EMA/COMP/86/2003 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Icatibant acetate for treatment of angioedema

First publication	9 April 2003
Rev.1: information about Marketing Authorisation	16 November 2009
Rev.2: sponsor's name and address change	16 September 2013

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.

On 17 February 2003, orphan designation (EU/3/03/133) was granted by the European Commission to Jerini AG, Germany, for icatibant acetate for the treatment of angioedema.

In September 2013, Jerini AG changed name to Shire Orphan Therapies GmbH.

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). This 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 (voice box), leading to airway obstruction. It can also appear in the gut. This may lead to pain in the abdomen, and vomiting. Faeces (stools) may become too liquid, and may be 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 approximately 2 – 3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 77,000 – 115,00 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 were authorised in the Community for treatment for angioedema. Certain medicines have been used to treat acute attacks of angioedema. These 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 included drugs that prevent new attacks. These include the male sex hormones called androgens.

Icatibant might be of potential significant benefit for the treatment of angioedema, particularly in terms of a selective action. 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. Certain proteins called proteases control this response. Proteases are a family of proteins that break up other proteins. In this case, the proteases involved cause the release of proteins called kinins. Kinins are small proteins that cause widening of blood vessels. They also alter the passage of fluids across the walls of the vessels.

The activation of kinins requires a series of reactions involving a protein called bradykinin. This is a very potent protein that causes widening of blood vessels, and other effects. Bradykinin is found in human blood. The plasma is the fluid in the blood, in which blood cells are suspended. Icatibant specifically blocks the action of human bradykinin, and hence interrupts the series of reactions that leads to angioedema.

What is the stage of development of this medicine?

The effects of icatibant were evaluated in an experimental model.

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

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 10 January 2003 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 382,800,000 (Eurostat 2003).

Update: Icatibant acetate (Firazyr) has been authorised in the EU since 11 July 2008 for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults (with C1-esterase-inhibitor deficiency).

More information on Firazyr can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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 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	Icatibant acetate	Treatment of angioedema
Bulgarian	Икатибант ацетат	Лечение на ангиоедема
Czech	Acetát icatibantu	Léčba angioedému
Danish	Icatibantacetat	Behandling af angioødem
Dutch	Icatibant acetaat	Behandeling van angiooedeem
Estonian	Ikatibant atsetaat	Angioödeemi ravi
Finnish	Ikatibantti asetaatti	Angioödeeman hoito
French	Acétate d'icatibant	Traitement de l'oedème angioneurotique
German	Icatibant acetat	Behandlung des Angioödems
Greek	Icatibant (οξεικό άλας)	Θεραπεία αγγειοοιδήματος
Hungarian	Icatibant acetate	Angioedema kezelése
Italian	Icatibant acetato	Trattamento dell'angioedema
Latvian	Ikatibants acetāts	Angioedēmas ārstēšana
Lithuanian	Ikatibanto acetatas	Treatment of angioedema
Maltese	Icatibant acetate	Kura ta' l-anġoedema
Polish	Octan Icatibantu	Leczenie obrzęku naczynioruchowego
Portuguese	Acetato de Icatibant	Tratamento de angioedema
Romanian	Acetat de icatibant	Tratamentul angioedemului
Slovak	Ikatibantacetát	Liečba angioedému
Slovenian	Ikatibant	Zdravljenje angioedema
Spanish	Acetato de Icatibant	Tratamiento del angioedema
Swedish	Icatibantacetat	Behandling av angioödem

[1] At the time of marketing authorisation