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Public summary of opinion on orphan designation

C1 esterase inhibitor (human) for treatment in solid organ transplantation

On 14 December 2018, orphan designation (EU/3/18/2114) was granted by the European Commission to Shire Pharmaceuticals Ireland Limited, Ireland, for C1 esterase inhibitor (human) for treatment in solid organ transplantation.

What is solid organ transplantation?

Solid organ transplantation is a surgical procedure in which a diseased organ, such as the heart, lungs, liver or kidney, is replaced with an organ from a donor.

Transplantation is a very complex procedure. During transplantation, the organ to be transplanted can become damaged because of the interruption and restoration of blood supply to the organ. In addition, graft rejection can occur after transplantation when the patient's body rejects the transplanted organ. Graft rejection is caused by the patient's immune system (the body's natural defences) recognising the transplanted graft as 'foreign' and attacking it.

These complications can be debilitating and life-threatening because they may result in the transplanted organ not working properly.

What is the estimated number of patients receiving solid organ transplants?

At the time of designation, approximately 1 in 10,000 people in the European Union (EU) were undergoing solid organ transplantation every year. This was equivalent to a total of around 52,000 people per year[*], and is below the ceiling for orphan designation. 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, several medicines were authorised in the EU to treat graft rejection in solid organ transplantation. These include antibodies such as antilymphocyte immunoglobulin and thymoglobulin, medicines that suppress the immune process such as azathioprine, ciclosporin,

[*]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 (European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 517,400,000 (Eurostat 2018).

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mycophenolate mofetil and tacrolimus, and corticosteroids such as prednisolone or methylprednisolone.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients undergoing solid organ transplantation. Initial studies in patients with a kidney transplant suggest that adding the medicine to standard treatment to control rejection can improve the functioning of the transplanted organ. 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?

C1 esterase inhibitor is a natural protein extracted from human blood that helps to control the action of various enzymes and processes, including the complement system. The complement system is made up of a group of proteins in the blood that help the immune system to work. The complement system plays a critical role in the development of graft rejection. Giving additional C1 esterase inhibitor to patients after solid organ transplantation is expected to reduce the action of the complement system, and so help reduce the likelihood of the transplanted organ being rejected.

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 the medicine in patients who have undergone solid organ transplantation were ongoing.

The medicine has been authorised in the EU for several years for the treatment and prevention hereditary angioedema, under the name Cinryze.

At the time of submission, the medicine was not authorised anywhere in the EU for treatment in solid organ transplantation 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 8 November 2018 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:

Contact details of the current sponsor for this orphan designation can be found on the 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	C1 esterase inhibitor (human)	Treatment in solid organ transplantation
Bulgarian	Човешки C1-естеразен инхибитор	Лечение при трансплантация на солиден орган
Croatian	Inhibitor C1-esteraze (ljudski)	Liječenje u transplantaciji solidnih organa
Czech	Humánní inhibitor C1-esterázy	Léčba pro transplantaci solidních orgánů
Danish	Human C1-esteraseinhibitor	Behandling i organ transplantation
Dutch	C1-esterase inhibitor (humaan)	Behandeling bij soliede orgaantransplantatie
Estonian	Inimese C1-esteraasi inhibiitor	Kasutamiseks elundite siirdamise ravis
Finnish	Ihmisen C1-esteraasin estäjä	Hoito kiinteän elimen siirron yhteydessä
French	Inhibiteur de la C1-estérase (humaine)	Traitement pour la transplantation d'organes solides
German	C1-Esterase Inhibitor (human)	Behandlung in Organtransplantation
Greek	Αναστολέας της C1-εστεράσης (ανθρώπινος)	Θεραπεία στη μεταμόσχευση συμπαγών οργάνων
Hungarian	Humán C1-észteráz-inhibitor	Szervtranszplantáció esetén alkalmazandó
Italian	Inibitore della C1-esterasi umano	Trattamento nel trapianto di organi solidi
Latvian	C1 esterāzes inhibitors (cilvēka)	Ārstēšanai norobežoto orgānu transplantācijā
Lithuanian	C1 esterazės inhibitorius (žmogaus)	Transplantacijos parenchiminiame organe gydymas
Maltese	Inibitur ta' C1-esteraży tal-bniedem	Kura fi trapjant ta' organi solidi
Polish	Inhibitor ludzkiej C1-esterazy	Leczenie w przebiegu transplantacji organów
Portuguese	Inibidor da esterase C1 humana	Tratamento em transplante de órgãos sólidos
Romanian	Inhibitor al C1-esterazei umane	Tratament în transplantul de organe solide
Slovak	Ľudský inhibítor C1-esterázy	Liečba pri transplantácii celého orgánu
Slovenian	Humani inhibitor C1-esteraze	Zdravljenje pri transplantaciji organov
Spanish	Inhibidor de la C1 esterasa humano	Tratamiento del transplante de organo solido
Swedish	human C1-esterashämmare	Behandling vid organtransplantation
Norwegian	C1-esterasehemmer (human)	Behandling ved transplantasjon av solide organer
Icelandic	Manna C1-esterasa hemill	Meðferð við líffæraígræðslu

[1] At the time of designation