30 March 2015
EMA/COMP/48508/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid for the treatment of hereditary angioedema

On 12 February 2015, orphan designation (EU/3/15/1431) was granted by the European Commission to BioCryst UK Ltd., the United Kingdom, for 3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid for the treatment of hereditary angioedema.

What is hereditary angioedema?

Angioedema is a disease characterised by attacks of swelling beneath the skin that can occur anywhere in the body, such as in the face, limbs, gut and larynx (voice box), causing discomfort and pain.

Angioedema can be caused by the deficiency (low levels) of 'C1 inhibitor', a protein in the blood that prevents the activation of some proteins involved in causing inflammation (swelling). The C1 inhibitor deficiency can be 'hereditary' or 'acquired'. Hereditary angioedema is caused by abnormalities in the gene responsible for the production of C1 inhibitor. Acquired angioedema is caused by conditions that increase the breakdown of C1 inhibitor such as cancer of the B cells (a type of white blood cell) and diseases where the body's own defence system attacks the C1 inhibitor protein.

Hereditary angioedema is a long-term debilitating disease that may be life threatening because, when the swelling occurs in the larynx, it can obstruct the airways and impede breathing.

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

At the time of designation, hereditary angioedema affected approximately 0.15 in 10,000 people in the European Union (EU). This was equivalent to a total of around 7,700 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).

[*]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 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

What treatments are available?

At the time of designation, several medicines were authorised in the EU for the treatment of hereditary angioedema. These included medicines containing human C1 inhibitor, conestat alfa and icatibant.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with hereditary angioedema because it will be available as an oral (by mouth) formulation, whereas the currently authorised products are to be given by injection. 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?

Because of the low levels of C1 inhibitor, a substance called 'kallikrein', which is involved in causing inflammation and swelling, is activated. This medicine is expected to work by attaching to and blocking the activity of kallikrein, thereby helping to relieve the symptoms of the disease.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with hereditary angioedema were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for hereditary angioedema or designated as an 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 9 January 2015 recommending the granting of this designation.

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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:

BioCryst UK Ltd.
(c/o Morgan Lewis & Bockius)
Condor House
5-10 St. Paul's Churchyard
London EC4M 8AL
United Kingdom
Tel. +44 (0)20 3201 5576
Fax +44 (0)20 3201 5001
E-mail: BioCrystUK@biocryst.com

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	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Treatment of hereditary angioedema
Bulgarian	3-[2-(4-карбамимидоил-фенилкарбамоил)-5-метокси-4-винил-фенил]-6-(циклопропилметил-карбамоил)-пиридин-2-карбоксилна киселина	Лечение на наследствен ангиоедем
Croatian	3-[2-(4-karbamimidoil-fenilkarbamoil)-5-metoksi-4-vinil-fenil]-6-(ciklopropilmetil-karbamoil)-piridin-2-karboksilatna kiselina	Liječenje hereditarnog angioedema
Czech	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-karboxylové kyseliny	Léčba hereditárního angioedému.
Danish	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Behandling af hereditært angioødem
Dutch	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxyliczuur	Behandeling van hereditair angioedema
Estonian	3-[2-(4-karbamimidoüül-fenüülkarbamoüüll)-5-metoksü-4-vinüül-fenüüll]-6-(tsüklopropüülmetüül-karbamoüül)-püridiin-2-karboksüülhape	Päriliku angioödeemi ravi
Finnish	3-[2-(4-karbamimidoyyli-fenyylikarbamoyyli)-5-metoksi-4-vinyyli-fenyyli]-6-(syklopropylmetyyli-karbamoyyli)-pyridiini-2-karboksyylihappo	Perinnöllisen angioödeeman hoito
French	Acide 3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylique	Traitement de l'angioedème héréditaire
German	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Behandlung des hereditären Angioödems
Greek	3-[2-(4-καρβαμιμιδοϋλ-φαινυλκαρβαμοϋλ)-5-μεθοξυ-4βινυλ-φαινυλ]-6-(κυκλοπροπυλμεθυλ-καρβαμοϋλ)-πυριδινο-2-καρβοκυλικό οξύ	Θεραπεία του συγγενούς αγγειοοιδήματος

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylsav	Örökletes angioedema kezelése
Italian	3-[2-(4-carbamimidoil-fenilcarbamil)-5-metossi-4-vinil-fenil]-6-(ciclopropilmethil-carbamoil)-piridina-2-acido carbossilico	Trattamento dell'angioedema ereditario
Latvian	3-[2-(4-karbamimidoil-fenilkarbamoil)-5-metoksi-4-vinil-fenil]-6-(ciklopropilmetil-karbamoil)-piridīna-2-karbonskābe	Iedzimtas angioedēmas ārstēšana
Lithuanian	3-[2-(4-karbamimidoil-fenilkarbamoil)-5-metoksi-4-vinil-fenil]-6-(ciklopropilmetil-karbamoil)-piridino-2-karboksirūgštis	Paveldimos angioedemos gydymas
Maltese	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Kura ta' anġoedema ereditarja
Polish	3-[2-(4-karbamimidoilo-fenylkarbamoilo)-5-metoksy-4-winylo-fenylo]-6-(cyklopropylmetylo-karbamoilo)-pirydyno-2-karboksylowy kwas	Leczenie dziedzicznego obrzęku naczynioruchowego
Portuguese	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Tratamento do angioedema hereditário
Romanian	Acid 3-[2-(4-carbamimidoil-fenilcarbamoil)-5-metoxi-4-vinil-fenil]-6-(ciclopropilmetil-carbamoil)-piridin-2-carboxilic	Tratamentul angioedemului ereditar
Slovak	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Liečba hereditárneho angioedému
Slovenian	3-[2-(4-carbamimidoil-phenilkarbamoil)-5-metoksi-4-vinil-fenil]-6-(ciclopropilmetil-karbamoil)-piridin-2-karboksilna kislina	Zdravljenje hereditarnega angioedema
Spanish	3-[2-(4-carbamimidoil-fenilcarbamoil)-5-metoxi-4-vinil-fenil]-6-(ciclopropilmethil-carbamoil)-piridine-2-carboxilic acid	Tratamiento de angioedema
Swedish	3-[2-(4-carbamimidoyl-phenylcarbamoyl)-5-methoxy-4-vinyl-phenyl]-6-(cyclopropylmethyl-carbamoyl)-pyridine-2-carboxylic acid	Behandling av hereditärt angioödem
Norwegian	3-[2-(4-karbamimidoyl-fenylkarbamoyl)-5-methoksy-4-vinyl-fenyl]-6-(syklopropylmetyl-karbamoyl)-pyridin-2-karboksylsyre	Behandling av heriditært angioødem

Language	Active ingredient	Indication
Icelandic	3-[2-(4-karbamímído-óýl-phenýlkarbamóýl)-5-methoxý-4-vínýl-phenýl]-6-(cýclóprópýlmethýl-karbamóýl)-pýridín-2-karboxýlic sýra	Meðferð við arfgengum æðabjúg