children. This will be done in one study comparing the medicine to standard treatment.
- 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 concerns, identified by the PDCO, are the potential toxicity of the medicine for longitudinal bone growth and the possible contamination of the product with cancer cells, if the cancer patient's bone marrow contains remaining tumour cells.

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 will perform the studies and trials 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 June 2021.

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).