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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human minibody against complement component C5 fused with RGD-motif for the prevention of the ischaemia/reperfusion injury associated with solid organ transplantation

First publication	24 June 2009
Rev.1: administrative update	8 November 2010
Rev.2: sponsor's name and address change	20 January 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.	

On 20 January 2009, orphan designation (EU/3/08/604) was granted by the European Commission to Adienne S.r.l., Italy, for recombinant human minibody against complement component C5 fused with RGD-motif for the prevention of the ischaemia/reperfusion injury associated with solid organ transplantation.

In January 2014, ADIENNE S.r.l. changed name to ADIENNE S.r.l.S.U.

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

Ischaemia and reperfusion injury are problems that can occur during an organ 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 is called ischaemia, and, if prolonged, can cause damage to the organ because of the lack of oxygen and nutrients. When the graft is attached to the recipient's blood circulation, the restoration of blood supply to the organ can cause inflammation and damage to the organ (reperfusion injury). These processes increase the risk of the graft not working or being rejected by the recipient. Because ischaemia/reperfusion injury associated with solid organ transplantation is a threat to the survival of the graft, it is a life-threatening condition.

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

At the time of designation, ischaemia/reperfusion injury associated with solid organ transplantation affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than absolute number of patients with a thousand separator e.g. 10,000 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?

To prevent problems during organ transplant, the grafts are usually stored in cold conditions in solutions that reduce the effects of ischaemia. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that recombinant human minibody against complement component C5 fused with RGD-motif might be of potential significant benefit for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation, mainly because it has a new mechanism of action that could limit the damage to, and improve the function of transplanted grafts. 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 expected to work by limiting the activation of the 'complement' system and decreasing the damage caused to the graft. Complement is part of the immune system (the body's natural defences) and plays a role in the inflammation and damage caused by ischaemia and reperfusion injury.

The medicine is made up of two elements that have been fused together:

- a 'minibody' (an engineered antibody) that has been designed to attach itself to one of the proteins of the complement system called component C5;
- a 'RGD-motif molecule' which has been design to attach itself to the cells lining blood vessels.

The medicine is used on the graft while it is being stored. The medicine attaches itself to the blood vessels via the RGD-motif molecule. Once the graft is transplanted and the blood supply is connected, the minibody part of the medicine can attach itself to component C5 in the blood vessels if the complement system is activated. This may limit the activation of the complement system within the transplanted organ.

What is the stage of development of this medicine?

The evaluation of the effects of recombinant human minibody against complement component C5 fused with RGD-motif in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients receiving grafts at risk of developing ischaemia/reperfusion injury associated with solid organ transplantation had been started.

At the time of submission, recombinant human minibody against complement component C5 fused with RGD-motif was not authorised anywhere in the world for ischaemia/reperfusion injury associated

*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 504,800,000 (Eurostat 2009).

