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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Adult human bone-marrow-derived, ex-vivo-expanded, pooled allogeneic mesenchymal stromal cells for treatment of thromboangiitis obliterans (Buerger's disease)

On 21 May 2015, orphan designation (EU/3/15/1499) was granted by the European Commission to Regulatory Resources Group Ltd, United Kingdom, for adult human bone-marrow derived, ex-vivo-expanded, pooled allogeneic mesenchymal stromal cells for 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 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).

*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 512,900,000 (Eurostat 2015).

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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 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 the medicine might be of significant benefit for patients with thromboangiitis obliterans because early studies show that the product reduces pain during rest and heals ulcers in patients with the condition. 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 made of cells, called mesenchymal stromal cells, extracted from the bone marrow of different adult donors, which are pooled together and grown in the laboratory. Mesenchymal stromal cells can produce several proteins important to regulate the immune system, control inflammation and the growth of cells. Although the mechanism by which the mesenchymal stromal cells in this medicine work is not fully known, the cells are expected to promote the growth of new blood vessels and tissue repair. This is expected to improve the blood supply in the limbs of patients with thromboangiitis obliterans, relieving the symptoms of 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 in patients with thromboangiitis obliterans were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for thromboangiitis obliterans 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 16 April 2015 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	Adult human bone-marrow-derived, ex-vivo-expanded, pooled allogeneic mesenchymal stromal cells	Treatment of thromboangiitis obliterans (Buerger's disease)
Bulgarian	Възрастни човешки костно-мозъчни алогенни мезенхимни стромални клетки, разширени ex-vivo	Лечение на облитериращ тромбоангиит (Болест на Бюргер)
Croatian	Združene, ex vivo umnožene, alogene mezenhimalne stromalne stanice podrijetla iz koštane srži odrasle osobe	Liječenje thromboangiitis obliteransa (Buergerove bolesti)
Czech	Izolované alogenní mezenchymální stromatické buňky, derivované z kostní dřeně dospělého člověka, rozšířené ex-vivo	Léčba obliterující tromboangiitidy(Bürgerova choroba)
Danish	Voksen, human knoglemarvafledt, ex-vivo udvidet, poolede allogene, mesenkymale, stromaceller	Behandling af thromboangiitis obliterans (Buergers sygdom)
Dutch	Uit adult humaan beenmerg afkomstige, ex-vivo geëxpandeerde, samengevoegde allogene mesenchymstromacellen	Behandeling van thromboangiitis obliterans (Buerger's ziekte)
Estonian	Täiskasvanu luuüdist pärinevad ex-vivo kasvatatud, ühendatud allogeensed mesenhümaalsed stroomarakud	Oblitereeruva tromboangiidi (Buergeri haigus) ravi
Finnish	Aikuisen ihmisen luuytimestä peräisin olevat, ex-vivo laajennetut, yhdistetyt allogeeniset mesenkymaaliset stroomasolut	Thromboangitis obliteransin (Bürgerin tauti) hoito
French	Cellules stromales mésenchymateuses allogéniques, derivées de moelle osseuse humaine, regroupées et développées ex-vivo	Traitement de la thromboangéite oblitérante (maladie de Buerger)
German	Aus adultem Knochenmark stammende, ex-vivo expandierte, gepoolte, allogene, mesenchymale Stammzellen	Behandlung der Thrombangiitis obliterans (Morbus Winiwater-Buerger)
Greek	Προερχόμενα εξ ανθρωπίνου ενηλίκου μυελού των οστών, πολλαπλασιασμένα ex-vivo, συγκεντρωμένα αλλογενή μεσεγχυματικά στρωματικά κύτταρα	Θεραπεία της αποφρακτικής θρομβαγγειίτιδας (νόσος Buerger)
Hungarian	A felnőtt emberi csontvelőből származó, ex-vivo expandált, egyesített allogén mesenchymalis stromális sejtek	Thromboangiitis obliterans (Bürger-kór) kezelésére
Italian	Cellule stromali mesenchimali allogeniche, derivate dal midollo osseo umano adulto, ragruppate e espanse ex-vivo	Trattamento della tromboangioite obliterante (malattia di Buerger)

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	No pieaugušo kaulu smadzenēm iegūtas, *ex-vivo* pavairotas, apkopotas alogēnas mezenhimālās stromas šūnas	Obliterējoša endarterīta (Bergera slimības) ārstēšana
Lithuanian	Iš suaugusio žmogaus kaulų čiulpų išskirtos, *ex-vivo* padaugintos, sukauptos alogeninės mezenchiminės stromos ląstelės	Obliteruojančio trombangito (*Buerger* liga) gydymas
Maltese	Ċelluli stromali mesenkimali alloġeniċi, imnisslin minn mudullun ta' adulti umani, miġburin flimkien u mwassa' ex-vivo	Kura tat-tromboanġite obliterans (marda ta' Buerger)
Polish	Koncentrat allogenicznych mezenchymalnych komórek zrębowych uzyskanych ze szpiku kostnego dorosłego dawcy, namnożonych *ex vivo*	Leczenie zakrzepowo-zarostowego zapalenie tętnic (choroby Buergera)
Portuguese	Células alogénicas mesenquimais estromais, derivadas de medula óssea humana adulta, agregadas e expandidas ex-vivo	Tratamento da tromboangeíte obliterante (Doença de Buerger)
Romanian	Celule stromale mezenchimale alogenice derivate din măduva osoasă umană adultă, regrupate şi multiplicate ex-vivo	Tratamentul trombangeitei obliterante (boala Bűrger)
Slovak	Združené allogénne mezenchýmové stromálne bunky pochádzajúce z kostmej drene dospelého človeka, expandované ex vivo	Liečba obliterujúcej trombangiitídy (Bürgerovej choroby)
Slovenian	Zbirne alogene mezenhimske matične celice iz kostnega mozga odraslih oseb, ex-vivo razširjeno	Zdravljenje obliterantnega trombagiitisa (Buergerjeva bolezen)
Spanish	Células estromales mesenquimales alogénicas agrupadas, derivadas de la médula ósea de adultos humanos, expandidas ex-vivo	Tratamiento de la tromboangeitis obliterante (enfermedad de Buerger)
Swedish	poolade humana, allogena benmärgsderiverade mesenchymala stromal celler från vuxna expanderade ex-vivo	Behandling av thromboangiitis obliterans (Buergers sjukdom)
Norwegian	Humane benmarg-avledede, ex-vivo ekspanderte, samlede allogene mesenkymale stromale celler fra voksne	Behandling av thromboangiitis obliterans (Buergers sykdom)
Icelandic	Beinmergsfrumur sem fjölgað er ex-vivo og blandað við ósamgena mesenkímal stróma frumur fullorðinna	Meðferð við thromboangiitis obliterans (Bürgers sjúkdómi)