2 June 2015
EMA/COMP/105743/2013 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Murine IgM monoclonal antibody binding to alpha beta T-cell receptor for the prevention of graft rejection following solid organ transplantation

First publication	26 March 2013
Rev.1: administrative update	2 June 2015

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 12 March 2013, orphan designation (EU/3/13/1113) was granted by the European Commission to CTI Clinical Trial and Consulting Services Europe GmbH, Germany, for murine IgM monoclonal antibody binding to alpha beta T-cell receptor 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'. 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 supress the patient's immune system, which can result in infections and malignancies.

What is the estimated number of at risk of graft rejection following solid organ transplantation?

At the time of designation, the number of patients at risk of organ graft rejection following solid organ transplantation was estimated to be not more than 0.9 people in 10,000 per year in the European

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Union (EU). This was equivalent to a total of not more than 46,000 people per year*, and is below the ceiling for orphan designation. 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 rabbit anti-human thymocyte immunoglobulin, which were used at time of transplantation.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit to patients at risk of graft rejection because early studies suggest it may be more effective than existing treatments. This assumption will have 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 a monoclonal antibody, a type of protein that has been designed to recognise and attach to a receptor called 'alpha beta T-cell receptor', which is present on the surface of cells of the immune system called alpha beta T-cells which are involved in the immune response following solid organ transplantation. Alpha beta T-cell receptor is responsible for identifying certain structures (antigens) produced by the transplanted organ as 'foreign', which initiates the immune response. By attaching to the alpha beta T-cell receptor, this medicine is expected to block its activity, making alpha beta T-cells unable to recognise the antigens. This is expected to reduce the immune reaction to the transplanted organ.

What is the stage of development of this medicine?

The effects of murine IgM monoclonal antibody binding to alpha beta T-cell receptor have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients who received a solid organ transplant were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for the prevention of graft rejection following solid organ transplantation. Orphan designation of the medicine had been granted in the United States of America for the prevention of this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 February 2013 recommending the granting of this designation.

*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.
At the time of designation, this represented a population of 512,200,000 (Eurostat 2013).

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:

CTI Clinical Trial and Consulting Services Europe GmbH
Schillerstrasse 1/15
89077 Ulm
Germany
Tel. +49 731 4000 8411
Fax +49 731 4000 8429
E-mail: info@ctifacts.com

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	Murine IgM monoclonal antibody binding to alpha beta T-cell receptor	Prevention of graft rejection following solid organ transplantation
Bulgarian	Мише IgM моноклонално антитяло, свързващо се с αβ Т-клетъчен рецептор	Предотвратяване на отхвърляне на присадката след трансплантация на солиден орган
Czech	Myší monoklonální protilátka IgM vážící se na αβ receptor T-buněk	Prevence rejekce štěpu po transplantaci solidního orgánu
Danish	Murint monoklonalt IgM-antistof, der binder til αβ T-celle-receptor	Forebyggelse af graftafstødning efter organtransplantation
Dutch	Murien IgM monoklonaal antilichaam welke bindt aan αβ T-celreceptor	Preventie van transplantaatafstoting na soliede orgaantransplantatie
Estonian	T-raku αβ-retseptoriga liituv hiire monokloonne IgM-antikeha	Siirdorgani äratõukamise ennetamine pärast soliidorgani siirdamist
Finnish	Hiiren monoklonaalinen IgM-luokan vasta-aine, joka sitoutuu T-solujen αβ –reseptoreihin	Siirrännäisen hylkimisreaktion ehkäisy elinsiirron jälkeen
French	Anticorps monoclonal IgM d'origine murine se liant au récepteur α/β des lymphocytes T	Prévention du rejet de greffe suite à la transplantation d'organes solides
German	Muriner monoklonaler IgM-Antikörper gegen αβ-T-Zellrezeptoren	Prävention einer Abstoßungsreaktion nach Organtransplantation
Greek	Μονοκλονικό IgM αντίσωμα ποντικού με πρόσδεση στον αβ υποδοχέα των Τ-κυττάρων	Πρόληψη της απόρρηψης μοσχεύματος μετά την μεταμόσχευση στερεών οργάνων
Hungarian	Az αβ T-sejt receptorhoz kötődő egér IgM monoklonális antitest	Szervtranszplantáció után a graft kilökődésének megelőzésére
Italian	Anticorpo monoclonale murino IgM che si lega al recettore α/β delle cellule T	prevenzione del rigetto di trapianto in seguito a trapianto di organi solidi
Latvian	Peļu IgM monoklonālā antiviela, kas saistās ar αβ T-šūnu receptoru	Transplantāta atgrūšanas profilaksei pēc orgāna transplantācijas
Lithuanian	Pelės IgM monokloninis antikūnas, susietas su αβ T ląstelės receptoriumi	Transplantato atmetimo prevencija po parenchiminio organo transplantacijos
Maltese	Antikorp monoklonali IgM tal-ġrieden li jintrabat ma' riċettur alfa beta taċ-ċelluli T	Prevenzjoni ta' rifjut ta' trapjant wara trapjant ta' organu solidu
Polish	Mysie przeciwciała monoklonalne IgM wiążące się z receptorem alfa-beta komórek T	Zapobieganie odrzucaniu przeszczepu po transplantacji narządów litych
Portuguese	Anticorpo monoclonal IgM murino que se liga ao receptor alpha/beta das células T.	Prevenção da rejeição de enxertos após transplante de órgãos sólidos

[1] At the time of designation

Language	Active ingredient	Indication
Romanian	Anticorp IgM monoclonal de origine murină cu legare de receptorul αβ al celulei T	Prevenirea respingerii grefei după transplantul de organ solid
Slovak	Myšacia monoklonálna IgM protilátka viažuca sa na αβ receptory T-lymfocytov	Prevencia odvrhnutia štepu po orgánovej transplantácii
Slovenian	Mišje monoklonsko protitelo IgM, ki se veže na receptor αβ limfocitov T	Preprečevanje zavrnitve presadka po transplantaciji čvrstih organov
Spanish	Anticuerpo monoclonal murino tipo IgM dirigido contra el receptor alfa-beta de las células T	Prevención del rechazo de injerto después de trasplante de órgano sólido
Swedish	Murin IgM monoklonal antikropp bindande till αβ T-cellsreceptor	Förebyggande av transplantatrejektion efter solid organtransplantation
Norwegian	Murint monoklonalt IgM-antistoff som bindes til en αβ T-cellereseptor	Forebygging av transplantat-avstøting etter solid organ-transplantasjon
Icelandic	Músa einstofna IgM mótefni sem binst alfa beta T-frumu viðtaka	Til að koma í veg fyrir höfnun eftir líffæraígræðslu