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EMA/COMP/786789/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Allogeneic peripheral blood mononuclear cells induced to an early apoptotic state for the prevention of graft-versus-host disease

On 15 January 2015, orphan designation (EU/3/14/1426) was granted by the European Commission to Richardson Associates Regulatory Affairs Ltd, United Kingdom, for allogeneic peripheral blood mononuclear cells induced to an early apoptotic state for the prevention of graft-versus-host disease.

What is graft-versus-host disease?

Graft-versus-host disease (GvHD) is a complication that can affect patients who have received allogeneic haematopoietic (blood) stem-cell transplantation. This is a complex procedure used to treat diseases of the blood such as leukaemia (a cancer of the white blood cells), whereby a patient receives stem cells from a matched donor to help restore the bone marrow, which produces new blood cells.

In GvHD, the transplanted cells recognise the patient as 'foreign' and attack the patient's organs, such as the stomach, gut, skin and liver, leading to organ damage. GvHD may happen shortly after transplantation or later on, in which case a wider range of organs can be involved.

GvHD is a serious and life-threatening disease with a high mortality rate.

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 GvHD was estimated to be approximately 0.4 people in 10,000 in the European Union (EU)· This was equivalent to a total of around 20,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 511,100,000 (Eurostat 2014).

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What methods of prevention are available?

At the time of designation, several medicines were authorised in the European Union (EU) for the prevention of GvHD, such as cyclosporine and antilymphocyte immunoglobulins (ATG). Treatment aimed to reduce the activity of immune cells involved in GvHD, thereby reducing their ability to attack the patient's organs.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients at risk of GvHD because preliminary studies suggest that the medicine can prevent severe acute GvHD when compared with published data for other treatments. 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 an advanced medicine that belongs to the group called 'somatic cell therapy products'. These are medicines that contain cells or tissues that have been manipulated to change their biological characteristics so that they can be used to cure, diagnose or prevent a disease.

This medicine contains certain immune cells derived from the blood of the donors who provide the stem-cell transplant. These immune cells are treated in the laboratory to induce and maintain them in an early stage of apoptosis (cell death). These 'dying' cells are then injected into the patients before they are given the stem-cell transplant. The dying cells are expected to help 'shut down' the cells that recognise the patient's cells as 'foreign', thereby preventing the patient's cells from being attacked and reducing the risk of GvHD.

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 the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients at risk of GvHD were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of GvHD. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 December 2014 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

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	Allogeneic peripheral blood mononuclear cells induced to an early apoptotic state	Prevention of graft-versus-host disease
Bulgarian	Алогенни периферни кръвни мононуклеарни клетки, индуцирани до начално апоптотично състояние	Профилактика на болестта на присадката срещу приемателя
Croatian	Alogene mononuklearne stanice periferne krvi inducirane u rano stanje apoptoze	Prevencija reakcije presatka protiv primatelja
Czech	Alogenní mononukleární buňky periferní krve, indukované k časnému stavu apoptózy	Prevence onemocnění štěpu proti hostiteli
Danish	Allogene perifere mononukleære celler induceret til et tidligt apoptotisk tilstand	Forebyggelse af graft versus host reaktion
Dutch	Allogene perifere mononucleaire cellen geïnduceerd tot een vroege apoptotische toestand	Preventie van "graft versus host" ziekte
Estonian	Allogeensed perifeerse vere mononukleaarsed rakud, mis on indutseeritud varajasse apoptootilisse olekusse	*Graft versus host* haiguse preventsioon
Finnish	Allogeeniset veren mononukleaarisolut, jotka on indusoitu varhaiseen ohjelmoituun solukuolemaan	Käänteishyljintäreaktion esto
French	Cellules mononuclées allogéniques du sang périphérique induites à un état d'apoptose précoce	Prévention de la réaction du greffon contre l'hôte
German	Allogene periphere mononukleäre Blutzellen zu einem frühen apoptotischen Zustand induziert	Prävention der Graft-versus-Host-Reaktion
Greek	Αλλογενή μονοπύρηνα κύτταρα περιφερικού αίματος που έχουν επαωθεί σε πρώιμη αποπτωτική κατάσταση	Πρόληψη της αντίδρασης του μοσχεύματος
Hungarian	Korai apoptotikus állapotra indukált allogén perifériás mononukleáris vérsejtek	Graft-versus-host betegség megelőzése
Italian	Cellule allogeniche mononucleari del sangue periferico indotte ad uno stato apoptotico precoce	Prevenzione della reazione del trapianto contro l'ospite
Latvian	Alogēnas perifērās asins mononukleārās šūnas, kas inducētas agrīnā apoptozes stadijā	Saimnieka-transplantāta slimības novēršana
Lithuanian	Alogeninės periferinio kraujo mononuklearinės ląstelės, sužadintos ankstyvos apoptozės būsenoje	Transplantato atmetimo ligos prevencija
Maltese	Ċelluli mononukleari alloġeneiċi tad-demm periferali indotti għal stat apoptotiku bikri	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Allogeniczne komórki jednojądrzaste krwi obwodowej indukowane do wczesnego stadium apoptozy	Zapobieganie chorobie przeszczep przeciw gospodarzowi
Portuguese	Células mononucleares do sangue periférico alogénicas induzidas para um estado de apoptose precoce	Prevenção da doença do enxerto contra o hospedeiro
Romanian	Celulele mononucleare alogene din sângele periferic induse catre o stare apoptotica timpurie	Prevenirea bolii grefă contra gazdă
Slovak	Alogénne mononukleárne bunky periférnej krvi, indukované na skorý stav apoptózy	Prevencia reakcie štepu proti hostiteľovi
Slovenian	Alogenske mononuklerarne celice periferne krvi inducirane na zgodnje apoptotično stanje	Preprečevanje zavrnitvene reakcije pri presaditvi
Spanish	Células mononucleares de sangre periférica alogénicos inducidos a un estado de apoptosis temprana	Prevención de la enfermedad de injerto contra huésped
Swedish	Allogena perifera mononukleära blodceller inducerade till ett tidig apoptotisk tillstånd	Förebyggande av graft-värd host reaktion
Norwegian	Allogene perifere mononukleære blodceller indusert til en tidlig apoptotisk tilstand	Forebygging av graft-versus-host - reaksjon
Icelandic	Ósamgena útæðablóðs einkjarna blóðfrumur sem eru hvattar til snemmbærs stýrðs frumudauða ástands	Forvörn gegn hýsilssótt