15 November 2010
EMA/COMP/182/04 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

recombinant human C1-inhibitor for the treatment of angioedema caused by C1 inhibitor deficiency

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in September 2010 on request of the sponsor.

On 11 May 2001, orphan designation (EU/3/01/036) was granted by the European Commission to Pharming N.V., Belgium, for recombinant human C1-inhibitor for the treatment of angioedema caused by C1 inhibitor deficiency.

The sponsorship of this orphan medicinal product was transferred to Pharming Group N.V., The Netherlands, in November 2002.

What is angioedema caused by C1 inhibitor deficiency?

Angioedema can be either hereditary or acquired. Patients with the inherited form of the disease are born lacking an inhibitor protein (C1-inhibitor) that normally prevents activation of a cascade of proteins leading to swelling and angioedema. Angioedema is a reaction involving different layers of the skin and is caused by dilatation of blood vessels. Patients with the acquired form of the disease either suffer from other diseases (most commonly B-cell disorder) or have auto-antibodies (protein produced by white blood cells) directed against the C1 inhibitor molecule. The symptoms of both conditions are similar. Patients can develop recurrent attacks of swollen tissues, pain in the abdomen and swelling of the voice-box (larynx), which can compromise breathing. The presence of abnormally large amounts of fluid in the tissue may lead to redness or mild allergic reaction (pale or red elevated patches) of the skin. Angioedema caused by C1 inhibitor deficiency is chronically debilitating and may be life-threatening.

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

At the time of designation, angioedema caused by C1 inhibitor deficiency affected approximately 2.1 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 79,000 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, a protein that 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.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that recombinant human C1-inhibitor might be of potential significant benefit for the treatment of angioedema caused by C1 inhibitor deficiency. The assumption 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?

Recombinant human C1-inhibitor is a glycoprotein (a protein linked to sugar), which stops the activity of an enzyme (molecule that speeds up chemical reactions in our body) called serine protease C1. Serine protease C1 has the ability to break up proteins in the body and in patients with angioedema its action is uncontrolled. This medicinal product is expected to oppose the activity of this enzyme and to substitute the C1 inhibitor deficiency in these patients.

What is the stage of development of this medicine?

The effects of recombinant human C1-inhibitor were evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials in patients with angioedema caused by C1 inhibitor deficiency were initiated.

Recombinant human C1-inhibitor was not marketed anywhere worldwide for the treatment of angioedema caused by C1 inhibitor deficiency, at the time of submission.

Orphan designation of recombinant human C1-inhibitor was granted in 1999 in the United States for prophylactic and acute treatment of hereditary and acquired angioedema.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 20 March 2001 recommending the granting of this designation.

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[*]Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition.

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 human C1-inhibitor	Treatment of angioedema caused by C1 inhibitor deficiency
Danish	Rekombinant human C1-inhibitor	Behandling af angioødem forårsaget af mangel på C1 inhibitor
Dutch	Recombinant humaan C1-remmer	Behandeling van angio-oedeem veroorzaalt door C1 inhibitor deficiëntie.
Finnish	Rekombinantti ihmisen C1-inhibiittori	C1 inhibiittorin puutteen aiheuttaman angioödeeman hoito angioödeeman (perinnöllinen tai hankittu) hoito ja enneltaehkäisy (akuutit kohtaukset)
French	Inhibiteur C1 humain recombinant	Traitement de l'oedème angioneurotique lié à un déficit en inhibiteur C1
German	Recombinant menschlicher C1-Inhibitor	Behandlung von Angioedema induziert durch C1-Inhibitor Mangel
Greek	Ανασυνδυασμένος ανθρώπινος αναστολεας C1	Θεραπεία αγγειακού οιδήματος που προέρχεται από ανεπάρκεια αναστολέα C1.
Italian	C1-inibitore umano ricombinante	Trattamento dell angioedema causato da deficit del C1-inibitore
Portuguese	Inibidor C1- humano recombinante	Tratamento de angioedema causado por deficiência de inibidor C1
Spanish	Inhibidor C1 humano recombinante	Tratamiento del angioedema causado por deficiencia del inhibidor C1
Swedish	Rekombinant human C1-inhibitor	Behandling av angioödem orsakat av C1 inhibitor brist

[1] At the time of designation