8 March 2017
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Leuprorelin acetate for the treatment of congenital hypogonadotropic hypogonadism

On 12 January 2017, orphan designation (EU/3/16/1821) was granted by the European Commission to Stichting Centre for Human Drug Research (CHDR), the Netherlands, for leuprorelin acetate (also known as NH901) for the treatment of congenital hypogonadotropic hypogonadism.

What is congenital hypogonadotropic hypogonadism?

Congenital hypogonadotropic hypogonadism is a genetic condition in which the sex organs (the testes in men and the ovaries in women) do not develop and work properly. Normally, the function of these organs is controlled by a complex pathway of hormones which regulate the testes and ovaries and their production of reproductive cells (sperm or eggs) as well as the sex hormones testosterone and oestrogen.

In patients with congenital hypogonadotropic hypogonadism, the first hormone in this pathway, gonadotropin-releasing hormone, is not produced, so the sex organs do not function correctly, making the patient infertile. The lack of testosterone and oestrogen from these organs also restricts the development of normal male and female characteristics and sexual function.

The condition is long-term debilitating due to loss of fertility and its effects on physical appearance and sexual function.

What is the estimated number of patients affected by the condition?

At the time of designation, congenital hypogonadotropic hypogonadism affected approximately 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 103,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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What treatments are available?

At the time of designation, several products were approved in the EU for the treatment of congenital hypogonadotropic hypogonadism or the associated infertility. These included a variety of hormones that directly stimulate the sex organs (gonadotropins) as well as sex hormones such as testosterone and estradiol.

The sponsor has provided sufficient information to show that leuprorelin acetate might be of significant benefit for patients with congenital hypogonadotropic hypogonadism because laboratory studies and published data have shown that it can increase sex hormone levels and has the potential to improve production of natural gonadotropins and improve fertility. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Normally, the hypothalamus (a region of the brain) produces bursts of gonadotropin-releasing hormone, which in turn stimulate the body to release gonadotropins. These gonadotropins play a key role in regulating the development and function of the testes and ovaries. In congenital hypogonadotropic hypogonadism the hypothalamus does not produce the releasing hormone, so this pathway does not operate and the sex organs fail to develop and function correctly. This medicine is a synthetic form of the releasing hormone which can replace the missing natural hormone. The medicine is available in a formulation to be taken by mouth once a day.

What is the stage of development of this medicine?

The effects of leuprorelin acetate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with leuprorelin acetate in patients with congenital hypogonadotropic hypogonadism had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for congenital hypogonadotropic hypogonadism or designated as an orphan medicinal product elsewhere for this condition. Long-lasting injectable forms of leuprorelin were authorised in the EU for the treatment of various hormone-related conditions including prostate cancer and endometriosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 December 2016 recommending the granting of this designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Leuprorelin acetate	Treatment of congenital hypogonadotropic hypogonadism
Bulgarian	Леупрорелин ацетат	Лечение на вроден хипогонадотропен хипогонадизъм
Croatian	Leuprorelin acetat	Liječenje prirođenog hipogonadotropnog hipogonadizma
Czech	Leuprorelin acetát	Léčba kongenitálního hypogonadotropního hypogonadismu
Danish	Leuprorelinacetat	Behandling af medfødt hypogonadotrop hypogonadisme
Dutch	Leuprorelineacetaat	Behandeling van congenitaal hypogonadotroop hypogonadisme
Estonian	Leuproreliinatsetaat	Kaasasündinud hüpogonadotroopse hüpogonadismi ravi
Finnish	Leuproreliiniasetaatti	Synnynnäisen hypogonadotrooppisen hypogonadismin hoito
French	Acétate de leuproréline	Traitement de l'hypogonadisme hypogonadotrophique congénital
German	Leuprorelinacetat	Behandlung von kongentitalem hypogonadotropem Hypogonadismus
Greek	Οξική λευπρορελίνη	Θεραπεία συγγενούς υπογοναδοτροπικού υπογοναδισμού
Hungarian	Leuprorelin-acetát	Veleszületett hypogonadotróp hypogonadizmus kezelése
Italian	Leuprorelina acetato	Trattamento dell' ipogonadismo ipogonadotropo congenito
Latvian	Leiprorelīna acetāts	Iedzimta hipogonadotropā hipogonādisma ārstēšana
Lithuanian	Leuprorelino acetatas	Įgimto hipogonadotropinio hipogonadizmo gydymas
Maltese	Leuprorelin aċetat	Kura ta' ipogonadiżmu ipogonadotropiċ konġenitali
Polish	Octan leuproreliny	Leczenie wrodzonego hipogonadyzmu hipogonadotropowego
Portuguese	Acetato de leuprorrelina	Tratamento de hipogonadismo hipogonadotrópico congénito
Romanian	Leuprorelină acetat	Tratamentul hipogonadismului hipogonadotropic congenital
Slovak	Leuprorelíniumacetát	Liečba kongenitálneho hypogonadotropného hypogonadizmu
Slovenian	Leuprorelin acetat	Zdravljenje kongenitalnega hipogonadotropnega hipogonadizma
Spanish	Acetato de leuprorelina	Tratamiento del hipogonadismo hipogonadotrópico congénita
Swedish	Leuprorelinacetat	Behandling av medfödd hypogonadotropism
Norwegian	Leuprorelinacetat	Behandling av kongenitalprimær hypogonadotropic hypogonadisme
Icelandic	Leuprórelín asetat	Meðferð frumkominnar kynkirtlavanseytingar

[1] At the time of designation