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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant homodimer of the human annexin V for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation

First publication	31 January 2012
Rev.1: sponsor's change of address	12 June 2013
Rev.2: withdrawal from the Community Register	21 March 2014

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.

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in February 2014 on request of the Sponsor.

On 11 January 2012, orphan designation (EU/3/11/946) was granted by the European Commission to Astellas Pharma Europe B.V., the Netherlands, for recombinant homodimer of the human annexin V for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation.

What is ischaemia/reperfusion injury associated with solid organ transplantation?

Ischaemia and reperfusion injury are problems that can occur to transplant organs as a result of being preserved during the time between donation and transplant. In the course of a transplant, the organ to be transplanted (the 'graft') needs to survive outside the body with no blood supply for a short while. This decrease in blood supply, if prolonged, can cause damage to the organ because of the lack of oxygen and nutrients, a condition called ischaemia. When the graft is attached to the recipient's blood circulation, the restoration of blood supply to the organ (reperfusion) can cause inflammation and damage to the organ, known as reperfusion injury. These processes increase the risk of the graft not working or being rejected by the recipient.

Because ischaemia/reperfusion injury in solid organ transplantation impairs the functioning of the graft, it is a life-threatening condition for the recipient of the graft.

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What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of ischaemia/reperfusion injury associated with solid organ transplantation was estimated to be approximately 0.6 people in 10,000 in the European Union (EU). This was equivalent to a total of around 31,000 people[*], which 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 methods of prevention are available?

At the time of designation, methods used to reduce the effects of ischaemia included storage of the organ in cold conditions in special preservation solutions. Two such solutions were authorised for organ preservation in some countries of the EU at the time of designation.

The sponsor has provided sufficient information to show that recombinant homodimer of the human annexin V might be of significant benefit for patients at risk of ischemia/reperfusion injury associated with solid organ transplantation because it works in a different way to existing methods and early studies indicate it may improve the prevention of this condition. 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 of a protein, annexin V, which is expected to work as an anticoagulant (a substance that prevents the blood from clotting). Since the formation of blood clots can occur during ischemia/reperfusion injury, this medicine is expected to prevent damage to the graft.

The medicine is produced by a method known as 'recombinant DNA technology': it is made by a bacterium that has received a gene (DNA), which makes it able to produce the medicine.

What is the stage of development of this medicine?

The effects of recombinant homodimer of the human annexin V have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with recombinant homodimer of the human annexin V in patients at risk of ischaemia/reperfusion injury associated with solid organ transplantation were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation. Orphan designation of the medicine had been granted in the United States of America for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 November 2011 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	Recombinant homodimer of the human annexin V	Prevention of ischaemia/reperfusion injury associated with solid organ transplantation
Bulgarian	Рекомбинантен хомодимер на човешки анексин V	Превенция на исхемия/реперфузия увреда, свързана с трансплантация на плътни органи.
Czech	Rekombinantní homodimer lidského annexinu V	Prevence ischemie/ reperfuzního poškození u transplantace solidních orgánů
Danish	Rekombinant homodimer af det humane annexin V	Prævention af den iskæmi/reperfusionsskade associeret med transplantation af solide organer
Dutch	Recombinant homodimeer van het humane annexine V	Preventie van ischemie- / reperfusieletsel geassociëerd aan soliede orgaantransplantatie
Estonian	Inimese anneksiin V rekombinantne homodimeer	Soliidorganite siirdamisega seotud isheemia/reperfusioonvigastuse ennetamine
Finnish	Ihmisen anneksiini-V:n rekombinantti homodimeeri	Iskemia-/reperfuusiovaurion esto elinsiirtoleikkauksessa
French	Homodimère recombinant de l'annexine V humaine	Prévention des lésions d'ischémie-reperfusion associées aux transplantations d'organes solides
German	Rekombinantes Homodimer des humanen Annexin V	Prävention von Ischämie-/Reperfusions-Syndromen bei Transplantation solider Organe
Greek	Ανασυνδυασμένο ομοδιμερές της ανθρώπινης αννεξίνης V	Πρόληψη της ισχαιμίας/ τραυματισμού λόγω επαναιμάτωσης που συσχετίζεται με τη μεταμόσχευση συμπαγών οργάνων
Hungarian	A humán annexin V rekombináns homodimerje	Szervátültetéssel összefüggő ischemiás/reperfúziós károsodás megelőzése
Italian	Omodimero ricombinante dell'annexina V umana	Prevenzione del danno da ischemia/riperfusione associato al trapianto di organi solidi
Latvian	Cilvēka aneksīna V rekombinants homodimērs	Išēmisko/reperfūzijas bojājumu profilakse saistībā ar orgānu transplantāciju
Lithuanian	Žmogaus aneksino V rekombinantinis homodimeras	Išemijos / reperfuzijos pažeidimo prevencija, susijusi su parenchiminių organų transplantacija
Maltese	Homodimer rikombinanti ta' annexin V uman	Prevenzjoni tad-dannu minn iskemija/riperfusjoni assoċjat mat-trapjant ta' organi solidi
Polish	Rekombinowany homodimer ludzkiej aneksyny V	Zapobieganie uszkodzeniu narządu spowodowanego niedokrwieniem/reperfuzją związanym z przeszczepem narządów litych
Portuguese	Homodímero recombinante de anexina V humana	Prevenção da lesão de isquémia/reperfusão associada ao transplante de órgãos sólidos
Romanian	Homodimer recombinant al anexinei V umane	Prevenirea leziunilor de ischemie /reperfuzie asociate cu transplantul de organe solide
Slovak	Rekombinantný homodimér ľudského anexínu V	Prevencia ischemicko-reperfúzneho poškodenia súvisiaceho s postupom pri transplantácii solídneho orgánu

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Rekombinantni homodimer človeškega aneksina V	Preprečevanje ishemične/reperfuzijske poškodbe, povezane s presaditvijo parenhimskih organov
Spanish	Homodímero recombinante de la anexina V humana	Prevención del daño por isquemia/reperfusión asociado al transplante de órganos sólidos
Swedish	Rekombinant homodimer av humant annexin V	Förebyggande av ischemia/reperfusionsskada i samband med organtransplantation
Norwegian	Rekombinant homodimer av humant annexin V	Forebygging av iskemi/reperfusjonsskade forbundet med solid organ-transplantasjon
Icelandic	Raðbrigða einsleit tvíliða manna annexíns V	Forvörn gegn blóðþurrðar/endurblóðvæðingar skaða í tengslum við líffæraígræðslu