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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous haematopoietic cells genetically modified with a lentiviral vector containing the human gp91(phox) gene for the treatment of X-linked chronic granulomatous disease

On 9 February 2012, orphan designation (EU/3/12/957) was granted by the European Commission to Généthon, France, for autologous haematopoietic cells genetically modified with a lentiviral vector containing the human gp91(phox) gene for the treatment of X-linked chronic granulomatous disease.

What is X-linked chronic granulomatous disease?

Chronic granulomatous disease (CGD) is a group of inherited diseases in which certain immune cells called phagocytes are unable to produce the substances needed to kill microbes. In X-linked CGD, this is caused by a defect in a gene on the X chromosome. This gene is responsible for the production of a protein called gp91(phox), which is lacking in these patients.

In CGD, the phagocytes are still able to engulf the microbes but, as they cannot kill them, the patients suffer repeated infections, and clumps of white blood cells called granulomas appear in various organs.

X-linked CGD is a long-term and life-threatening disease due to severe infections and the formation of granulomas in internal organs.

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

At the time of designation, X-linked CGD affected less than 0.02 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of fewer than 1,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).

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What treatments are available?

At the time of designation, the main treatments for X-linked CGD included lifelong use of antibiotics and anti-fungal agents to prevent infections from occurring, interferon gamma to stimulate the immune system and aggressive early treatment of infections.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with X-linked CGD because it works in a different way to existing treatments by directly targeting the genetic defect that causes the condition, which could improve the outcome of patients. 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?

This medicine is made up of immature haematopoietic (blood) cells that are taken from the patient. These cells are able to develop into different types of blood cell. To make this medicine, the cells are modified by a virus that contains the gene for the gp91(phox) protein, so that this gene is carried into the cells. When these modified cells are transplanted back into the patient, they are expected to populate the bone marrow and produce healthy phagocytes with the gp91(phox) protein, which is lacking in patients with X-linked CGD. 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?

At the time of submission of the application for orphan designation, the evaluation of the effects of autologous haematopoietic cells genetically modified with a lentiviral vector containing the human gp91(phox) in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with X-linked CGD had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for X-linked CGD 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 7 December 2011 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	Autologous haematopoietic cells genetically modified with a lentiviral vector containing the human *gp91(phox)* gene	Treatment of X-linked chronic granulomatous disease
Bulgarian	Автологични хемопоетични клетки, генетично модифицирани с лентивирусен вектор, съдържащ човешкия ген *gp91(phox)*	Лечение на Х-свързана хронична грануломатозна болест
Czech	Autologní hematopoetické buňky geneticky modifikované pomocí lentivirálního vektoru, který obsahuje lidský gen *gp91(phox)*	Léčba chronické granulomatózy vázané na chromozom X
Danish	Autologe hæmatopoietisk celler, der er genetisk modificerede med en lentiviral vektor, der indeholder det humane *gp91(phox)* gen	Behandling af X-bundet, kronisk granulomatøs sygdom
Dutch	Autologe hematopoëtische cellen, genetisch gewijzigd met een lentivirale vector, die het humane *gp91(phox)* gen bevat	Behandeling van x-gebonden chronische granulomateuze ziekte
Estonian	Autoloogsed vereloome rakud, mida on geneetiliselt lentiviirus-vektoriga, mis sialdab inimese *gp91 (phox)* geeni, modifitseeritud	X-liitelise kroonilise granulomatooshaiguse ravi
Finnish	Lentivirusvektorilla geneettisesti modifioituja autologisia hematopoieettisia soluja, jotka sisältävät ihmisgeenin *gp91(phox)*	X-kromosomiin liittyvän kroonisen granulomatoottisen sairauden hoito
French	Cellules hématopoïétiques autologues, génétiquement modifiées par un vecteur lentiviral contenant le gène humain *gp91 (phox)*	Traitement de la granulomatose chronique liée à l'X
German	Autologe hämatopoetische Zellen, genetisch modifiziert mit einem lentiviralen-Vektor, der das humane *gp91(phox)* Gen enthält	Behandlung der X-chromosomal rezessiven chronischen Granulomatose
Greek	Αυτόλογα αιμοποιητικά κύτταρα γενετικά τροποποιημένα με φορέα λεντιιών, ο οποίος περιέχει το ανθρώπινο γονίδιο *gp91(phox)*	Θεραπεία της χρόνιας κοκκιωμάτωσης συνδεόμενη με το χρωμόσωμα Χ
Hungarian	Humán *gp91(phox)* gént tartalmazó lentivirális vektorral genetikailag módosított autológ hematopoietikus sejtek	X-kromoszómához kötődő krónikus granulómás betegség kezelése
Italian	Cellule staminali ematopoietiche autologhe, geneticamente modificate con vettore	Trattamento della X-linked granulomatosi cronica

[1] At the time of designation

Language	Active ingredient	Indication
	lentivirale contenente il gene umano *gp91 (phox)*	
Latvian	Autologas hematopoētiskās šūnas, ģenētiski modificētas ar lentivīrusa vektoru, kas satur cilvēka *gp91(phox)* gēnu	X-saistītās hroniskās granulomatozes ārstēšana
Lithuanian	Autologinės hematopoetinės ląstelės, genetiškai modifikuotos lentivirusiniu vektoriumi, pernešančiu žmogaus *gp91 (phox)* geną	Su X chromosoma susijusios lėtinės granulomatozės gydymas
Maltese	Ċelluli ematopojetiċi awtologi, ġeneralment modifikati b'vettur lentivirali li fih il-ġene uman *gp91(phox)*	Kura tal-marda granulomatu kronika X-kollegata
Polish	Autologiczne hematopoetyczne komórki zmodyfikowane genetycznie za pomocą wektora lentiwirusowego zawierającego gen ludzki *gp91 (phox)*	Leczenie przewlekłej choroby ziarniniakowej sprzężonej z chromosomem X
Portuguese	Células hematopoiéticas autólogas, geneticamente modificadas com um vector lentiviral que contém o gene humano *gp91(phox)*	Tratamento da doença granulomatosa crónica ligada ao cromossoma X
Romanian	Celule hematopoietice autologe, modificate genetic cu un vector lentiviral care conţine gena umană *gp91(phox)*	Tratamentul granulomatozei cronice X-linkate
Slovak	Autológne hematopoetické bunky geneticky modifikované pomocou lentivírusového vektora obsahujúceho ľudský gén *gp91(phox)*	Liečba chronickej granulomatózy viazanej na chromozóm X
Slovenian	Avtologne krvotvorne celice, genetsko modificirane z lentivirusnim vektorjem, ki vsebuje človeški gen *gp91 (phox)*	Zdravljenje s kromosomom X povezane kronične granulomatozne bolezni
Spanish	Células hematopoyéticas autólogas, genéticamente modificadas con un vector lentiviral que contiene el gen humano *gp91(phox)*	Tratamiento de la enfermedad granulomatosa crónica ligada al cromosoma X
Swedish	Autologa hematopoetiska celler, genetiskt modifierade med en lentiviral vektor innehållande den humana *gp91 (phox)* genen	Behandling av X-kromosombunden kronisk granulomatös sjukdom
Norwegian	Autologe, hematopoetiske celler, genetisk modifiserte med en lentiviral vektor som inneholder det humane *gp91(phox)*-genet	Behandling av X-bundet, kronisk granulomatøs sykdom
Icelandic	Eigin blóðmyndandi frumur, erfðafræðilega breyttar með lentiveiru ferju sem inniheldur manna *gp91 (phox)* gen	Meðferð við X-tengdum langvinnum átfrumugalla