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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sirolimus for the prevention of arteriovenous access dysfunction in patients undergoing surgical creation of an arteriovenous access for haemodialysis

On 13 November 2013, orphan designation (EU/3/13/1204) was granted by the European Commission to S-Cubed Limited, United Kingdom, for sirolimus for the prevention of arteriovenous access dysfunction in patients undergoing surgical creation of an arteriovenous access for haemodialysis.

What is arteriovenous access dysfunction?

Arteriovenous access dysfunction occurs when blood vessels that are used for haemodialysis become blocked. Haemodialysis is a technique used to clear waste products (such as urea) from the blood of patients whose kidneys are not working properly, since their kidneys are not able to perform this function.

Patients undergoing haemodialysis usually have two needles inserted into a blood vessel in the arm, one to draw the blood out, and one to return the purified blood back to the patient. This blood vessel is surgically prepared beforehand to allow a good blood flow. However, following the surgery a narrowing can develop which can block the access to the blood vessels. If the narrowing becomes severe, the access closes and haemodialysis can no longer be carried out effectively.

Arteriovenous access dysfunction is a long-term debilitating and potentially life-threatening condition because it makes the dialysis less effective and can lead to further damage to the kidneys.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients undergoing haemodialysis at risk of arteriovenous access dysfunction was estimated to be between 2.9 and 4.4 in 10,000 people in the European Union (EU). This was equivalent to between 149,000 and 225,000 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 512,200,000 (Eurostat 2013).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What treatments are available?

At the time of designation, there were no satisfactory methods authorised in the EU for the prevention of arteriovenous access failure in haemodialysis patients. Some patients with arteriovenous access dysfunction were treated with angioplasty (a procedure to unblock blood vessels) to improve access or surgery to create a new access.

How is this medicine expected to work?

This medicine is an implant that contains sirolimus, an immunosuppressant medicine that has been used for several years to prevent organ rejection following a transplant.

For the prevention of arteriovenous access dysfunction, this medicine is expected to be implanted around the blood vessels that have been prepared for haemodialysis. The implant is expected to deliver sirolimus to the walls of the blood vessels where it blocks the action of 'mammalian target of rapamycin' (mTOR), a protein involved in the growth of muscle cells within the blood vessel wall. By blocking this process, sirolimus is expected to reduce or prevent the growth of the muscle cells that leads to narrowing and blockage of the blood vessels, helping to keep them open.

What is the stage of development of this medicine?

The effects of this 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 undergoing haemodialysis were completed and additional studies were planned.

At the time of submission, the medicine was not authorised anywhere in the EU for preventing arteriovenous access dysfunction in patients undergoing surgical creation of an arteriovenous access for haemodialysis. Orphan designation of the medicine been granted in the United States for the 'prevention of arteriovenous (AV) fistula or AV graft failure in patients with end stage renal disease, receiving haemodialysis or preparing for haemodialysis'.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 October 2013 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:

S-Cubed Limited
99 Park Drive
Milton Park
Abingdon
Oxfordshire OX14 4RY
United Kingdom
Tel. +44 123 5854 055
Fax +44 123 5854 001
E-mail: info@s-cubed.co.uk