with solid organ transplantation or designated as 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 5 November 2008 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	Recombinant Human minibody against complement component C5 fused with RGD-motif	Prevention of the ischaemia/reperfusion injury associated with solid organ transplantation
Bulgarian	Рекомбинантно човешко минитяло срещу C5 компонента на комплемента	Превенция на исхемия/реперфузия увреда, свързана с трансплантация на плътни органи.
Czech	Rekombinantní lidská miniprotilátka proti C5 složce komplementu fuzovaná s RGD-motivem	Prevence ischemie/ reperfuzního poškození u transplantace solidních orgánů
Danish	Rekombinant humant antistoffragment mod komplement komponent C5 fusioneret med RGD-motiv	Prævention af den iskæmi/reperfusionsskade associeret med transplantation af solide organer
Dutch	Recombinant humaan minilichaam gericht tegen complement component C5 gefuseerd aan RGD-motief	Preventie van ischemie- / reperfusieletsel geassocieerd aan soliede orgaantransplantatie
Estonian	Komplemendi osa C5 vastane rekombinantne inimese minikeha, mis on liidetud RGD-motif.	Soliidorganite siirdamisega seotud isheemia/reperfusioonvigastuse ennetamine
Finnish	RGD-motiiviin kytketty rekombinantti humaani minivasta-aine komplementti komponentti C5:a vastaan	Iskemia-/reperfuusiovaurion esto elinsiirtoleikkauksessa
French	Minibody humain recombinant dirigé contre l'élément C5 du complément fusionné au motif RGD	Prévention des lésions d'ischémie-reperfusion associées aux transplantations d'organes solides
German	Humaner rekombinanter Minibody gegen den Komplementfaktor C5	Prävention (Vorbeugung) der Ischämie/Organperfusion verursacht durch die Transplantation solider Organe
Greek	Ανασυνδιασμενο ανθρώπινο μινίσωμα ενάντια στον παράγοντα C5 του συμπληρώματος συνδεδεμένου με RGD-μοτίβο	Πρόληψη της ισχαιμίας/ τραυματισμού λόγω επαναιμάτωσης που συσχετίζεται με τη μεταμόσχευση συμπαγών οργάνων
Hungarian	C5 komplement-komponens ellenes rekombináns humán minitest	Szervátültetéssel összefüggő ischemiás/reperfúziós károsodás megelőzése
Italian	Minianticorpo umano ricombinante diretto contro la componente C5 del complemento fuso con il motivo RGD	Prevenzione del danno da ischemia/riperfusione associato all'intervento di trapianto di organi solidi
Latvian	Rekombinantas cilvēka minivielas pret komplementa C5 komponenti saistītas ar RGD motīvu	Išēmisko/reperfūzijas bojājumu novēršana saistībā ar orgānu transplantāciju

[1] At the time of designation

Language	Active Ingredient	Indication
Lithuanian	Rekombinantinis žmogaus minikūnelis prieš komplemento komponentą C5, sulietas su RGD-motyvu	Išemijos / reperfuzijos pažeidimo prevencija, susijusi su parenchiminių organų transplantacija
Maltese	Minikorp uman rikombinanti kontra l-komponent Ċ5 tal-komplement mgħaqud mal-motif RGD	Prevenzjoni tad-dannu minn iskemija/riperfusjoni assoċjat mat-trapjant ta' organi solidi
Polish	Rekombinowane ludzkie miniciało przeciwko składowej dopełniacza C5 połączone z motywem RGD	Zapobieganie uszkodzeniu narządu spowodowanego niedokrwieniem/reperfuzją związanym z przeszczepem narządów litych
Portuguese	Minicorpo recombinante de origem humana anti- componente C5 do complemento fundido com o motivo RGD.	Prevenção da lesão de isquémia/reperfusão associada ao transplante de órgãos sólidos
Romanian	Minianticorp uman recombinant anti componenta C5 a complementului fuzionat cu motiv-RGD	Prevenirea leziunilor de ischemie /reperfuzie asociate cu transplantul de organe solide
Slovak	Rekombinantná ľudská miniprotilátka proti zložke komplementu C5 fúzovaný s RGD motívom	Prevencia ischemicko-reperfúzneho poškodenia súvisiaceho s postupom pri transplantácii solídneho orgánu
Slovenian	Rekombinantno humano minitelo proti sestavini komplementa C5, spojeni z motivom RGD	Preprečevanje ishemične/reperfuzijske poškodbe, povezane s presaditvijo parenhimskih organov
Spanish	Minianticuerpo recombinante humano fusionado con el motivo RGD contra el factor C5 del complemento	Prevención del daño por isquemia/reperfusión asociado al transplante de órganos sólidos
Swedish	Recombinant human minikropp riktat mot komplement komponenten C5 fusionerat med RGD-motiv	Förebyggande av ischemia/reperfusionsskada i samband med organtransplantation
Norwegian	Rekombinant humant antistoffragment mot komplementfaktor C5 fusert til RGD-motiv	Forebygging av iskemi/reperfusjonsskade forbundet med solid organ-transplantasjon
Icelandic	Raðbrigða manna mótefnabrot gegn komplementþætti C5	Forvörn gegn blóðþurrðar/endurblóðvæðingar skaða í tengslum við líffæraígræðslu.