



EMA/COMP/472601/2009 Rev.1  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue for the treatment of anal fistula

First publication	14 October 2009
Rev.1: sponsor's name change	7 June 2013
<b>Disclaimer</b> 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 8 October 2009, orphan designation (EU/3/09/667) was granted by the European Commission to Cellerix S.A., Spain, for expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue for the treatment of anal fistula.

In February 2013, Cellerix S.A. changed name to TiGenix S.A.U.

### 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).



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

At the time of designation, anal fistula affected approximately 2.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 116,000 people<sup>\*</sup>, 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 designation, no satisfactory method were authorised in the EU for the treatment of anal fistula. Some anal fistulae heal without any specific treatment, but surgery is usually necessary. This involves stretching the gut tissue or cutting the sphincter muscles (the muscles that control the opening and closing of the anus), although this may cause problems such as incontinence.

## **How is this medicine expected to work?**

This medicine is made up of 'mesenchymal stem cells' that are extracted from the adipose (fat) tissue of a donor. 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?**

The effects of expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue have been evaluated in experimental models.

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

At the time of submission, this medicine was not authorised anywhere in the EU for anal fistula 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 8 July 2009 recommending the granting of this designation.

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<sup>\*</sup>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 504,800,000 (Eurostat 2009).

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue	Treatment of anal fistula
Bulgarian	Човешки алогенни мезенхимни стволови клетки, извлечени от мастна тъкан на възрастни индивиди	Лечение на анална фистула
Czech	Lidské allogenní mezenchymální dospělé buňky, odebrané z adipózní tkáně	Léčba anální píštěle
Danish	Humane allogene mesenkymale adulte stamceller, ekstraheret fra fedtvæv	Behandling af analfistler
Dutch	Geëxpandeerde humaan allogene mesenchymale volwassen stamcellen, geëxtraheerd uit adipeus weefsel	Behandeling van anusfistel
Estonian	Rasvkoest saadud inimese allogeensed mesenhümaalsed täisealised tüvirakud	Anaalfistuli ravi
Finnish	Ihmisen allogeenisia mesenkymaalisia somaattisia kantasoluja, jotka on otettu rasvakudoksesta	Anaalifistelin hoito
French	Cellules souches humaines mésenchymateuses allogéniques adultes extraites de tissu adipeux	Traitement des fistules anales
German	Humane aus Fettgewebe extrahierte allogene mesenchymale adulte Stammzellen	Behandlung von Analfisteln
Greek	Ανθρώπινα αλλογενή μεσεγγυματικά ενήλικα βλαστικά κύτταρα προερχόμενα από λιπώδη ιστό	Θεραπεία πρωκτικού συριγγίου
Hungarian	Zsírszövetből kivont allogén mesenchimalis felnőtt emberi őssejtek	Végbélsípoly kezelése
Italian	Cellule staminali mesenchimali adulte umane allogeniche, estratte da tessuto adiposo	Trattamento della fistola anale
Latvian	No taukaudiem iegūtas ekspensētas pieauguša cilvēka allogēnas mezenhimālās cilmes šūnas	Anālas fistulas ārstēšana
Lithuanian	Pagausintos žmogaus alogeninės mezenchimos brandžios kamieninės ląstelės, gautos iš riebalinio audinio	Analinės fistulės gydymas
Maltese	Ċelluli staminali adulti alloġeneiċi mesenkimali umani estratti mit-tessut adipożu	Kura ta' fistla anali
Polish	Ludzkie alogeniczne mezenchymalne dorosłe komórki macierzyste uzyskane z tkanki tłuszczowej	Leczenie przetok odbytu
Portuguese	Células estaminais alogénicas adultas de mesênquima humano extraídas do tecido adiposo	Tratamento de fístulas anais

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Romanian	Celule stem umane adulte mezenchimale alogene multiplicata (expandate ex vivo) extrase din țesut adipos	Tratamentul fistulei anale
Slovak	Expandované ľudské alogénne mezenchýmové adultné kmeňové bunky získané z tukového tkaniva	Liečba análnej píšťaly
Slovenian	Človeške alogenske mezenhimske odrasle zarodne celice, vzete iz maščobnega tkiva	Zdravljenje analne fistule
Spanish	Células madre expandidas alogénicas humanas adultas de origen mesenquimal extraídas de tejido adiposo	Tratamiento de la fístula anal
Swedish	Humana allogena mesenkymala vuxna stamceller extraherade ur fettvävnad	Treatment of Anal Fistula Behandling av analfistel
Norwegian	Humane allogene mesenkymale voksne stamceller ekstrahert fra adipøst vev	Behandling av analfistel
Icelandic	Fullorðnar stofnfrumur úr bandvefskími úr ósamgena einstaklingi dregnar úr fituvef.	Meðferð við endaparmsfistli