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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous bone marrow-derived mononuclear cell fraction for the treatment of thromboangiitis obliterans (Buerger's 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 20 September 2010, orphan designation (EU/3/10/775) was granted by the European Commission to t2cure GmbH, Germany, for autologous bone marrow-derived mononuclear cell fraction for the treatment of thromboangiitis obliterans (Buerger's disease).

What is thromboangiitis obliterans (Buerger's disease)?

Thromboangiitis obliterans, also known as Buerger's disease, is a disease in which the blood vessels become inflamed. Because of the inflammation, clots form within the blood vessels, blocking them and causing pain. The small blood vessels in the limbs (especially in the hands, legs and feet) are most often affected, and the lack of blood flow can cause skin ulcers (sores) and gangrene (decay and death of tissue). Ultimately, the limb may need to be amputated. Although the causes of the inflammation in thromboangiitis obliterans are not known, the disease is known to be closely linked to smoking.

Thromboangiitis obliterans is a long-term debilitating condition because of the development of ulcers and gangrene, and the risk of amputation.

What is the estimated number of patients affected by the condition?

At the time of designation, thromboangiitis obliterans affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 people*, and is below the

*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. At the time of designation, this represented a population of 506,300,000 (Eurostat 2010).



threshold 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 treatments are available?

At the time of designation, iloprost was authorised in some EU Member States for the treatment of advanced thromboangiitis obliterans. Other medicines were also used to control the symptoms of the disease such as pain, and to promote the healing of the skin ulcers. Vascular surgery (surgery on the blood vessels) was used in a small number of cases.

The sponsor has provided sufficient information to show that autologous bone marrow-derived mononuclear cell fraction might be of significant benefit for patients with thromboangiitis obliterans because it works in a different way to existing treatments and might act on the original underlying lesions causing the disease. 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?

Autologous bone marrow-derived mononuclear cell fraction is an advanced medicine 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.

Autologous bone marrow-derived mononuclear cell fraction is made of stem cells extracted from the patient's own bone marrow. Stem cells are cells that can develop into different types of cell. This medicine is expected to be injected directly into the patient's affected blood vessels, where the stem cells are expected to move towards the damaged areas and promote the growth of new blood vessels. This will improve the blood supply in these areas, relieving the symptoms of the disease.

What is the stage of development of this medicine?

The effects of autologous bone marrow-derived mononuclear cell fraction have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with autologous bone marrow-derived mononuclear cell fraction in patients with thromboangiitis obliterans were ongoing.

At the time of submission, autologous bone marrow-derived mononuclear cell fraction was not authorised anywhere in the EU for thromboangiitis obliterans. Orphan designation had been granted in the United States of America for thromboangiitis obliterans.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 2 June 2010 recommending the granting of this designation.

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 European Union) 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:

t2cure GmbH
Kennedyallee 93
60596 Frankfurt am Main
Germany
Telephone: + 49 69 7561 46 878
Telefax: + 49 69 7561 46 879
E-mail: info@t2cure.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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous bone marrow-derived mononuclear cell fraction	Treatment of thromboangiitis obliterans (Buerger's disease)
Bulgarian	Автоложна, моноклеарна клетъчна фракция, с костно-мозъчен произход.	Лечение на облитериращ тромбоангиит (Болест на Бюргер)
Czech	Mononukleární buněčná frakce autologní kostní dřeně	Léčba obliterující tromboangiitidy (Bürgerova choroba)
Danish	Autolog knoglemarvslideret mononukleær cellefraktion	Behandling af thromboangiitis obliterans (Buergers sygdom)
Dutch	Autologe mononucleaire cel-fractie verkregen uit beenmerg	Behandeling van thromboangiitis obliterans (Buerger's ziekte)
Estonian	Autoloogsest luuüdist lähtuvad mononukleaarsete rakkude fraktsioon	Oblitereeruva tromboangiidi (Buergeri haigus) ravi.
Finnish	Autologinen, luuytimeistä peräisin oleva, mononukleäärinen solufraktio	Thromboangitis obliteransin (Bürgerin tauti) hoito
French	Fractions cellulaires mononucléées autologues d'origine médullaire	Traitement de la thromboangéite oblitérante (maladie de Buerger)
German	Fraktion autologer, mononukleärer Zellen aus dem Knochenmark	Behandlung der Thrombangiitis obliterans (Morbus Winiwater-Buerger)
Greek	Κλάσμα μονοπύρηνων κυττάρων προερχόμενα από αυτόλογο μυελό οστών	Θεραπεία της αποφρακτικής θρομβοαγγειίτιδας (νόσος Buerger)
Hungarian	Autológ csontvelőből származó mononukleáris sejtfrakció	Thromboangiitis obliterans (Bürger-kór) kezelése
Italian	Frazione di cellule mononucleate derivata da midollo osseo autologo	Trattamento della tromboangioite obliterante (malattia di Buerger)
Latvian	No autologām kaulu smadzenēm atvasināta mononukleāro šūnu frakcija	Obliterējoša endarterīta (Bergera slimības) ārstēšana
Lithuanian	Mononuklearinių ląstelių frakcija, išgauta iš autologinių kaulų čiulpų	Obliteruojančio trombangito (Buerger liga) gydymas
Maltese	Frazzjoni ta' celluli mononukleari imnissla minn mudullun awtologuż	Kura tat-tromboangite obliterans (marda ta' Buerger)
Polish	Frakcja autogennych komórek jednojądrowych szpiku kostnego	Leczenie zakrzepowo-zarostowego zapalenie tętnic (choroby Buergera)
Portuguese	Fracção de células mononucleares derivadas de medula óssea autóloga	Tratamento da tromboangeíte obliterante (Doença de Buerger)
Romanian	Fracţiuni celulare mononucleare autologe derivate din măduva osoasă	Tratamentul trombangeitei obliterante (boala Búrger)
Slovak	Mononukleárna bunková frakcia z autológnej kostnej drene	Liečba obliterujúcej trombangiitídy (Bürgerovej choroby)
Slovenian	Frakcija mononuklearnih avtolognih celic kostnega mozga	Zdravljenje obliterantnega trombagiitisa (Buergerjeva bolezen)
Spanish	Fracción celular mononuclear derivada de médula ósea autóloga	Tratamiento de la tromboangeitis obliterante (enfermedad de Buerger)

¹ At the time of designation

Language	Active ingredient	Indication
Swedish	Autolog mononukleär cellfraktion från benmärg	Behandling av thromboangiitis obliterans (Buergers sjukdom)
Norwegian	Autolog mononukleær cellefraksjon fra beinmarg	Behandling av thromboangiitis obliterans (Buergers sykdom)
Icelandic	Samgena einkjarna frumu hluti unnið úr beinmerg	Meðferð við thromboangiitis obliterans (Bürgers sjúkdómi)