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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant inhibitor of human plasma kallikrein for the treatment of angioedema

First publication	29 January 2003
Rev.1: sponsor's change of address	20 August 2009
Rev.2: withdrawal from the Community Register	3 October 2014

Disclaimer

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.

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in June 2014 on request of the Sponsor.

On 18 December 2002, orphan designation (EU/3/02/126) was granted by the European Commission to Dyax s.a., Belgium, for recombinant inhibitor of human plasma kallikrein for the treatment of angioedema.

What is angioedema?

Angioedema is a reaction of the blood vessels. The reaction allows the passage of more fluids across the blood vessels, into the surrounding tissue. The excess fluid builds up in confined areas under the skin producing swelling (oedema). Most of the time oedema is painless and does not itch. The oedema often appears in the face, and the neck. Here it may involve the lips, the floor of the mouth, and the tongue. It may also involve the larynx, leading to airway obstruction. It can also appear in the gut. This may lead to colicky pain in the abdomen, and vomiting. Faeces may become too liquid, and produced too frequently (diarrhoea). Angioedema can occur as a result of various causes. The condition may be inherited via the genes from the parents. It may also develop after birth. In some cases, it is related to the use of certain medications. Angioedema can be a life-threatening condition due to airway obstruction.

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

At the time of designation, angioedema affected between 2 and 3 in 10,000 people in the European Union (EU). This was equivalent to a total of between 76,000 and 114,000 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?

Methods of treatment have been authorised in the Community for treatment for angioedema. Certain medicines have been used to treat acute attacks of angioedema. These have included agents that prevent the break-down of a protein called fibrin. This protein is found in blood clots. Such agents are called antifibrinolytic agents. Other agents include those that inhibit a protein called C1, as abnormal activation of this protein leads to oedema. Such agents are called C1-esterase inhibitors. Other therapies include drugs that prevent new attacks like, for example, the male sex hormones called androgens.

Recombinant inhibitor of human plasma kallikrein might be of potential significant benefit for the treatment of angioedema, particularly in terms of a selective action and potentially wide availability. The assumption of benefit is yet to be proven, and will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Angioedema involves fluid leakage from small blood vessels beneath the skin. This response is mediated by certain proteins called proteases. Proteases are a family of proteins that break up other proteins. In the case of angioedema, the proteases involved are called kinins. Kinins are small proteins that cause dilation of blood vessels. They also alter the passage of fluids across the walls of the vessels. An example of a kinin is the protein called bradykinin. This is a very potent protein that causes dilation of blood vessels, and other effects.

The activation of kinins requires a series of reactions involving a protein called kallikrein. Kallikrein is found in the human plasma. The plasma is the fluid of the blood, in which blood cells are suspended. Recombinant inhibitor of human plasma kallikrein specifically blocks the action of human plasma kallikrein, and hence interrupts the series of reactions that leads to angioedema.

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 angioedema were ongoing.

The medicinal product was not marketed anywhere worldwide for angioedema or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 November 2002 recommending the granting of this designation.

*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.
At the time of designation, this represented a population of 380,600,000 (Eurostat 2002).

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	Recombinant inhibitor of human plasma kallikrein (scientific name)	Treatment of angioedema
Danish	Rekombinant inibitor af humant plasmakallikrein (videnskabeligt navn)	Behandling af angioødem
Dutch	Recombinante inhibitor van menselijk plasmakallikreïne (generieke naam)	Behandeling van angio-oedeem
Finnish	Ihmisplasman kallikreiinin rekombinantti-inhibiittori (tieteellinen nimi)	Angioödeeman hoito
French	Antikallikréine recombinante plasmatique humaine (dénomination scientifique)	Traitement de l'œdème angioneurotique
German	Rekombinant hergestellter Hemmstoff für menschliches Plasmakallikrein (wissenschaftliche Bezeichnung)	Behandlung von angineurotischen Ödemen
Greek	Ανασυνδυασμένος αναστολέας της καλλικρεΐνης του ανθρώπινου πλάσματος (επιστημονική ονομασία)	Θεραπεία αγγειοοιδήματος
Italian	Inibitore ricombinante della callicreina plasmatica umana (termine scientifico)	Trattamento dell'angioedema
Portuguese	Inibidor recombinante da calicreína plasmática humana (nome científico)	Tratamento do angioedema
Spanish	Inhibidor recombinante de la calicreína plasmática humana (nombre científico)	Tratamiento del angioedema
Swedish	Rekombinant inhibitor av mänskligt plasmakallikrein (vetenskapligt namn)	Behandling av angioödem

[1] At the time of designation