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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Allogeneic bone marrow derived mesenchymal cells expanded *ex vivo* in synthetic media for the treatment of graft-versus-host disease

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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 7 June 2013, orphan designation (EU/3/13/1129) was granted by the European Commission to Cell2B Advanced Therapeutics, SA, Portugal, for allogeneic bone marrow derived mesenchymal cells expanded *ex vivo* in synthetic media for the treatment 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 affected by the condition?

At the time of designation, GvHD affected not more than 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 30,000 people*, and is below the ceiling for

*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. This represents a population of 509,000,000 (Eurostat 2013).

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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?

At the time of designation, several medicines were authorised in the European Union (EU) for GvHD, such as ciclosporin, antilymphocyte immunoglobulins (ATG) and corticosteroids. 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 with GvHD because early studies indicate that it might improve the treatment particularly of patients who do not respond to current 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 medicinal product 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.

The medicine is made of mesenchymal cells extracted from the bone marrow of a donor and grown in a laboratory. Mesenchymal cells are able to regulate the immune system. Once injected into the patient's blood, the mesenchymal cells are expected to reduce the activity of the immune cells involved in GvHD, reducing their ability to attack the patient's organs, thereby relieving the symptoms of the disease.

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 with GvHD were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for condition 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 17 April 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 mesenchymal cells expanded *ex vivo* in synthetic media	Treatment of graft-versus-host disease
Bulgarian	Алогенни, извлечени от костен мозък мезенхимни клетки, ex vivo експанзирани в синтетична среда	Лечение на реакция на присадката срещу приемателя
Czech	Alogenní mesenchymální buňky kostní dřeně expandované ex-vivo v syntetických mediích	Léčba reakce štěpu proti hostiteli
Danish	Allogene knoglemarvsderiverede mesenchymalceller ekspanderet ex vivo i syntetisk medium	Behandling af graft versus host reaktion
Dutch	Uit allogeen beenmerg afgeleide mesenchymale cellen, welke ex vivo in synthetisch media zijn geëxpandeerd.	Behandeling van graft versus host ziekte
Estonian	Allogeensest luuüdist lähtunud mesenhümaalsed rakud, mida on paljundatud *ex vivo* sünteetilises keskkonnas	Graft versus host haiguse ravi
Finnish	Allogeenisia, synteettisessä mediumissa ex vivo rikastettuja luuytimen mesenkymaalisia soluja	Käänteishyljintäreaktion hoito
French	Cellules mésenchymateuses dérivées de cellules souches allogéniques développées ex vivo sur milieu synthètique	Traitement de la réaction du greffon contre l'hôte
German	Allogene, aus dem Knochenmark stammende mesenchymale Zellen, die ex vivo in synthetischen Medien vermehrt wurden	Behandlung der Graft-versus-Host-Reaktion
Greek	Αλλογενή μεσεγχυματικά κύτταρα προερχόμενα από μυελό οστών, πολλαπλασιασμένα ex vivo σε συνθετικά μέσα.	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	Ex vivo szintetikus táptalajon szaporított allogén csontvelő eredetű mesenchimális sejtek	Graft-versus-host betegség kezelése
Italian	Cellule mesenchimali derivate da midollo osseo espanse in mezzo di coltura sintetico	Trattamento della reazione del trapianto contro l'ospite
Latvian	No allogēnām kaulu smadzenēm iegūtas un ex vivo attīstītas mezenteriālās šūnas	Saimnieka-transplantāta slimības ārstēšana
Lithuanian	Alogeninės iš kaulų čiulpų išskirtos mezenchiminės ląstelės, padaugintos sintetinėse terpėse ex vivo	Transplantato atmetimo ligos gydymas
Maltese	Ċelluli mesenkimali alloġeniċi imnissla minn mudullun mwassa' ex vivo f'sustanzi sintetiċi	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Allogeniczne komórki mezenchymatyczne szpiku po ekspansji w warunkach ex vivo w mediach syntetycznych	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Células mesenquimais derivadas da medula óssea alogênico expandidas *ex vivo*, em meio sintético	Tratamento da reacção do enxerto contra o hospedeiro
Romanian	Celule mezenchimale derivate din celule stem alogenice dezvoltate ex vivo pe medii sintetice	Tratamentul reacţiei grefei contra gazdei
Slovak	Alogénne mezenchýmové bunky odvodené z kostnej drene expandované ex vivo v syntetických médiách	Liečba reakcie štepu proti hostiteľovi
Slovenian	Alogene mezenhimske celice kostnega mozga spodbujene ex vivo v sintetičnem mediju	Zdravljenje bolezni presadka proti gostitelju
Spanish	Células mesenquimales alogénicas derivadas de la médula ósea expandidas ex vivo en medio sintético	Tratamiento de la enfermedad de injerto contra huésped
Swedish	Allogena benmärgsderiverade mesenchymala celler expanderade ex vivo i syntetiskt medium	Behandling av graft-värd host reaktion
Norwegian	Allogene beinmargsderiverte mesenkymale celler ekspandert ex vivo i syntetisk medium	Behandling av graft-versus-host -reaksjon
Icelandic	Ósamgena mesenkýmal beinmergsfrumur ræktaðar ex vivo í tilbúnu æti	Til meðferðar á hýsilssótt