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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human *ABCD1* cDNA for the treatment of adrenoleukodystrophy

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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 6 June 2012, orphan designation (EU/3/12/1003) was granted by the European Commission to bluebird bio France, France, for autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human *ABCD1* cDNA for the treatment of adrenoleukodystrophy.

What is adrenoleukodystrophy?

Adrenoleukodystrophy (ALD) is an inherited disease, seen almost exclusively in males, that affects the brain, nerves and the adrenal glands (small glands located above the kidneys). ALD is caused by abnormalities in a gene called *ABCD1* which is responsible for the production of a protein called ALDP (adrenoleukodystrophy protein). Patients with the disease lack ALDP which is needed to break down fatty substances in the body called very long chain fatty acids (VLCFA). Because patients with ALD cannot break these fatty substances down, they gradually build up in cells in the body, particularly in the brain, nerves and adrenal glands. In the brain and spinal cord, the build-up of VLCFA leads to inflammation and destruction of the protective sheath (myelin) that insulates and improves the way the nerves function. In the adrenal gland,s its build-up causes their dysfunction (adrenal insufficiency) and reduces their ability to produce hormones, such as cortisol. This leads to a wide range of symptoms, including behavioural problems, problems with vision, hearing and coordination, seizures (fits) and dementia.

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ALD is life-threatening and long-term debilitating due to the progressive damage to the brain and nerves.

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

At the time of designation, ALD affected not more than 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 20,000 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).

What treatments are available?

At the time of application, there was no satisfactory treatment authorised in the EU for ALD. Haematopoietic (blood) stem-cell transplantation (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) had been used in some patients. Corticosteroids were also used to treat the adrenal insufficiency.

How is this medicine expected to work?

This medicine is made up of immature bone marrow cells that are taken from the patient. These cells are able to develop into different types of cells, including brain cells. To make this medicine, the cells are modified by a virus that contains a functional copy of the gene *ABCD1* for the ALDP protein, so that this gene is carried into the cells. When these modified cells are transplanted back into the patient, they are expected to develop into healthy cells that produce the ALDP protein, which is lacking in patients with ALD. As a result, any accumulated VLCFA will be broken down and this will help to reduce the symptoms of the disease.

The type of virus used in this medicine ('lentivirus') is modified in order not to cause disease in humans.

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, preliminary clinical trials with the medicine in patients with ALD had been conducted.

At the time of submission, the medicine was not authorised anywhere in the EU for ALD 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 12 April 2012 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 509,000,000 (Eurostat 2012).

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	Autologous haematopoietic stem cells transduced with lentiviral vector Lenti-D encoding the human *ABCD1* cDNA	Treatment of adrenoleukodystrophy
Bulgarian	Автоложни, хематопоетични стволови клетки трансдуцирани с лентивирусен вектор Lenti-D, кодиращ човешката *ABCD1* cDNA	Лечение на аденолевкодистрофия
Czech	Autologní hematopotické kmenové buňky transdukované lentivirálním vektorem Lenti-D kódujícím lidský ABCD1 cDNA.	Léčba adrenoleukodystrofie
Danish	Autologe hæmatopoietiske stamceller transduceret med lentiviral vector Lenti-D som koder for humant *ABCD1* cDNA	Behandling af adrenoleukodystrofi
Dutch	Autologe haematopoiëtische stamcellen getransudeerd met lentivirale vector Lenti-D die het humane *ABCD1* cDNA codeert	Behandeling van adrenoleukodystrofie
Estonian	Autoloogsed hematopoeetilised tüvirakud, mis sisaldavad lentiviraalset vektorit, mis kodeerib inimese *ABCD1* cDNA	Adenoleukodüstroofia ravi
Finnish	Ihmisen *ABCD1* cDNA:ta koodaavalla Lenti-D -lentivirusvektorilla muunnettuja autologisia hematopoieettisia kantasoluja	Adrenoleukodystrofian hoito
French	Cellules souches hématopoïétiques autologues transduites par le vecteur lentiviral Lenti-D codant pour l'ADNc *ABCD1*	Traitement de l'adrénoleucodystrophie
German	Autologe hämatopoetische Stammzellen, die mit einem lentiviralen Vektor (Lenti-D) transduziert sind ; dieser kodiert fuer die humane cDNA des *ABCD1* Gens	Behandlung der Adrenoleukodystrophie
Greek	Αυτόλογα αιμοποιητικά βλαστικά κύτταρα επιμολυσμένα με λεντι-ιϊκό φορέα Lenti-D που κωδικοποιεί για το ανθρώπινο *ABCD1* cDNA	Θεραπεία της αδρενολευκοδυστροφίας
Hungarian	A humán *ABCD1* cDNS gént kódoló lentivirális vectorral Lenti-D transzdukált autológ hematopoietikus őssejtek	Adrenoleukodisztrófia kezelése
Italian	Cellule staminali ematopoietiche autologhe transdotte con un vettore lentivirale Lenti-D codificante il cDNA della *ABCD1* umana	Trattamento dell'adrenoleucodistrofia
Latvian	Autologas hematopoētiskas climes šūnas pārveidotas ar lentivīrusa vektoru Lenti-D, kas kodē cilvēka *ABCD1* cDNS	Treatment of adrenoleukodystrophy Adrenoleikodistrofijas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	Autologinės hematopoetinės kamieninės ląstelės lentiviruso vektoriumi Lenti-D perkeltos į koduojančią žmogaus *ABCD1* cDNR	Adrenoleukodistrofijos gydymas
Maltese	Ċelluli steminali ematopojetiċi awtologużi trasformati permezz tal-vettur lentivirali Lenti-D li jikkodifika il-ġene uman *ABCD1* cDNA	Kura tal-adrenolewkodistrofija
Polish	Autologiczne hematopoetyczne komórki macierzyste transdukowane wektorem lentiwirusowym Lenti-D kodującym ludzki *ABCD1* cDNA	Leczenie adrenoleukodystrofii
Portuguese	Células estaminais hematopoiéticas autólogas transfectadas com o vetor lentiviral Lenti-D codificação o cDNA *ABCD1* humano	Tratamento da adrenoleucodistrofia
Romanian	Celule stem hematopoietice autologe prelucrate prin transducţie cu vector lentiviral Lenti-D ce codifică ADNc al genei umane *ABCD1*	Tratmentul adrenoleucodistrofiei
Slovak	Autológne hematopoetické kmeňové bunky transdukované lentivírusovým vektorom Lenti-D kódujúcim ľudskú *ABCD1* cDNA	Liečba adrenoleukodystrofie
Slovenian	Autologne hematopoetične matične celice transducirane z lentivirusnim vektorjem Lenti-D, ki enkodira humani *ABCD1* cDNA	Zdravljenje adrenolevkodistrofije
Spanish	Células hematopoyéticas pluripotenciales autólogas transducidas con un vector lentivírico Lenti-D que contiene el cDNA del *ABCD1* humano	Tratamiento de la adrenoleucodistrofia
Swedish	Autologa stamceller transfekterade med lentivirusvektor Lenti-D innehållande humant *ABCD1* cDNA	Behandling av adrenoleukodystrofi
Norwegian	Autologe hematopoetiske stamceller transdusert med lentiviral vektor Lenti-D som inneholder cDNA for humant ABCD1	Behandling av adrenoleukodystrofi
Icelandic	Samgena blóðstofnfrumur, fluttar með lentiveiru ferju Lenti-D, sem kóða fyrir manna ABCD1 cDNA	Meðferð við adrenal hvítavefkyrkingi