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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

A mixture of anti-CD3 mAb (SPV-T3a)-ricin A chain fusion protein and anti-CD7 mAb (WT1)-ricin A chain fusion protein for the treatment of graft-versus-host-disease

On 26 August 2005, orphan designation (EU/3/05/317) was granted by the European Commission to Henogen SA, Belgium, for a mixture of anti-CD3 mAb (SPV-T3a)-ricin A chain fusion protein and anti-CD7 mAb (WT1)-ricin A chain fusion protein for the treatment of graft-versus-host-disease.

The sponsorship was transferred to Xenikos BV, The Netherlands, in January 2010.

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 with healthy marrow) is a treatment used against certain diseases of the bone marrow. A frequent complication of bone marrow transplantation is the development of a disease called graft-versus-host-disease (GvHD). This disease involves a reaction between the donor cells and the recipient's native tissues leading to injury of the recipient's tissues. GvHD occurs in acute and chronic form. The organs most commonly affected in acute GvHD are the stomach and the intestines, the skin, and the liver. Chronic GvHD involves a much wider range of tissues 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 approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 19,000 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 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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 466,600,000 (Eurostat 2005).

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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 of 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). A mixture of anti-CD3 mAb (SPV-T3a)-ricin A chain fusion protein and anti-CD7 mAb (WT1)-ricin A chain fusion protein might be of potential significant benefit for the treatment of GvHD, particularly in terms of a selective action against those cells that are responsible for the disease. This assumption remains to be proven. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

A mixture of anti-CD3 mAb (SPV-T3a)-ricin A chain fusion protein and anti-CD7 mAb (WT1)-ricin A chain fusion protein is a combination of a toxic substance with an antibody. Antibodies are proteins that specifically recognise and attach themselves to cell structures such as proteins found on the surface of the cells. In the case of this antibody, the target is a protein (CD-3 and CD7) found on certain cells of the immune system, so-called mature T-cells. The antibody is expected to bind to these cells and to induce their destruction, by release of the toxin into the cells. This might thereby prevent the graft-versus-host-disease.

What is the stage of development of this medicine?

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

A mixture of anti-CD3 mAb (SPV-T3a)-ricin A chain fusion protein and anti-CD7 mAb (WT1)-ricin A chain fusion protein was not marketed anywhere worldwide for treatment of graft-versus-host-disease or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 13 July 2005 a positive opinion recommending the grant of the above-mentioned 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 European Union) 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	A mixture of anti-CD3 mAb (SPV-T3a)-ricin A chain fusion protein and anti-CD7 mAb (WT1)-ricin A chain fusion protein	Treatment of graft versus host disease
Bulgarian	Смес от анти – CD3 mAb (SPV-T3a)- рицин А верижен фюжън протеин и анти - CD7 mAb (WT1)- рицин А верижен фюжън протеин.	Лечение на реакция на присадката срещу приемателя
Czech	Kombinace anti-CD3 (SPV-T3a) a anti-CD7 (WT1) monoklonálních protilátek, které jsou vázané na ricin A	Léčba reakce štěpu proti hostiteli
Danish	En blandning af anti-CD3 monoklonal antistof (SPV-T3a)-ricin A kæde fusion protein og anti-CD7 monoklonal antistof (WT1)-ricin A kæde fusion protein	Behandling af graft versus host reaktion
Dutch	Mengeling van anti-CD3 mAb (SPV-T3a)-ricine A keten fusieproteïne en anti-CD7 mAb (WT1)-ricine A keten fusieproteïne	Behandeling van graft versus host ziekte
Estonian	Mikstuur anti-CD3 monoklonaalse antikeha (SPV-T3a) ja ritsiin A-ahelaga liitproteiinist ning anti-CD7 monoklonaalse antikeha (WT1) ja ritsiin A-ahelaga liitproteiinist.	*Graft versus host* haiguse ravi
Finnish	Anti-CD3-monoklonaalinen vasta-aine (SPV-T3a)-risiini A ketju fuusioproteiini ja anti-CD7 monoklonaalinen vasta-aine (WT1)-risiini A ketju fuusioproteiini sekoitus	Käänteishyljintäreaktion hoito
French	Mélange d'anticorps anti-CD3 mAb (SPV-T3a)-protéine de fusion chaîne A de ricine et anticorps anti-CD7 (WT1)- protéine de fusion chaîne A de ricine	Traitement de la réaction du greffon contre l'hôte
German	Ein Gemisch von anti-CD3 (SPVT3-a)-Ricin A Ketten Fusionsprotein und anti-CD7 (WT1)-Ricin A Ketten Fusionsprotein	Behandlung der Graft-versus-Host-Reaktion
Greek	Μίγμα μονοκλωνικού αντισώματος anti-CD3 (SPV-T3a) συνδεδεμένο με πρωτεϊνη σύντηξης Α αλυσίδας ricin και μονοκλωνικού αντισώματος anti-CD7 (WT1) συνδεδεμένο με πρωτεϊνη σύντηξης Α αλυσίδας ricin, .	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	Anti-CD3 mAb(SPV-T3a)-ricin A lánc fúziós fehérje és anti-CD7 mAb(WT1)-ricin A lánc fúziós fehérje kombinációja	Graft-versus-host betegség kezelése
Italian	Mistura di proteina di fusione anticorpo monoclonale anti-CD3 (SPV-T3a)-catena A della ricina e proteina di fusione anticorpo monoclonale anti-CD7 (WT1)-catena A della ricina	Trattamento della reazione del trapianto contro l'ospite

