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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Human autologous mesenchymal adult stem cells extracted from adipose tissue for the treatment of anal fistula

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Rev.1: administrative update	9 October 2009
Rev.2: correction of translation table	13 October 2009
Rev.3: sponsor's name change	7 June 2013

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 August 2005, orphan designation (EU/3/05/303) was granted by the European Commission to Cellerix S.L., Spain, for human autologous mesenchymal adult stem cells extracted from adipose tissue for the treatment of anal fistula.

The sponsor changed name to Cellerix S.A. in September 2008 and then to TiGenix S.A.U. in February 2013.

What is anal fistula?

An anal fistula is an abnormal passageway that develops between the rectum (the lower part of the large intestine that stores faeces) and the outside of the body. This results in abnormal discharge of faeces through an opening other than the anus.

Anal fistulae are usually caused by an infection or an abscess (collection of pus) in the anus. They can also result from other diseases that cause long-term inflammation of the bowel. Patients with an anal fistula have constant pain, sometimes accompanied by swelling and irritation of skin around the anus, leakage of pus, diarrhoea and fever.

Anal fistula is a long-term debilitating disease because it can lead to incontinence (a lack of control over the opening of the bowels) and sepsis (blood infection).

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

At the time of designation, anal fistula affected approximately 1.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 84,000 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 treatments are available?

At the time of submission of the application for orphan designation, no satisfactory method had been authorised in the European Union for treatment of the condition. Certain anal fistulas heal spontaneously, however fistula surgery is usually necessary. Fistula surgery involves cutting a small portion of the anal sphincter (a ring of muscle fibers controlling the opening and closing of the anus) to open the tunnel, joining the external and internal opening and converting the tunnel into a groove that will then heal from within outward.

How is this medicine expected to work?

This medicine is made up of 'mesenchymal stem cells' that are extracted from the patient's own adipose (fat) tissue. To make this medicine, the cells are isolated and cultivated using a technique called *ex vivo* expansion to increase their number. When these cells are injected into the walls of the fistula, they are expected to send signals that reduce the activity of the immune system and inflammation. Once the inflammation in the fistula has subsided, new tissue can start to grow, helping the fistula to heal.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of human autologous mesenchymal adult stem cells extracted from adipose tissue in experimental models was ongoing.

At the time of submission of the application for orphan designation, clinical trials in patients with anal fistula were ongoing.

Human autologous mesenchymal adult stem cells extracted from adipose tissue was not authorised anywhere worldwide for treatment of anal fistula or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 July 2005 recommending the granting of this designation.

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*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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

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	Human autologous mesenchymal adult stem cells extracted from adipose tissue	Treatment of anal fistula
Czech	Lidské autologní mesenchymální dospělé buňky, odebrané z adipózní tkáně	Léčba análního píštěle
Danish	Humane autologe mesenkymale voksne stamceller ekstraheret fra fedtvæv	Behandling af analfistler
Dutch	Humane autologe mesenchymale stamcellen, geëxtraheerd uit vetweefsel van volwassenen	Behandeling van anusfistel
Estonian	Rasvkoest saadud inimese autoloogilised mesenhümaalsed täisealised tüvirakud	Anaalfistuli ravi
Finnish	Ihmisen autologisia mesenkymaalisia (adult) kantasoluja, jotka on otettu rasvakudoksesta	Anaalifistelin hoito
French	Cellules souches humaines adultes autologues de type mesenchymal extraites de tissus adipeux	Traitement des fistules anales
German	Menschliche autologe mesenchymale Stammzellen aus dem Fettgewebe von Erwachsenen	Behandlung von Analfisteln
Greek	Ανθρώπινα αυτόλογα μεσεγχυματικά ενήλικα βλαστικά κύτταρα εκχυλισμένα από λιπώδη ιστό	Θεραπεία πρωκτικού συριγγίου
Hungarian	Zsírszövetből nyert humán autolog mesenchimalis felnőtt őssejtek	Végbélsipoly kezelése
Italian	Cellule staminali mesenchimali adulte umane autologhe estratte da tessuto adiposo	Trattamento di fistola anale
Latvian	Cilvēka autologas mezenhimālas pieaugušas no taukaudiem iegūtas cilmšūnas	Anālas fistulas ārstēšana
Lithuanian	Žmogaus autologinės mezenchimos brandžios kamieninės ląstelės, gautos iš riebalinio audinio	Analinės fistulos gydymas
Polish	Ludzkie autologiczne mezenchymalne komórki macierzyste uzyskane z tkanki tłuszczowej dorosłych	Leczenie przetok odbytu
Portuguese	Células estaminais autólogas adultas de mesênquima humano extraídas do tecido adiposo	Tratamento de fístulas anais
Slovak	Ľudské autológové mezenchymálne zrelé kmeňové bunky extrahované z tukového tkaniva	Liečba análnej píšťaly
Slovenian	Humane avtologne mezenhimske odrasle zarodne celice, pridobljene iz maščobnega tkiva	Zdravljenje analne fistule
Spanish	Células madre humanas autólogas mesenquimales adultas extraídas de tejido adiposo	Tratamiento de la fístula anal
Swedish	Humana autologa mesenkymala vuxna stamceller extraherade ur fettvävnad	Treatment of Anal FistulaBehandling av analfistel
Norwegian	Humane autologe mesenkymale voksne stamceller ekstrahert fra fett vev	Behandling av analfistel

[1] At the time of designation

Language	Active ingredient	Indication
Icelandic	Stofnfrumur fullorðinna unnar úr bandvefskími fituvefs sama einstaklings	Meðferð við endaþarmsfistli