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	Sirolimus	Prevention of arteriovenous access dysfunction in patients undergoing surgical creation of an arteriovenous access for haemodialysis
Bulgarian	Сиролимус	Профилактика на дисфункция на артериовенозен достъп при пациенти, подлагащи се на хирургично създаване на артериовенозен достъп за хемодиализа
Czech	Sirolimus	Prevence selhání arteriovenózního vstupu u pacientů podstupujících implantaci arteriovenózního hemodialyzačního vstupu
Croatian	Sirolimus	Prevencija disfunkcije arteriovenskog pristupa u bolesnika koji su podvrgnuti operativnom kreiranju arteriovenskog pristupa za hemodijalizu
Danish	Sirolimus	Forebyggelse af dysfunktion i arteriovenøs adgang hos patienter, der gennemgår kirurgisk dannelse af arteriovenøs adgang til hæmodialyse
Dutch	Sirolimus	Preventie van het falen van de arterioveneuze toegang in patiënten bij wie chirurgisch een arterioveneuze toegang voor hemodialyse wordt gecreëerd
Estonian	Siroliimus	Arteriovenoosse juurdepääsu häirete ärahoidmine patsientidel, kellele luuakse kirurgilisel teel arteriovenoosse juurdepääs hemodialüüsiks
Finnish	Sirolimuusi	Verisuoniyhteyden toimintahäiriön ehkäisy, kun potilaalla on kirurgisesti rakennettu verisuoniyhteys hemodialyysihoitoa varten
French	Sirolimus	Prévention du dysfonctionnement de l'accès artério-veineux chez les patients subissant une intervention chirurgicale visant à créer un accès artério-veineux pour l'hémodialyse
German	Sirolimus	Prävention einer Störung des arteriovenösen Gefäßzugangsbei Patienten, denen chirurgisch ein arteriovenöser Gefäßzugang für die Hämodialyse angelegt wird
Greek	Σιρόλιμους	Πρόληψη δυσλειτουργίας αγγειακής προσπέλασης σε ασθενείς που υποβάλλονται σε χειρουργική δημιουργία αγγειακής προσπέλασης για αιμοδιάλυση
Hungarian	Szirolimusz	Sebészi úton kialakított arteriovenozus fisztula dysfunkciójának megelőzése haemodializisre szoruló betegeknél
Italian	Sirolimus	Prevenzione di disfunzioni nella fistola arterovenosa in pazienti sottoposti a creazione chirurgica di una fistola arterovenosa per emodialisi
Latvian	Sirolimus	Arteriovenozās pieejas disfunkcijas novēršana pacientiem, kuriem tiek ķirurģiski veidota arteriovenozā fistula hemodialīzei
Lithuanian	Sirolimuzas	Arterioveninės jungties disfunkcijos prevencija pacientams, kuriems chirurgiškai formuojama arterioveninė jungtis hemodializei

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Sirolimus	Prevenzjoni ta' taħsir ta' funzjoni tal-aċċess arterjovenuż f'pazjenti li jkun qiegħed jinħolqilhom kirurġikament aċċess arterjovenuż għall-emodijalisi
Polish	Syrolimus	Zapobieganie dysfunkcjom dostępu tętniczo-żylnego u pacjentów poddawanych chirurgicznemu wytworzeniu dostępu tętniczo-żylnego w celu przeprowadzania hemodializy
Portuguese	Sirolimus	Prevenção de disfunção do acesso arteriovenoso em doentes submetidos a criação cirúrgica de um acesso arteriovenoso para hemodiálise
Romanian	Sirolimus	Prevenirea disfuncţiei căii de acces arterio-venoase la pacienţii supuşi unei intervenţii chirurgicale de realizare a unei căi de acces arterio-venoase pentru hemodializă
Slovak	Sirolimus	Prevencia dysfunkcie arteriovenózneho vstupu u pacientov s chirurgicky vytvoreným arteriovenóznym hemodialyzačným vstupom
Slovenian	Sirolimus	Preprečevanje motenega delovanja arterijsko venskega pristopa pri bolnikih s kirurško ustvarjenim arterijsko venskim pristopom za hemodializo
Spanish	Sirolimus	Prevención de la disfunción del acceso arteriovenoso en los pacientes sometidos a la creación quirúrgica de un acceso arteriovenoso para la hemodiálisis
Swedish	Sirolimus	Förebyggande av arteriovenös tillgångsdysfunktion hos patienter som genomgår kirurgiskt anläggande av en arteriovenös tillgång för hemodialys
Norwegian	Sirolimus	Forebygging av arteriovenøs tilgangsdysfunksjon hos pasienter som gjennomgår kirurgisk anlegging av en arteriovenøs tilgang for hemodialyse
Icelandic	Sírólímus	Til að koma í veg fyrir lokun á samtengingu slagæðar og bláæðar hjá sjúklingum sem gangast undir skurðaðgerð til að veita æðaaðgengi fyrir blóðskilun