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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ex vivo cultured human mesenchymal stromal cells for the prevention of graft rejection following solid organ transplantation

On 26 March 2014, orphan designation (EU/3/14/1253) was granted by the European Commission to iCell Science AB, Sweden, for ex vivo cultured human mesenchymal stromal cells for the prevention of graft rejection following solid organ transplantation.

What is graft rejection following solid organ transplantation?

Graft rejection following solid organ transplantation is a problem that can occur when the recipient's body rejects the transplanted organ. Graft rejection is caused by the patient's immune system (the body's natural defences) recognising the transplanted graft as 'foreign' and attacking it. This results in inflammation and damage to the organs.

Graft rejection following solid organ transplantation is a life-threatening condition because the transplanted organ may fail and because medication is required to suppress the patient's immune system, which can result in infections and malignancies.

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 graft rejection following solid organ transplantation was estimated to be not more than 0.9 people in 10,000 in the European Union (EU). This was equivalent to a total of not more than 46,000 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 to suppress the immune system in order to prevent rejection after transplantation were authorised in the EU. These include the antibodies basiliximab and

[*]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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antithymocyte immunoglobulin, calcineurin inhibitors such as ciclosporin or tacrolimus, azathioprine, mycophenolate mofetil and corticosteroids such as prednisolone or methylprednisolone.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients at risk of graft rejection following solid organ transplantation because early results suggest that combination with existing treatments improves the survival of transplanted organs compared with existing treatments alone and can reduce the need for medicines to suppress the immune system. 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 human mesenchymal stromal cells (hMSCs) that have been extracted from donor tissue and grown in a laboratory to increase their numbers. In the body, hMSCs help to regulate the immune system, reducing the activation and growth of cells responsible for attacking foreign bodies and encouraging the growth of other immune cells that can protect the transplanted tissue. By supplying additional hMSCs, the medicine is expected to reduce the immune system's attack on the graft, decreasing inflammation and damage to the graft and lowering the risk of graft rejection, and hence the need for other medicines to suppress the immune system.

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 at risk of graft rejection were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of graft rejection following solid organ transplantation 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 6 February 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	Ex-vivo-cultured human mesenchymal stromal cells	Prevention of graft rejection following solid organ transplantation
Bulgarian	Ex-vivo култивирани човешки мезенхимални стромни клетки	Предотвратяване на отхвърляне на присадката след трансплантация на солиден орган
Czech	Ex-vivo kultivované lidské mesenchymální buňky	Prevence rejekce štěpu po transplantaci solidního orgánu
Croatian	Ex-vivo uzgojene ljudske mezenhimalne stromalne stanice	Prevencija odbacivanja presatka nakon transplantacije solidnih organa
Danish	Ex-vivo dyrkede humane mesenkymale stromaceller	Forebyggelse af graftafstødning efter organtransplantation
Dutch	Ex-vivo gekweekte humane mesenchymale stromacellen	Preventie van transplantaatafstoting na soliede orgaantransplantatie
Estonian	*Ex-vivo* kultureeritud inimese mesenhümaalsed stroomirakud	Siirdorgani äratõukamise ennetamine pärast soliidorgani siirdamist
Finnish	Ihmisen ex vivo -kasvatetut mesenkymaaliset stroomasolut	Siirrännäisen hylkimisreaktion ehkäisy elinsiirron jälkeen
French	Cellules stromales mésenchymateuses humaines, cultivées ex vivo	Prévention du rejet de greffe suite à la transplantation d'organes solides
German	Ex vivo kultivierte humane mesenchymale Stromazellen	Prävention einer Abstoßungsreaktion nach Organtransplantation
Greek	Ex-vivo καλλιεργημένα ανθρώπινα μεσεγχυματικά στρωματικά κύτταρα	Πρόληψη της απόρριψης μοσχεύματος μετά την μεταμόσχευση στερεών οργάνων
Hungarian	Ex-vivo szaporított humán mesenchymális stroma sejtek	Szervtranszplantáció után a graft kilökődésé-megelőzése
Italian	Cellule stromali mesenchimali coltivate ex-vivo	Prevenzione del rigetto di trapianto in seguito a trapianto di organi solidi
Latvian	*Ex vivo* kultivētas cilvēka mezenhīmas stromas šūnas	Transplantāta atgrūšanas profilaksei pēc orgāna transplantācijas
Lithuanian	Žmogaus mezenchimos stromos ląstelės, kultivuotos *ex vivo*	Transplantato atmetimo prevencija po parenchiminio organo transplantacijos
Maltese	Ċelluli stromali mesenkimali umani mkabbra ex-vivo	Prevenzjoni ta' rifjut ta' trapjant wara trapjant ta' organu solidu
Polish	Ludzkie mezenchymalne komórki macierzyste zrębu namnożone *ex vivo*	Zapobieganie odrzucaniu przeszczepu po transplantacji narządów litych
Portuguese	Células mesenquimais do estroma humano cultivadas *ex-vivo*	Prevenção da rejeição de enxertos após transplante de órgãos sólidos
Romanian	Celule stromale mezenchimale umane cultivate ex- vivo	Prevenirea respingerii grefei după transplantul de organ solid
Slovak	Ľudské mezenchýmové stromálne bunky kultivované ex-vivo	Prevencia odvrhnutia štepu po orgánovej transplantácii

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Ex-vivo vzgojene človeške mezenhimske stromalne celice	Preprečevanje zavrnitve presadka po transplantaciji čvrstih organov
Spanish	Células mesenquimales del estroma humano cultivadas ex-vivo	Prevención del rechazo de injerto después de trasplante de órgano sólido
Swedish	Mänskliga mesenkymala stromaceller odlade ex vivo	Förebyggande av transplantatrejektion efter solid organtransplantation
Norwegian	Humane mesenkymale stromale celler dyrket ex vivo	Forebygging av transplantat-avstøting etter solid organ-transplantasjon
Icelandic	Manna mesenchýmal stróma frumur ræktaðar *ex vivo*	Til að koma í veg fyrir höfnun eftir líffæraígræðslu