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EMA/COMP/732370/2014
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 prevention of graft-versus-host disease

On 16 December 2014, orphan designation (EU/3/14/1388) 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 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 had 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 the condition?

At the time of designation, the number of people at risk of GvHD was less than 0.4 in 10,000 people 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).

### 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

*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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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 this medicine might be of significant benefit for patients at risk of GvHD because early studies showed that it reduced the frequency of GvHD in patients receiving haematopoietic stem-cell transplantation. 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 matched healthy donor and grown in a laboratory. Mesenchymal cells are able to regulate the activity of 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 the immune cells' ability to attack the patient's organs, thereby preventing 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 for the prevention of GvHD were planned.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of GvHD 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 13 November 2014 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 | Prevention of graft-versus-host disease |
| Bulgarian | Алогенни, извлечени от костен мозък мезенхимни клетки, ex vivo експанзирани в синтетична среда | Профилактика на болест на присадката срещу приемателя |
| Croatian | Alogene mezenhimalne stanice dobivene iz koštane srži umnožene ex vivo u sintetičnom mediju | Prevencija reakcije presatka protiv primatelja |
| Czech | Alogenní mesenchymální buňky kostní dřeně expandované ex-vivo v syntetických mediích | Prevence onemocnění štěpu proti hostiteli |
| Danish | Allogene knoglemarvsderiverede mesenchymalceller ekspanderet ex vivo i syntetisk medium | Forebyggelse af graft versus host reaktion |
| Dutch | Uit allogeen beenmerg afgeleide mesenchymale cellen, welke ex vivo in synthetisch media zijn geëxpandeerd. | Preventie van “graft versus host” ziekte |
| Estonian | Allogeensest luuüdist lähtunud mesenhümaalsed rakud, mida on paljundatud *ex vivo* sünteetilises keskkonnas | *Graft versus host* haiguse preventsioon |
| Finnish | Allogeenisia, synteettisessä mediumissa ex vivo rikastettuja luuytimen mesenkymaalisia soluja | Käänteishyljintäreaktion esto |
| French | Cellules mésenchymateuses dérivées de cellules souches allogéniques développées ex vivo sur milieu synthètique | Prévention de la réaction du greffon contre l'hôte |
| German | Allogene, aus dem Knochenmark stammende mesenchymale Zellen, die ex vivo in synthetischen Medien vermehrt wurden | Prävention der Graft-versus-Host-Reaktion |
| Greek | Αλλογενή μεσεγχυματικά κύτταρα προερχόμενα από μυελό οστών, πολλαπλασιασμένα ex vivo σε συνθετικά μέσα. | Πρόληψη της αντίδρασης του μοσχεύματος |
| Hungarian | Ex vivo szintetikus táptalajon szaporított allogén csontvelő eredetű mesenchimális sejtek | Graft-versus-host betegség megelőzése |
| Italian | Cellule mesenchimali derivate da midollo osseo espanse in mezzo di coltura sintetico | Prevenzione della reazione del trapianto contro l’ospite |
| Latvian | No allogēnām kaulu smadzenēm iegūtas un ex vivo attīstītas mezenteriālās šūnas | Saimnieka-transplantāta slimības novēršana |
| Lithuanian | Alogeninės iš kaulų čiulpų išskirtos mezenchiminės ląstelės, padaugintos sintetinėse terpėse ex vivo | Transplantato atmetimo ligos prevencija |
| 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 | Zapobieganie chorobie przeszczep przeciw gospodarzowi |
| Portuguese | Células mesenquimais derivadas da medula óssea alogênico expandidas *ex vivo*, em meio sintético | Prevenção da doença do enxerto contra o hospedeiro |
| Romanian | Celule mezenchimale derivate din celule stem alogenice dezvoltate ex vivo pe medii sintetice | Prevenirea bolii grefă contra gazdă |
| Slovak | Alogénne mezenchýmové bunky odvodené z kostnej drene expandované ex vivo v syntetických médiách | Prevencia reakcie štepu proti hostiteľovi |
| Slovenian | Alogene mezenhimske celice kostnega mozga spodbujene ex vivo v sintetičnem mediju | Preprečevanje zavrnitvene reakcije pri presaditvi |
| Spanish | Células mesenquimales alogénicas derivadas de la médula ósea expandidas ex vivo en medio sintético | Prevención de la enfermedad de injerto contra huésped |
| Swedish | Allogena benmärgsderiverade mesenchymala celler expanderade ex vivo i syntetiskt medium | Förebyggande av graft-värd host reaktion |
| Norwegian | Allogene beinmargsderiverte mesenkymale celler ekspandert ex vivo i syntetisk medium | Forebygging av graft-versus-host - reaksjon |
| Icelandic | Ósamgena mesenkýmal beinmergsfrumur ræktaðar ex vivo í tilbúnu æti | Forvörn gegn hýsilssótt |