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Public summary of opinion on orphan designation

Human frataxin fused to TAT cell-penetrating peptide for the treatment of Friedreich's ataxia

On 21 August 2020, orphan designation EU/3/20/2328 was granted by the European Commission to YES Pharmaceutical Development Services GmbH, Germany, for human frataxin fused to TAT cell-penetrating peptide (also known as CTI-1601) for the treatment of Friedreich's ataxia.

What is Friedreich's ataxia?

Friedreich's ataxia is an inherited disease that causes a range of symptoms that worsen over time, including difficulty walking, inability to co-ordinate movements, muscle weakness, speech problems, damage to the heart muscle and diabetes.

Patients with Friedreich's ataxia do not have enough frataxin, a protein that regulates iron in mitochondria (energy-producing components of cells). As a result, iron builds up within the cells, which in turn results in the production of toxic forms of oxygen that damage cells in the brain, the spinal cord and nerves, as well as in the heart and pancreas.

Friedreich's ataxia is a debilitating and life-threatening disease because of the worsening of symptoms over time.

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

At the time of designation, Friedreich's ataxia affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 26,000 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 designation, no satisfactory methods were authorised in the EU for the treatment of Friedreich's ataxia. Different treatments were used to relieve the symptoms of the disease, such as medicines for diabetes and heart problems. Patients were also offered walking aids to allow them to

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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remain as independent as possible, and other devices to assist them with everyday tasks such as eating and taking care of themselves. Speech therapy and physiotherapy were also used.

How is this medicine expected to work?

This medicine is made up of frataxin, the protein lacking in patients with Friedreich's ataxia, linked to a peptide (a short chain of amino acids, the building blocks of proteins) called TAT which is capable of entering cells. Once in the cells, frataxin is transported to mitochondria, thus delivering additional frataxin to patients with Friedreich's ataxia. This is expected to stop or slow down the progression of the disease.

What is the stage of development of this medicine?

The effects of human frataxin fused to TAT cell-penetrating peptide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with Friedreich's ataxia were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of Friedreich's ataxia. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 16 July 2020, recommending the granting of this designation.

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

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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	Human frataxin fused to TAT cell-penetrating peptide	Treatment of Friedreich's ataxia
Bulgarian	Човешки фратаксин, фузиран с клетъчно-проникващ TAT пептид	Лечение на атаксия на Фридрайх
Croatian	Ljudski frataksin fuzioniran s peptidom TAT koji prodire u stanice i djeluje kao transaktivator transkripcije (TAT)	Liječenje Friedreichove ataksije
Czech	Lidský frataxin fúzovaný s TAT peptidem penetrujícím buňku	Léčba Friedrichovy ataxie
Danish	Humant frataxin fusioneret med cellepenetrerende TAT-peptid	Behandling af Friedreichs ataksi
Dutch	Humaan frataxine gefuseerd met een celpenetrerend TAT peptide	Behandeling van de ataxie van Friedreich
Estonian	Inimese frataksiiniga liidetud rakku sisenev TAT-peptiid	Friedreichi ataksia ravi
Finnish	Soluun penetroituvan TAT-peptidiin liitetty ihmisen frataksiini	Friedreichin ataksian hoito
French	Frataxine humaine couplée au peptide de pénétration cellulaire TAT	Traitement de l'ataxie de Friedreich
German	Menschliches Frataxin fusioniert mit dem zellpenetrienrenden TAT Peptid	Therapie der Friedreichschen Ataxie
Greek	Ανθρώπινη φραταξίνη συζευγμένη με κυτταροδιεισδυτικό πεπτίδιο TAT	Θεραπεία της αταξίας Friedreich
Hungarian	Sejtpenetráló transzkripciós transzaktivátor [TAT] peptiddel fuzionált humán frataxin	Friedreich ataxia kezelése
Italian	Fratassina umana fusa con un peptide TAT a penetrazione cellulare	Trattamento dell'atassia di Friedreich
Latvian	Ar šūnas penetrējošu *TAT* peptīdu sapludināts cilvēka frataksīns	Frīdreiha ataksijas ārstēšana
Lithuanian	Žmogaus frataksinas, sulietas su TAT, į ląsteles prasiskverbiančiu, peptidu	Fridreicho ataksijos gydymas
Maltese	Fratassin uman magħqud ma' peptide TAT (Transattivatur tat-traskrizzjoni) li jippenetra ċ-ċelloli	Kura tal-atassja ta' Friedreich
Polish	Ludzka frataksyna połączona fuzyjnie z peptydem TAT penetrującym komórkę	Leczenie ataksji Friedreicha
Portuguese	Frataxina humana acoplada com o péptido de penetração celular TAT	Tratamento da ataxia de Friedreich
Romanian	Frataxină umană fuzionată cu un peptid penetrant celular TAT	Tratamentul ataxiei Friedreich

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Ľudský frataxín fúzovaný s TAT peptidom penetrujúcim bunku	Liečba Friedreichovej ataxie
Slovenian	Humani frataksin, spojen s peptidom TAT, ki prehaja skozi celično membrano	Zdravljenje Friedreichove ataksije
Spanish	Frataxina humana fusionada a un péptido de penetración celular TAT	Tratamiento de la ataxia de Friedreich
Swedish	Humant frataxin fusionerat med cellpenetrerande TAT-peptid	Behandling av Friedreichs ataxi
Norwegian	Humant frataksin fusjonert med cellepenetrerende TAT-peptid	Behandling av Friedreichs ataksi
Icelandic	Mannafrataxín sameinað TAT-peptíði sem kemst inn í frumur	Meðferð arfgengs mænuslingurs