30 March 2011
EMA/COMP/146358/2009 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Nanobody directed towards the human A1 domain of von Willebrand factor for the treatment of thrombotic thrombocytopenic purpura

On 30 April 2009, orphan designation (EU/3/09/629) was granted by the European Commission to Ablynx NV, Belgium, for nanobody directed towards the human A1 domain of von Willebrand factor for the treatment of thrombotic thrombocytopenic purpura.

What is thrombotic thrombocytopenic purpura?

Thrombotic thrombocytopenic purpura (TTP) is a disease of the blood clotting system. It is characterised by the formation of multiple blood clots in the narrow blood vessels and by low levels of platelets (components that help the blood to clot) in the blood (thrombocytopenia). Because 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 TTP develop symptoms affecting the nervous system, such as seizures (fits), altered behaviour, confusion, stroke and headache. Symptoms of the disease may also include anaemia (low red blood cell counts) and fever. The patients may develop problems with their heart or kidneys if blood clots form in the blood vessels supplying them.

TTP is often caused by the inactivation of an enzyme called 'ADAMTS13', which breaks down large aggregations of a substance in the body called 'von Willebrand factor'. These aggregations are involved in the blood clotting process by linking platelets together. When ADAMTS13 is inactivated, the aggregations of von Willebrand factor are not broken down, so more blood clots are formed in the blood vessels. ADAMTS13 is inactivated either because of an inborn genetic mutation, or by the immune system (the body's natural defences) attacking the enzyme. TTP can also develop after pregnancy or some medical conditions, such as infections and cancer. TTP has also been associated with the use of certain medicines.

TTP is a life-threatening disease because it can severely damage the brain, the heart and the kidneys.

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

At the time of designation, TTP affected between 2.2 and 2.9 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of between 111,000 and 150,000 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?

At the time of designation, there were no authorised medicines for TTP in the EU. The standard therapy of TTP consisted of 'plasma exchange', a procedure that helps restore the inactivated enzyme from the blood by replacing the patient's plasma (the liquid part of the blood) with plasma from a donor.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for the patients because of the way the medicine is expected to work. This could reduce the need for plasma exchange. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Nanobody directed towards the human A1 domain of von Willebrand factor is a very small antibody (a type of protein) that has been made to recognise and attach to a specific part of von Willebrand factor. By attaching to von Willebrand factor, this medicine is expected to prevent the factor from linking to platelets and inducing the formation of blood clots, reducing the symptoms of the disease.

What is the stage of development of this medicine?

The effects of nanobody directed towards the human A1 domain of von Willebrand factor have been evaluated in experimental models.

At the time of submission of the application for orphan designation, a clinical trial in healthy volunteers had finished, and further trials were ongoing or were planned.

At the time of submission, this medicine was not authorised anywhere in the EU for TTP or designated as 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 4 March 2009 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. This represents 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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Nanobody directed towards the human A1 domain of von Willebrand factor	Treatment of thrombotic thrombocytopenic purpura
Bulgarian	Нанотяло, насочено срещу участък A1 от човешкия фактор на von Willebrand	Лечение на тромботична тромбоцитопенична пурпура
Czech	Nanobody směrované k doméně A1 humánního von Wilenbrandova faktoru	Léčba trombotické trombocytopenické purpury
Danish	Nanobody rettet mod A1-domænet i human von Willebrand faktor	Behandling af trombotisk trombocytopenisk purpura
Dutch	Nanolichaam gericht tegen het A1-domein van humane von Willebrand factor	Behandeling van trombotische trombocytopenische purpura
Estonian	Inimese vonWillebrandi faktori A1 piirkonnale suunatud Nanobody	Trombootilise trombotsütopeenilise purpura ravi
Finnish	Ihmisen von Willebrand -tekijän A1-domeeniin suunnattu nanovasta-aine	Tromboottisen trombosytopeenisen purppuran hoito
French	Nanobody dirigé contre le domaine A1 du facteur von Willebrand humain	Traitement du purpura thrombocytopénique thrombotique
German	Auf die A1-Domäne des humanen von Willebrand Faktors gerichteter Nanobody	Behandlung von thrombotisch thrombozytopenischer Purpura
Greek	Νανόσωμα κατευθυνόμενο προς το ανθρώπινο πεδίο A1 του παράγοντα von Willebrand	Θεραπεία της θρομβοτικής θρομβοκυτοπενικής πορφύρας
Hungarian	A von Willebrand faktor humán A1 tartományára irányuló Nanobody	Thromboticus thrombocytopeniás purpura kezelése
Italian	Nanoparticella diretta nei confronti del dominio A1 del fattore von Willebrand umano	Trattamento della porpora trombotica trombocitopenica
Latvian	Nanovielas, kas vērsta uz cilvēka fon Villebranda faktora A1 domēnu	Trombotiskās trombocitopēniskās purpura ārstēšana
Lithuanian	Nanokūnas nukreiptas į žmogaus von Vilebrando faktoriaus domeną A1	Trombozinės trombocitopeninės purpuros gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Nanobody dirett kontra l-qasam uman A1 tal- fattur von Willebrand	Kura tal-purpura trombotika trombocitopenika
Polish	Nanociało skierowane przeciwko ludzkiej domenie A1 czynnika von Willebranda	Leczenie zakrzepowej plamicy małopłytkowej
Portuguese	Nanobody (nanocorpo) específico para o domínio A1 do factor von Willebrand humano	Tratamento da púrpura trombótica trombocitopénica
Romanian	Nano-anticorp orientat împotriva domeniului A1 al factorului von Willebrand uman	Tratamentul purpurei trombotice trombocitopenice
Slovak	Nanoprotilátky smerované k doméne A1 ľudského von Willebrandovho faktora	Liečba trombotickej trombocytopenickej purpury
Slovenian	Nanobody proti domeni A1 humane beljakovine von Willebrandovega faktorja	Zdravljenje trombotične trombocitopenične purpure
Spanish	Nanocuerpo dirigido contra el dominio A1 del factor de von Willebrand humano	Tratamiento de la púrpura trombótica trombocitopénica
Swedish	Nanobody riktad mot den humana A1-domänen i von Willebrand faktor	Behandling av trombotisk trombocytopen purpura
Norwegian	Nanobody rettet mot det humane A1-domenet til von Willebrands faktor	Behandling av trombotisk trombocytopenisk purpura
Icelandic	Nanobody sem beinist að A1-svæði von Willebrands faktors hjá mönnum	Meðferð við blóðflagnafæðarpurpura með segamyndun