



Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of ex-vivo cultured adult human mesenchymal stem cells for the treatment of graft-versus-host-disease

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.

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 is equivalent to a total of fewer than 46,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and 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.

*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. This represents a population of 459,700,000 (Eurostat 2004).

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.).

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on January 10 2006 a positive opinion recommending the grant of the above-mentioned designation.

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 Community) 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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Patients’ association contact point: Not available

**Translations of the active ingredient and indication in all EU languages
and 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 <i>ex vivo</i>	Léčba reakce štěpu proti hostiteli
Danish	<i>Ex vivo</i> dyrkede voksne humane mesenchymale stamceller	Behandling af graft versus host reaktion
Dutch	<i>Ex vivo</i> gekweekte adult humane mesenchymale stamcellen	Behandeling van graft versus host ziekte
Estonian	Täiskasvanud inimese <i>ex vivo</i> kultiveeritud mesenhümaalsed tüvirakud	Graft versus host haiguse ravi
Finnish	<i>Ex vivo</i> viljellyt aikuisen ihmisen mesenkymaaliset kantasolut	Käänteishyljintäreaktion hoito
French	Cellules souches mésenchymateuses humaines adultes mises en culture <i>ex vivo</i>	Traitement de la réaction du greffon contre l'hôte
German	<i>Ex vivo</i> kultivierte humane erwachsene Mesenchymstammzellen	Behandlung der Graft-versus-Host-Reaktion
Greek	<i>Ex vivo</i> καλλιεργημένα ανθρώπινα αρχέγονα μεσεγγυματικά κύτταρα ενηλίκου	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	<i>Ex vivo</i> tenyésztett felnött 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
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 reacção do enxerto contra o hospedeiro
Romanian	Celule stem mezenchimale umane adulte cultivate <i>ex vivo</i>	Tratamentul reacţiei grefei contra gazdei
Slovak	Dospelé ľudské mezenchýmové kmeňové bunky kultivované <i>ex vivo</i> .	Liečba reakcie štepu proti hostiteľovi
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