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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human apolipoprotein A-I in a complex with phospholipids for the treatment of ATP-binding cassette transporter A1 deficiency

On 22 August 2014, orphan designation (EU/3/14/1314) was granted by the European Commission to Cerenis Therapeutics Holding SA, France, for recombinant human apolipoprotein A-I in a complex with phospholipids for the treatment of ATP-binding cassette transporter A1 deficiency.

What is ATP-binding cassette transporter A1 deficiency?

ATP-binding cassette transporter A1 (ABCA1) is a protein that regulates the movement of cholesterol and other fatty substances out of cells. The cholesterol removed from the cells then attaches to specific fatty molecules containing a substance called apolipoprotein A-I, forming particles of 'high-density lipoprotein', or HDL. The cholesterol found in HDL particles is commonly referred to as 'good' cholesterol. These particles are then transported to the liver where they can be broken down and the cholesterol removed from the body.

In patients with ABCA1 deficiency, the ABCA1 protein is not produced in significant amounts due to a mutation (defect) in their *ABCA1* genes, and so cholesterol is not effectively transported out of the cells and does not attach to the fatty molecules containing apolipoprotein A-I. This results in very low levels of HDL particles in the blood and in damaging build-up of cholesterol in blood vessels, nerves, liver, skin, gut and eyes.

ABCA1 deficiency is a long-term debilitating and life-threatening condition due to the cholesterol deposits in organs and tissues, particularly the arteries (atherosclerosis), where it increases the risk of heart disease.

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

At the time of designation, ABCA1 deficiency 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 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 511,100,000 (Eurostat 2014).

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What treatments are available?

No satisfactory methods of treatment were authorised in the EU for ABCA1 deficiency at the time of designation. Patients were usually managed with measures such as a low-fat diet and medicines to lower lipids (fats) in the blood.

How is this medicine expected to work?

In patients with ABCA1 deficiency cholesterol does not leave the cells in sufficient amounts and therefore HDL particles are not adequately formed.

The medicine contains replacement HDL-like particles containing apolipoprotein A-I in a form that absorbs cholesterol very efficiently. By absorbing efficiently cholesterol that is present in the blood, this medicine is expected to facilitate the loss of cholesterol from tissues where it has been accumulating, particularly in the walls of blood vessels.

The apolipoprotein A-I in this medicine is made by a method known as 'recombinant DNA technology': it is made by cells that have received a gene (DNA) that makes them able to produce the apolipoprotein.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with ABCA1 deficiency were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for ABCA1 deficiency or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 2014 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:

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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 apolipoprotein A-I in a complex with phospholipids	Treatment of ATP-binding cassette transporter A1 deficiency
Bulgarian	Рекомбинантен човешки аполипопротеин A-I в комплекс с фосфолипиди	Лечение на дефицит на АТР-свързващ касетъчен транспортер А1
Croatian	Rekombinantni ljudski apolipoprotein A-I u kompleksu s fosfolipidima	Liječenje nedostatka ATP-ovisnog prijenosnika A1
Czech	Rekombinantní humánní apolipoprotein A-I v komplexu s fosfolipidy	Léčba deficience kazetového transportéru vážícího ATP, A1
Danish	Rekombinant humant apolipoprotein A-1 i et kompleks med fosfolipider	Behandling af mangel på ATP-bindende kassettetransportør A1
Dutch	Recombinant humaan apolipoproteïne A-I in een complex met fosfolipiden	Behandeling van ATP bindende cassette transporter A1 deficiëntie
Estonian	Rekombinantne inimese apolipoproteiin A-I kompleksis fosfolipiididega	ATP-siduva kassett transportvalgu A1 puudulikkuse ravi
Finnish	Yhdistelmä-DNA-tekniikalla valmistettu humaani-apolipoproteiini A-I:tä ja fosfolipidejä sisältävä kompleksi	ATP:tä käyttävän kuljettimen ATP-binding cassette transporter A1 puutoksen hoito
French	Apolipoprotéine A-I humaine recombinante dans un complexe avec des phospholipides	Traitement de la déficience en transporteur A1 de type cassette liant l'ATP
German	Rekombinantes humanes Apolipoprotein A-I in einem Komplex mit Phospholipiden	Behandlung von ATP-binding-cassette-Transporter A1 Mangel
Greek	Ανασυνδυασμένη ανθρώπινη απολιποπρωτεΐνη A-I σε σύμπλεγμα με φωσφολιπίδια	Θεραπεία της ανεπάρκειας μεταφορικής πρωτεΐνης δέσμευσης του ATP τύπου A1
Hungarian	Rekombináns humán apolipoprotein A-I foszfolipid komplexben	ATP-kötő kazetta transzporter A1 hiány kezelése
Italian	Apolipoproteina A1 ricombinante umana in un complesso fosfolipidico	Trattamento del deficit di trasportatore ATP-binding cassette transporter A1
Latvian	Rekombinants cilvēka A-I apolipoproteīns, kas saistīts ar fosfolipīdiem	ATF saistošās kasetes A1 nesējvielas deficīta ārstēšana
Lithuanian	Rekombinantinis žmogaus apolipoproteinas A-I junginyje su fosfolipidais	ATF surišančios kasetės transporterio A1 stokos gydymas
Maltese	Apolipoproteina A-I umana rikombinanti magħquda ma' fosfolipidi	Kura tan-nuqqas ta' trasportattur A1 tat-tip cassette li jingħaqad mal-ATP
Polish	Kompleks rekombinowanej ludzkiej apolipoproteiny A-I z fosfolipidami	Leczenie niedoboru białka transportowego A1 zależnego od ATP
Portuguese	Apolipoproteína A-I humana recombinante num complexo com fosfolípidos	Tratamento da deficiência de transportador de efluxo com domínio de ligação ao trifosfato de adenosina
Romanian	Apolipoproteina A-I umană recombinantă într-un complex cu fosfolipide	Tratamentul deficitului de transportor A1 al casetei de legare a ATP

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Rekombinantný ľudský apolipoproteín A-I v komplexe s fosfolipidmi	Liečba nedostatku ATP- viažuceho kazetového transportéra A1
Slovenian	Kompleks rekombinantnega humanega apolipoproteina A-I s fosfolipidi	Zdravljenje pomanjkanja prenašalca z ATP-vezavno kaseto A1
Spanish	Apolipoproteína A-I humana recombinante en un complejo fosfolipídico	Tratamiento de la deficiencia de transportador A1 del casete de unión a ATP
Swedish	Rekombinant humant apolipoprotein A-I i ett komplex med fosfolipider	Behandling av brist på ATP-bindande kassett-transportör A1
Norwegian	Rekombinant humant apolipoprotein A-I i et kompleks med fosfolipider	Behandling av mangel på ATP-bindende kassett-transportør A1
Icelandic	Raðbrigða manna apólípóprótein A-I í flóka með fosfólípíðum	Meðferð við skorti á ATP-bindispólu-flutningspróteini A1