European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of recombinant human ADAMTS-13 for the treatment of thrombotic thrombocytopenic purpura

On 3 December 2008, orphan designation (EU/3/08/588) was granted by the European Commission to Baxter AG, Austria, for recombinant human ADAMTS-13 for the treatment of thrombotic thrombocytopenic purpura.

What is thrombotic thrombocytopenic purpura?
Thrombotic thrombocytopenic purpura (TTP) is a disease characterised by the formation of multiple blood clots in the narrow blood vessels and by a low number of platelets in the blood (thrombocytopenia). As platelets are consumed in the blood clotting process, there are fewer platelets in the blood resulting in spontaneous bleeding and bruising of the skin in purple spots (called 'purpura'). Patients with this condition develop neurological symptoms, such as confusion or seizures (fits) . Other signs of the disease are anaemia (low red blood cell counts) and, in some, cases fever. TTP may be idiopathic, which means that the cause of the disorder is unknown. It may also be secondary to various other conditions such as pregnancy, infections, cancer, and some drugs. A few patients have a familial form of TTP, caused by the deficiency of an enzyme called 'ADAMTS13' due to an inborn mutation (change) in the gene coding for the enzyme. In other patients, the immune system reacts against the enzyme and blocks its function. TTP is a life-threatening disease.

What is the estimated number of patients affected by the condition?
At the time of designation thrombotic thrombocytopenic purpura affected approximately 2.2 in 10,000 people in the European Union (EU) [*]. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 111,000 people.

What treatments are available?
There are no authorised medicines for TTP in the European Union (EU). At the time of submission for orphan drug designation, the standard therapy of TTP consisted of 'plasma exchange', a procedure in which the patient's blood is taken out of the body and the blood cells are separated from the liquid part (plasma). For TTP, the blood cells are returned to the patient together with plasma from a donor. However, plasma exchange has been associated with several risks for the patients. The sponsor has provided sufficient information to show that recombinant human ADAMTS13 might be of potential significant benefit for the patients as it could be safer compared to plasma exchange and has a mechanism of action closely related to the pathophysiology of the disease which could result in improved efficacy. These assumptions will need to be confirmed at the time of marketing authorisation, to maintain the orphan status.

[*]Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.europa.eu http://www.emea.europa.eu

How is this medicine expected to work?
ADAMTS13 normally breaks down large aggregations of a substance in the body called 'von Willebrand factor', which is involved in the blood clotting process by linking to platelets. When ADAMTS13 is inactivated, the aggregations of von Willebrand factor are not broken down and more blood clots are formed in the blood vessels. Human recombinant ADAMTS13 is expected to replenish the function of patients' inactivated ADAMTS13. By doing this it is expected that the product will partly restore the normal clotting process.

What is the stage of development of this medicine?
The effects of human recombinant ADAMTS13 have been evaluated in experimental models.

At the time of submission, human recombinant ADAMTS13 was not authorised anywhere in the world for thrombotic thrombocytopenic purpura. Orphan designation had been granted in the United States for treatment and prevention of thrombotic thrombocytopenic purpura including its congenital, acquired idiopathic, and secondary forms.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 October 2008 recommending the granting of this 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information:
Sponsor's contact details:
Baxter AG
Industriestrasse 67
A-1221 Vienna
Austria
Telephone: +43 12 01 00 34 88
Telefax: +43 12 01 00 771
E-mail: bruce_ewenstein@baxter.com

Patients' associations contact points:

Association ADAMTS 13
45 Chemin du Dauphin
72230 Guecelard
France
Telephone: +33 2 43 87 10 46

TTP Network - Thrombotic Thrombocytopenic Purpura Network
Web-Based Only
United Kingdom
E-mail: jo@ttpnetwork.org.uk

Translations of the active ingredient and indication in all official EU languages, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Recombinant human ADAMTS-13	Treatment of thrombotic thrombocytopenic purpura
Bulgarian	Рекомбинантен човешки ADAMTS-13	Лечение на тромботична тромбоцитопенична пурпура
Czech	Lidský rekombinantní ADAMTS-13	Léčba trombotické trombocytopenické purpury
Danish	rekombinant humant ADAMTS-13	Behandling af trombotisk trombocytopenisk purpura
Dutch	Recombinant humaan ADAMTS-13	Behandeling van trombotische trombocytopenische purpura
Estonian	Rekombinantne inimese ADAMTS-13	Trombootilise trombotsütopeenilise purpura ravi
Finnish	Rekombinantti ihmisen ADAMTS-13	Tromboottisen trombosytopeenisen purppuran hoito
French	ADAMTS-13 humain recombinant	Traitement du purpura thrombocytopénique thrombotique
German	Rekombinante humane ADAMTS-13	Behandlung von thrombotisch thrombozytopenischer Purpura
Greek	Ανασυνδυασμένη ανθρώπινη ADAMTS-13	Θεραπεία της θρομβοτικής θρομβοκυτοπενικής πορφύρας
Hungarian	Rekombináns humán ADAMTS-13	Thromboticus thrombocytopeniás purpura kezelése
Italian	ADAMTS-13 umana ricombinante	Trattamento della porpora trombotica trombocitopenica
Latvian	Rekombinantais cilvēka ADAMTS-13	Trombotiskās trombocitopēniskās purpura ārstēšana
Lithuanian	Rekombinantinis žmogaus ADAMTS-13	Trombozinės trombocitopeninės purpuros gydymas
Maltese	ADAMTS-13 uman rikombinanti	Kura tal-purpura trombotika tromboċitopenika
Polish	Rekombinowane ludzkie ADAMTS-13	Leczenie zakrzepowej plamicy małopłytkowej
Portuguese	ADAMST-13 humano recombinante	Tratamento da púrpura trombótica trombocitopénica
Romanian	ADAMTS-13 uman recombinant	Tratamentul purpurei trombotice trombocitopenice
Slovak	Rekombinantný ľudský ADAMTS-13	Liečba trombotickej trombocytopenickej purpury
Slovenian	Rekombinantni človeški ADAMTS-13	Zdravljenje trombotične trombocitopenične purpure
Spanish	ADAMTS-13 recombinante humana	Tratamiento de la púrpura trombótica trombocitopénica
Swedish	Rekombinant humant ADAMTS-13	Behandling av trombotisk trombocytopen purpura
Norwegian	Rekombinant human ADAMTS-13	Behandling av trombotisk trombocytopenisk purpura
Icelandic	Raðbrigða manna ADAMTS-13	Meðferð við blóðflagnafæðarpurpura með segamyndun