

EMA/COMP/29248/2007 Rev.2  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### Ex-vivo cultured adult human mesenchymal stem cells for the treatment of graft-versus-host-disease

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| First publication                                                                                                                                                                                                                                                                                                       | 11 June 2007     |
| Rev.1: transfer of sponsorship                                                                                                                                                                                                                                                                                          | 12 November 2009 |
| Rev.2: transfer of sponsorship                                                                                                                                                                                                                                                                                          | 3 May 2013       |
| <b>Disclaimer</b><br>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 February 2007, orphan designation (EU/3/07/432) was granted by the European Commission to Quintiles UK Limited, United Kingdom, for ex-vivo cultured adult human mesenchymal stem cells for the treatment of graft-versus-host-disease.

The sponsorship was transferred to Genzyme Europe BV, The Netherlands, in October 2009 and to Voisin Consulting S.A.R.L., France, in February 2013.

### What is graft-versus-host-disease?

The bone marrow is the spongy tissue inside the large bones in the body. The bone marrow makes red blood cells (which carry oxygen and other materials to all tissues of the body), white blood cells (which fight infection), and platelets (which make the blood clot). Bone marrow transplantation (replacing the existing bone marrow with that of a donor) is a treatment used for certain diseases. A frequent complication of bone marrow transplantation is the development of a disease called graft-versus-host-disease (GvHD). GvHD involves an immune reaction of the donor cells against the organs of the patient, leading to damage to the organs themselves. GvHD may occur in an acute or a chronic form. The organs most commonly affected in acute GvHD are the stomach, gut, skin and liver. Chronic GvHD occurs later after transplantation, involves a much wider range of organs, and has a different pathology than the acute form. The condition is chronically debilitating and life-threatening.

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

At the time of designation, graft-versus-host-disease affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 50,000 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?**

The methods of treatment authorised for GvHD in the Community, at the time of submission of the application for orphan designation, consisted in certain steroid hormones (corticosteroids, a group of chemical substances, which modulate the activity of certain organs and of the immune system) administered at high doses. Other therapies include drugs that inhibit the immune response (immunosuppressants). "Ex-vivo cultured adult human mesenchymal stem cells" might be of potential significant benefit for the treatment of GvHD. This assumption remains to be proven. This will be necessary to maintain the orphan status.

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

"Ex-vivo cultured adult human mesenchymal stem cells" are derived from bone marrow of healthy donors; it is thought that these cells have the ability to home to the sites of injury and inflammation in damaged organs, and reduce the immune and inflammatory responses and restore damaged tissue. This is expected to help in treating graft-versus-host-disease.

## **What is the stage of development of this medicine?**

The effects of "ex-vivo cultured adult human mesenchymal stem cells" were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with graft-versus-host-disease were ongoing.

"Ex-vivo cultured adult human mesenchymal stem cells" were not authorised anywhere in the world for graft-versus-host-disease.

The product had been designated by the FDA on 14 December 2005 as an orphan medicinal product for the treatment of only the acute form of Graft-versus-Host rejection to the sponsor Osiris Pharmaceuticals Inc. (which is associated with the EU sponsor Quintiles UK Ltd.).

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 January 2006 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 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 500,300,000 (Eurostat 2007).

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    | <i>Ex vivo</i> cultured adult human mesenchymal stem cells                                   | Treatment of Graft-versus-Host disease                          |
| Bulgarian  | Ex vivo култивирани човешки мезенхимални стволони клетки от възрастни                        | Лечение на реакция на присадката срещу приемателя               |
| Czech      | Lidské dospělé mesenchymální kmenové buňky, kultivované ex vivo                              | Léčba reakce štěpu proti hostiteli                              |
| Danish     | Ex vivo dyrkede voksne humane mesenchymale stamceller                                        | Behandling af graft versus host reaktion                        |
| Dutch      | Ex vivo gekweekte adult humane mesenchymale stamcellen                                       | Behandeling van graft versus host ziekte                        |
| Estonian   | Täiskasvanud inimese ex vivo kultiveeritud mesenhümaalsed tüvirakud                          | Graft versus host haiguse ravi                                  |
| Finnish    | Ex vivo viljellyt aikuisen ihmisen mesenkymaaliset kantasolut                                | Käänteishyljintäreaktion hoito                                  |
| French     | Cellules souches mésenchymateuses humaines adultes mises en culture ex vivo                  | Traitement de la réaction du greffon contre l'hôte              |
| German     | Ex vivo kultivierte humane erwachsene Mesenchymstammzellen                                   | Behandlung der Graft-versus-Host-Reaktion                       |
| Greek      | Ex vivo καλλιεργημένα ανθρώπινα αρχέγονα μεσεγχυματικά κύτταρα ενηλίκου                      | Θεραπεία της αντίδρασης του μοσχεύματος                         |
| Hungarian  | Ex vivo tenyésztett felnőtt humán mesenchimális őssejtek                                     | Graft-versus-host betegség kezelése                             |
| Italian    | Cellule staminali mesenchimali da umano adulto, coltivate <i>ex vivo</i>                     | Trattamento della reazione del trapianto contro l'ospite        |
| Latvian    | Ārpus organisma kultivētas pieauguša cilvēka mezenhimālās cilmes šūnas                       | Saimnieka-transplantāta slimības ārstēšana                      |
| Lithuanian | Suaugusiojo žmogaus mezenchimos kamieninės ląstelės, kultivuotos <i>ex vivo</i>              | Transplantato atmetimo ligos gydymas                            |
| Maltese    | Ċelluli staminali adulti mesenkimali umani mkabbra ex-vivo                                   | Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih |
| Polish     | Ludzkie mezenchymalne komórki macierzyste od dorosłych wyhodowane w warunkach <i>ex vivo</i> | Leczenie choroby przeszczep przeciw gospodarzowi                |
| Portuguese | Células estaminais mesenquimatosas humanas adultas cultivadas <i>ex vivo</i>                 | Tratamento da reação do enxerto contra o hospedeiro             |
| Romanian   | Celule stem mezenchimale umane adulte cultivate <i>ex vivo</i>                               | Tratamentul reacției grefei contra gazdei                       |
| Slovak     | Dospelé ľudské mezenchýmové kmeňové bunky kultivované ex vivo.                               | Liečba reakcie štepů proti hostiteľovi                          |

<sup>1</sup> At the time of transfer of sponsorship

| Language  | Active Ingredient                                                             | Indication                                             |
|-----------|-------------------------------------------------------------------------------|--------------------------------------------------------|
| Slovenian | Ex vivo odrasle človeške mezenhimske matične celice, gojene v celični kulturi | Zdravljenje bolezni presadka proti gostitelju          |
| Spanish   | Células madre mesenquimales humanas adultas cultivadas <i>ex vivo</i>         | Tratamiento de la enfermedad de injerto contra huésped |
| Swedish   | Ex vivo-odlade humana, mesenkymala stamceller från vuxen                      | Behandling av graft-värd host reaktion                 |
| Norwegian | Ex vivo dyrkede, humane mesenkymale stamceller fra voksen                     | Behandling av graft-versus-host - reaksjon             |
| Icelandic | Bandvefskíms stofnfrumur úr fullorðnum mönnum ræktaðar <i>ex vivo</i>         | Til meðferðar á hýsilssótt                             |