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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human IgG1 kappa light chain monoclonal antibody targeting plasma kallikrein for the treatment of hereditary angioedema

On 9 October 2015, orphan designation (EU/3/15/1551) was granted by the European Commission to Dyax Ltd, United Kingdom, for recombinant human IgG1 kappa light chain monoclonal antibody targeting plasma kallikrein 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 low levels of 'C1 inhibitor', a protein in the blood involved in the control of the 'kallikrein-kinin' system. This system plays a role in causing the swelling and inflammation seen in angioedema. Patients with low levels of C1 inhibitor have excessive activity of this system, which leads to the symptoms of angioedema.

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 in some cancers and autoimmune diseases.

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 less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 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).

*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).

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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 inhibitors (Cinryze and Berinert), conestat alfa (Ruconest) and icatibant (Firazyr).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with hereditary angioedema, with early studies showing that the medicine reduces angioedema attacks and compares favourably with existing treatments. 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?

This medicine is a monoclonal antibody (a type of protein) that has been designed to recognise and attach to kallikrein proteins, and thereby block the activity of the kallikrein-kinin system. Since this system plays a role in causing the swelling and inflammation seen in angioedema, this medicine is expected to reduce the number of angioedema attacks.

What is the stage of development of this medicine?

The effects of the 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. Orphan designation of the medicine had been granted in the United States for the treatment of hereditary angioedema.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 3 September 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

For details of the current sponsor of the orphan designation please refer to the information on the main web page of this Public Summary of Opinion.

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 IgG1 kappa light chain monoclonal antibody targeting plasma kallikrein	Treatment of hereditary angioedema
Bulgarian	Рекомбинантна IgG1 каппа лека верига от човешко моноклонално антитяло срещу плазмен калликреин	Лечение на наследствен ангиоедем
Croatian	Rekombinantno ljudsko IgG1 monoklonsko protutijelo lakog kapa lanca usmjereno na plazmatski kalikrein	Liječenje hereditarnog angioedema
Czech	Rekombinantní, lidská monoklonální protilátka IgG1 s lehkými řetězci kappa cílená na plazmatický kallikrein	Léčba hereditárního angioedému.
Danish	Rekombinant, humant IgG1 kappa let-kæde monoklonalt antistof rettet mod plasma kallikrein	Behandling af hereditært angioødem
Dutch	Recombinant humaan IgG1 kappa lichte keten monoklonaal antilichaam tegen plasma-kallikreïne	Behandeling van hereditair angioedema
Estonian	Plasma kallikreiini vastane rekombinantne inimpäritolu IgG1 kapa-tüüpi kerge-ahelaga monoklonaalne antikeha	Päriliku angioödeemi ravi
Finnish	Rekombinantti, ihmisen monoklonaalinen IgG1 kappakevytketju vasta-aine plasman kallikreiiniille	Perinnöllisen angioödeeman hoito
French	Anticorps monoclonal à chaîne légère IgG1 kappa, humain et recombinant, ciblant la kallicréine plasmatique	Traitement de l'angioedème héréditaire
German	Rekombinanter, humaner, monoklonaler IgG1 Kappa-Leichtketten-Antikörper gegen aktives Kallikrein im Blutplasma	Behandlung des hereditären Angioödems
Greek	Ανασυνδυασμένο, ανθρώπειο, IgG1 κάππα ελαφράς αλύσου μονοκλωνικό αντίσωμα με στόχο την ενεργό καλλικρεΐνη πλάσματος	Θεραπεία του συγγενούς αγγειοοιδήματος
Hungarian	Plazma kallikreint célzó rekombináns humán IgG1 kappa könnyű láncú, monoklonális antitest	Örökletes angioedema kezelése
Italian	Anticorpo monoclonale umano, ricombinante a catena leggera kappa delle IgG1, contro la callicreina plasmatica	Trattamento dell'angioedema ereditario
Latvian	Rekombinanta cilvēka IgG1 kappa vieglās ķēdes monoklonāla antiviela, kas vērsta pret plazmas kalikreīnu	Iedzimtas angioedēmas ārstēšana
Lithuanian	Rekombinantinio žmogaus IgG1 kapa lengvosios grandinės monokloninis antikūnas, nukreiptas į plazmos kalikreiną	Paveldimos angioedemos gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Antikorp monoklonali uman rikombinanti b' katina ħafifa ta' IgG1 kappa immirat għal kallikrein mill-plasma	Kura ta’ anġoedema ereditarja
Polish	Rekombinowane ludzkie przeciwciało monoklonalne klasy IgG1 o łańcuchu lekkim kappa skierowane przeciwko kalikreinie osoczowej	Leczenie dziedzicznego obrzęku naczynioruchowego
Portuguese	Anticorpo monoclonal recombinante humano - cadeia leve Kappa da IgG1- dirigido à calicreína plasmática	Tratamento do angioedema hereditário
Romanian	Lanţ uşor tip kappa al anticorpului monoclonal IgG1 uman recombinantîndreptat împotrivakalikreinei plasmatice	Tratamentul angioedemului ereditar
Slovak	Rekombinantná, ľudská monoklonálna protilátka IgG1 s kappa ľahkým reťazcom proti plazmatickému kalikreínu	Liečba hereditárneho angioedému
Slovenian	Rekombinantno monoklonsko protitelo, s humano IgG1 kapa lahko verigo, proti plazemskemu kalikreinu	Zdravljenje hereditarnega angioedema
Spanish	Anticuerpo monoclonal recombinante humano - cadena ligera kappa de la IgG1- anti-calicreína plasmática	Tratamiento del angioedema hereditario
Swedish	Rekombinant, human monoklonal antikropp av IgG1-kappa med lätta kedjor mot plasma-kallikrein	Behandling av hereditärt angioödem
Norwegian	Rekombinant humant IgG1 kappa lett kjede monoklonalt antistoff innrettet på plasmakallikrein	Behandling av heriditært angioødem
Icelandic	Raðbrigða, einstofna IgG1-kappaléttkeðjumótefni úr mönnum sem beinist að blóðvökvakallíkreini	Meðferð við arfgengum æðabjúg