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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein for the for the treatment of hypophosphatasia

First publication	5 January 2009
Rev.1: administrative update	24 April 2009
Rev.2: transfer of sponsorship	7 March 2011
Rev.3: transfer of sponsorship	18 February 2013
Rev.4: sponsor's change of address	12 March 2015

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 3 December 2008, orphan designation (EU/3/08/594) was granted by the European Commission to Europa Rx Limited, United Kingdom, for recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein for the treatment of hypophosphatasia.

The sponsorship was transferred to Dr Ulrich Granzer, Germany, in September 2010 and Alexion Europe SAS, France, in September 2012.

What is hypophosphatasia?

Hypophosphatasia is a rare inherited metabolic disorder. It is caused by defects in the gene for tissue non-specific alkaline phosphatase (TNSALP), an enzyme that is involved in the development of bone, particularly the hardening of the bones. Patients with hypophosphatasia have symptoms such as early loss of teeth, malformed (unusually shaped) bones and frequent bone fractures (breaks).

There are five forms of the disease. Perinatal and infantile hypophosphatasia affect unborn babies and children, and are life-threatening either in the womb or in early infancy because of the incomplete development of the bones and lungs. The other three forms (childhood and adult hypophosphatasia, and odontohypophosphatasia) are generally not lethal but are debilitating and long-lasting.

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

At the time of designation, hypophosphatasia affected less than 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 500 people[*], and is below the threshold 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).

What treatments are available?

At the time of submission of the application for orphan drug designation, there were no satisfactory methods authorised for the treatment of hypophosphatasia. Treatment has been aimed at relieving the symptoms of the disease such as setting fractures in plaster casts, controlling pain and controlling the levels of calcium in the blood. Patients are sometimes treated with surgery, and dental hygiene is carefully monitored.

How is this medicine expected to work?

Recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein contains TNSALP, the enzyme that is missing in patients with hypophosphatasia. The enzyme is produced by a method known as 'recombinant DNA technology': it is made by a cell that has received a gene (DNA), which makes it able to produce TNSALP. In this medicine, the TNSALP is attached to a protein called deca-aspartate, which guides the TNSALP to the bones. Providing TNSALP is expected to replace the missing enzyme in the bones, improving their development and making them harder.

What is the stage of development of this medicine?

The evaluation of the effects of recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein in experimental models is ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with hypophosphatasia had been started.

At the time of submission, recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein was not authorised anywhere in the world for hypophosphatasia. Orphan designation of the product had been granted in the United States of America for hypophosphatasia.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 October 2008 recommending the granting of this designation.

[*]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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 502,800,000 (Eurostat 2008).

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:

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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	Recombinant human tissue non-specific alkaline phosphatase - Fc - deca-aspartate fusion protein	Treatment of hypophosphatasia
Bulgarian	Човешка рекомбинантна тъканно-неспецифична алкална фосфатаза - Fc – дека-аспартат фузионен протеин	Лечение на хипофосфатазия
Czech	Lidský rekombinantní tkáňově nespecifický fúzní protein alkalická fosfatáza-Fc-dekaaspartát	Léčba hypofosfatázie
Danish	Humant rekombinant vævs-uspecifikt alkalisk fosfatase - Fc - deca-aspartat fusionsprotein	Behandling af hypofosfatasi
Dutch	Humaan recombinant weefsel niet-specifiek alkalische fosfatase - Fc - deca-aspartaatfusieproteïne	Behandeling van hypofosfatasemie
Estonian	Rekombinantne inimese mittekoespetsiifilise leelisfosfataasi - Fc - deka-aspartaadi liitvalk	Hüpofosfataasia ravi
Finnish	Rekombinantti humaani kudoksen ei-spesifinen alkaliinifosfataasi – Fc – deka-aspartaattifuusioproteiini	Hypofosfatasian hoito
French	Protéine de fusion humaine recombinante de phosphatase alcaline non spécifique des tissus-Fc - déca-aspartate	Traitement de l'hypophosphatasie
German	Humanes rekombinantes Fusionsprotein Gewebeunspezifische-alkalische Phosphatase-Fc-Deca-Aspartat	Behandlung der Hypophosphatasie
Greek	Ανασυνδυασμένη πρωτεΐνη σύντηξης ανθρώπινης μη-ειδικής για ιστό αλκαλικής φωσφατάσης - Fc - δέκα-ασπαρτάτης	Θεραπεία υποφωσφατασίας
Hungarian	Rekombináns, nem humán szövetspecifikus alkalikus foszfatáz - Fc - dekaaszpartát fúziós protein	Hypophosphatasia kezelése
Italian	Proteina di fusione fosfatasi alcalina tessuto-aspecifica - Fc - deca-aspartato umana ricombinante	Trattamento dell'ipofosfatasia
Latvian	Cilvēka rekombinantais audu nespecifiskās sārmainās fosfatāzes - Fc - dekaaspartāta sajūgtais proteīns	Hipofosfatāzijas ārstēšana
Lithuanian	Baltymas, sulietas iš rekombinantinės žmogaus audiniui nespecifinės šarminės fosfatazės-Fc-deka-aspartato	Hipofosfatazijos gydymas
Maltese	Proteina ta' fużjoni umana rikombinanti ta' alkaline phosphatase mhux speċifiku għat-tessut - Fc - deca-aspartate	Kura ta' l-ipofosfatasija

[1] At the time of designation

Language	Active Ingredient	Indication
Polish	Ludzka, rekombinowana, tkankowo niespecyficzna alkaliczna fosfataza - Fc - deka-asparaginian (białko fuzyjne)	Leczenie hipofosfatazji
Portuguese	Proteína de fusão recombinante humana de fosfatase alcalina não específica de tecidos - Fc - deca-aspartato	Tratamento da hipofosfatasia
Romanian	Proteină de fuziune umană recombinantă fosfatază alcalină fără specificitate tisulară - Fc - deca-aspartat	Tratamentul hipofosfataziei
Slovak	Rekombinantný ľudský tkanivovo nešpecifický fúzny proteín Fc-dekaasparátu alkalickej fosfatázy	Liečba hypofosfatázie
Slovenian	Humana rekombinantna tkivno nespecifična alkalna fosfataza-Fc-deka-aspartatni fuzijski protein	Zdravljenje hipofosfatazije
Spanish	Proteína de fusión recombinante humana sin especificidad tisular de fosfatasa alcalina - Fc - deca-aspartato	Tratamiento de la hipofosfatasia
Swedish	Rekombinant Humant vävnadsospecifikt alkaliskt fosfatas - Fc - deka-aspartatfusionsprotein	Behandling av hypofosfatasia
Norwegian	Human rekombinant vevsuspesifikk alkalisk fosfatase - Fc - deka-aspartatfusjonsprotein	Behandling av hypofosfatasi
Icelandic	Vefjaósértækt manna-, raðbrigða-, alkalísks fosfatasa - Fc - deca-aspartat samrunaprótein	Meðferð við blóðfosfatasaskorti