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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Eculizumab for the prevention of graft rejection following solid organ transplantation

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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 26 March 2014, orphan designation (EU/3/14/1254) was granted by the European Commission to Alexion Europe SAS, France, for eculizumab 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).

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

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 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 eculizumab might be of significant benefit for patients at risk of graft rejection following solid organ transplantation because early results suggest that use in combination with existing treatments improves the survival of transplanted organs compared with existing treatments alone. 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?

Eculizumab has been authorised in the EU as Soliris for the treatment of two rare genetic diseases, paroxysmal nocturnal haemoglobinuria and atypical haemolytic uraemic syndrome. It is a monoclonal antibody, a type of protein that has been designed to recognise and attach to a specific structure (called an antigen) that is found in the body. Eculizumab has been designed to attach to and block a protein called C5 that plays an important role in the complement system, part of the immune system. The complement system is involved in producing the inflammation and damage seen in graft rejection.

By attaching to the C5 complement protein, eculizumab is expected to block the activation of the complement system in patients who have undergone solid organ transplantation, thus limiting the development of inflammation and damage, and helping to prevent rejection of the graft.

What is the stage of development of this medicine?

The effects of eculizumab have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with eculizumab in patients at risk of graft rejection were ongoing.

At the time of submission, eculizumab was not authorised anywhere in the EU for prevention of graft rejection following solid organ transplantation or designated as an orphan medicine in 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.

*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 512,900,000 (Eurostat 2014).

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:

Alexion Europe SAS
1-15, avenue Edouard Belin
92500 Rueil-Malmaison
France
Tel. +33 1 47 32 36 21
Fax +33 1 47 10 24 46
E-mail: medicalinformation.europe@alxn.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	Eculizumab	Prevention of graft rejection following solid organ transplantation
Bulgarian	Екулизумаб	Предотвратяване на отхвърляне на присадката след трансплантация на солиден орган
Czech	Eculizumab	Prevence rejekce štěpu po transplantaci solidního orgánu
Croatian	Ekulizumab	Prevencija odbacivanja presatka nakon transplantacije solidnih organa
Danish	Eculizumab	Forebyggelse af graftafstødning efter organtransplantation
Dutch	Eculizumab	Preventie van transplantaatafstoting na soliede orgaantransplantatie
Estonian	Ekulizumab	Siirdorgani äratõukamise ennetamine pärast soliidorgani siirdamist
Finnish	Ekulitsumabi	Siirrännäisen hylkimisreaktion ehkäisy elinsiirron jälkeen
French	Eculizumab	Prévention du rejet de greffe suite à la transplantation d'organes solides
German	Eculizumab	Prävention einer Abstoßungsreaktion nach Organtransplantation
Greek	Εκουλιζουμάμπη	Πρόληψη της απόρριψης μοσχεύματος μετά την μεταμόσχευση στερεών οργάνων
Hungarian	Ekulizumab	Szervtranszplantáció után a graft kilökődésé-megelőzése
Italian	Eculizumab	Prevenzione del rigetto di trapianto in seguito a trapianto di organi solidi
Latvian	Ekulizumabs	Transplantāta atgrūšanas profilaksei pēc orgāna transplantācijas
Lithuanian	Ekulizumabas	Transplantato atmetimo prevencija po parenchiminio organo transplantacijos
Maltese	Eculizumab	Prevenzjoni ta' rifjut ta' trapjant wara trapjant ta' organu solidu
Polish	Ekulizumab	Zapobieganie odrzucaniu przeszczepu po transplantacji narządów litych
Portuguese	Eculizumab	Prevenção da rejeição de enxertos após transplante de órgãos sólidos
Romanian	Eculizumab	Prevenirea respingerii grefei după transplantul de organ solid
Slovak	Ekulizumab	Prevencia odvrhnutia štepu po orgánovej transplantácii
Slovenian	Ekulizumab	Preprečevanje zavrnitve presadka po transplantaciji čvrstih organov
Spanish	Eculizumab	Prevención del rechazo de injerto después de trasplante de órgano sólido
Swedish	Eculizumab	Förebyggande av transplantatrejektion efter solid organtransplantation
Norwegian	Ekulizumab	Forebygging av transplantat-avstøting etter solid organ-transplantasjon
Icelandic	Ekúlízúmab	Til að koma í veg fyrir höfnun eftir líffæraígræðslu

[1] At the time of designation