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Latvian	Anti-CD3 mAb (SPV-T3a)-rīcina A ķēdes savienojošā proteīna un anti-CD7 mAb (WT1)-rīcina A ķēdes savienojošā proteīna maisījums	Saimnieka-transplantāta slimības ārstēšana
Lithuanian	Anti-CD3 mAb (SPV-T3a)-ricinos A grandinės jungties baltymo ir anti-CD7 mAb (WT1)-ricinos A grandinės jungties baltymo mišinys	Transplantato atmetimo ligos gydymas
Maltese	Taħlita ta' proteina tal-fużjoni ta' antikorp monoklonali CD3 (SPV-T3a)-katina A ta' ricin u proteina tal-fużjoni ta' antikorp monklonali CD7 (WT1)-katina A ta' ricin	Kura tal-marda tat tessut għat trapjant kontra dak li jirċievih
Polish	Mieszanina przeciwciał monoklonalnych: anty-CD 3 (SPV-T3a) – sprzężonego z łańcuchem A białka fuzyjnego rycyny i anty- CD7 (WT1) – sprzężonego z łańcuchem A białka fuzyjnego rycyny	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Uma mistura das proteínas de fusão do anti-CD3 mAb (SPV-T3a) da cadeia A da ricina e das proteínas de fusão do anti-CD7 mAb (WT1) da cadeia A da ricina.	Tratamento da reacção do enxerto contra o hospedeiro
Romanian	Mixtură de anticorp monoclonal anti-CD3 (SPV-T3a)-proteină de fuziune lanţ ricin A şi anticorp monoclonal anti CD7(WT1)- proteină de fuziune lanţ ricin A	Tratamentul reacţiei grefei contra gazdei
Slovak	Zmes anti-CD3 mAb (SPV-T3a) proteínu spojeného s A reťazcom ricínu a anti-CD7 mAb (WT1) proteínu spojeného s A reťazcom ricínu	Reakcia štepu protihostiteľovi
Slovenian	Zmes anti-CD3 mAb (SPV-T3a)-ricin A verižnega fuzijskega proteina in anti-CD7 mAb (WT1)-ricin A verižnega fuzijskega proteina	Zdravljenje bolezni presadka proti gostitelju
Spanish	Combinación de las proteínas de fusión anticuerpo monoclonal anti-CD3 (SPV-T3a) cadena A de la ricina y anticuerpo monoclonal anti-CD7 (WT1) cadena A de la ricina	Tratamiento de la enfermedad de injerto contra huésped
Swedish	En blandning av anti-CD3 monoklonal antikropp (SPV-T3a)-ricin A kedja fusionerat protein och anti-CD7 monoklonal antikropp (WT1)-ricin A kedja fusionerat protein	Behandling av graft-värd host reaktion
Norwegian	En blanding av anti-CD3 mAb(SPV-T3a)-ricin A-kjede fusjonsprotein mAb og anti-CD7 mAb (WT1)-ricin A-kjede fusjonsprotein	Graft-versus-host -reaksjon
Icelandic	Blanda af anti-CD3 mAb (SPV-T3a) og antiCD7 mAb (WT1), bæði bundinricin A tengipróteini	Til meðferðar á hýsilsótt