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Human Medicines Research and Development Support Division

# Public summary of the evaluation of a proposed product-specific waiver

## Enclomifene for the treatment of hypogonadotropic hypogonadism

On 17 July 2015, the Paediatric Committee of the European Medicines Agency agreed a product-specific waiver* for enclomifene for the treatment of hypogonadotropic hypogonadism (EMEA-001779-PIP01-15).

### What is enclomifene, and how is it expected to work?

Enclomifene is not authorised in the European Union. Its safety and efficacy have not been studied in adults or children.

This medicine is proposed in adults for the treatment of hypogonadotrophic hypogonadism (secondary hypogonadism) in adult men.

Enclomifene is one of the two components (isomers) of clomifene. Clomifene has been authorised for several decades, for the treatment of infertility in women with infertility due to anovulation*.

Enclomifene is expected to have a similar effect to that of clomifene, but to be more potent. It is a modulator of the effects of estrogens (female hormones), and by blocking these effects at the level of the hypothalamus in the brain, it increases the production of certain hormones from the pituitary gland, called gonadotropins. In turn, these hormones stimulate the ovaries (in women) or the testes (in men) to produce other hormones, called sex steroids (mainly estrogens and progesterone in women, and mainly testosterone in men).

For these reasons, enclomifene is expected to be beneficial for the treatment of conditions where the the testes do not produce enough testosterone, but only because they are not sufficiently stimulated by the pituitary gland.

### What was the proposal from the applicant?

For children, the applicant proposed not to do any study in children (from birth to less than 18 years of age), because the condition does not exist in some subsets of the paediatric population, and because there would be no significant benefit of this product in the other subsets.

Therefore, the applicant requested an exemption (waiver*) from the obligation to study the medicine in any children, in the condition “treatment of hypogonadotrophic hypogonadism”.

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## Is there a need to treat children affected by hypogonadotrophic hypogonadism?

This condition does occur in children of all ages. While treatment is not usually required or appropriate before the age of onset of puberty, it becomes necessary to address the delayed puberty associated with the condition. Taking into account the proposed indication in adults, and the characteristics of the medicine, the Paediatric Committee did not consider that this medicine could be of significant benefit for the treatment of hypogonadotrophic hypogonadism in children.

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

The Committee agreed with the request of the applicant to be exempt from performing studies in children from birth to less than 18 years. The Committee concluded that this medicinal product does not seem to have a potential significant benefit over existing treatments for the treatment of hypogonadotrophic hypogonadism.

The Committee came to this conclusion because the product seems to be more appropriate for the induction of ovulation in the treatment of infertility, in adult women. Other products are currently available for the treatment of hypogonadism in children.

## What happens next?

The applicant has now received the EMA Decision (P/0XXX/20XX)* on this medicine. The Decision itself is necessary for the applicant to request in the future a marketing authorisation* for this medicine in adults.

## *Definitions:

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| Anovulation | Condition characterised by absence or disturbance of the normal production of one or more eggs from the ovaries. It can cause infertility (difficulty in becoming pregnant) in women. |
| 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 18$^{th}$ 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 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). |