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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Allogeneic bone-marrow-derived ex-vivo-expanded multipotent adult progenitor cells for the prevention of graft-versus-host disease

On 16 January 2014, orphan designation (EU/3/13/1233) was granted by the European Commission to ReGenesys BVBA, Belgium, for allogeneic bone-marrow derived ex-vivo expanded multipotent adult progenitor cells 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 such as leukaemia or multiple myeloma (cancers 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 less than 0.4 people in 10,000 in the European Union (EU). This was equivalent to a total of fewer than 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 512,200,000 (Eurostat 2013).

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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 allogeneic bone-marrow derived ex-vivo expanded multipotent adult progenitor cells might be of significant benefit for patients at risk of GvHD because preliminary results in experimental models suggest that the medicine can improve survival and initial observations in patients have shown a reduced frequency of severe GvHD. 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?

The medicine contains multipotent progenitor cells originally derived from the bone marrow of healthy donors and grown outside the body to increase their numbers. Multipotent progenitor cells are cells with the ability to develop into many other kinds of cells. Early studies indicate that these cells can prevent and regulate the inflammation caused when transplanted immune cells attack the host by restoring the body's normal control systems for such cells, thus preventing GvHD.

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, a clinical trial with the medicine in patients at risk of GvHD had completed.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of GvHD. Orphan designation of allogeneic bone-marrow derived ex-vivo expanded multipotent adult progenitor cells had been granted in the United States for the prevention of the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 December 2013 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	Allogeneic bone-marrow derived ex-vivo expanded multipotent adult progenitor cells	Prevention of graft-versus-host disease
Bulgarian	Алогенни, доразвити ex vivo мултипотентни прогениторни клетки, получени от костен мозък на възрастен.	Профилактика на болест на присадката срещу приемателя
Czech	Allogenní kostní dřeň ex-vivo expandovaná s multipotentními progenitorovými buňkami dospělých	Prevence onemocnění štěpu proti hostiteli
Croatian	Alogene multipotentne adultne progenitorske stanice podrijetla iz koštane srži	Prevencija reakcije presatka protiv primatelja
Danish	Allogen knoglemarv deriverede ex vivo formerede voksne multipotente progenitor celler	Forebyggelse af graft versus host reaktion
Dutch	Ex-vivo geëxpandeerde multipotente adulte progenitorcellen afgeleid uit allogeen beenmerg	Preventie van “graft versus host” ziekte
Estonian	Allogeensest luuüdist lähtuvad *ex-vivo* paljundatud multipotentsed täiskasvanud progenitoorsed rakud	*Graft versus host* haiguse preventsioon
Finnish	Allogeeniset, luuytimestä peräisin olevat, ex vivo -viljellyt multipotentit aikuiset esisolut	Käänteishyljintäreaktion esto
French	Cellules progénitrices multipotentes adultes, développées ex vivo, et derivées de moelle osseuse allogénique	Prévention de la réaction du greffon contre l'hôte
German	Aus dem Knochenmark gewonnene, allogene, ex vivo expandierte, multipotente Vorläuferzellen	Prävention der Graft-versus-Host-Reaktion
Greek	Αλλογενή πολυδύναμα προγονικά κύτταρα προερχόμενα από το μυελό των οστών και πολλαπλασιασμένα ex vivo	Πρόληψη της αντίδρασης του μοσχεύματος
Hungarian	Allogen csontvelőből származó ex-vivo tenyésztett multipotens felnőtt progenitor sejtek	Graft-versus-host betegség megelőzése
Italian	Cellule progenitrici multipotenti adulte derivate da midollo allogenico espanse ex-vivo	Prevenzione della reazione del trapianto contro l’ospite
Latvian	Alogēnas no kaulu smadzenēm iegūtas, *ex vivo* pavairotas multipotentas pieaugušas celmšūnas	Saimnieka-transplantāta slimības novēršana
Lithuanian	Alogeniniai kaulų čiulpai, išskirti ex vivo iš suaugusiojo multipotentinių pirminių ląstelių	Transplantato atmetimo ligos prevencija
Maltese	Ċelloli proġenituri adulti multipotenti imnisslin minn mudullun allogeniku mwassa’ ex vivo	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih
Polish	Allogeniczne wielofunkcyjne dorosłe komórki progenitorowe uzyskane ze szpiku kostnego namnożone ex vivo	Zapobieganie chorobie przeszczep przeciw gospodarzowi

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	Medula óssea alogénica derivada de células progenitoras adultas multipotentes expandidas ex-vivo	Prevenção da doença do enxerto contra o hospedeiro
Romanian	Celule progenitoare multipotente adulte derivate din maduva hematogenă alogenă multiplicate ex-vivo	Prevenirea bolii grefă contra gazdă
Slovak	Alogénne ex-vivo expandované multipotentné progenitorové bunky dospelých získané z kostnej drene	Prevencia reakcie štepu proti hostiteľovi
Slovenian	Alogene multipotentne matične celice kostnega mozga odraslih, ekspandirane ex vivo	Preprečevanje zavrnitvene reakcije pri presaditvi
Spanish	Células progenitoras adultas multipotentes derivadas de la médula ósea expandidas ex vivo	Prevención de la enfermedad de injerto contra huésped
Swedish	Allogena benmärgsderiverade, ex-vivo expanderade multipotenta vuxna progenitorceller	Förebyggande av graft-värd host reaktion
Norwegian	Allogene beinmargsderiverte ex-vivo ekspanderte multipotente adulte progenitorceller	Forebygging av graft-versus-host -reaksjon
Icelandic	Ósamgena fjölhæfar forstigs beinmergs frumur fullorðinna ræktaðar ex-vivo	Forvörn gegn hýsilssótt