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Public summary of opinion on orphan designation

Recombinant human ectonucleotide pyrophosphatase/phosphodiesterase 1 fused to the Fc fragment of IgG1 for the treatment of ectonucleotide pyrophosphatase/phosphodiesterase 1 deficiency

On 31 July 2018, orphan designation (EU/3/18/2049) was granted by the European Commission to Inozyme Pharma Ireland Ltd, Ireland, for recombinant human ectonucleotide pyrophosphatase/phosphodiesterase 1 fused to the Fc fragment of IgG1 (also known as INZ-701) for the treatment of ectonucleotide pyrophosphatase/phosphodiesterase 1 deficiency.

What is ectonucleotide pyrophosphatase/phosphodiesterase 1 deficiency?

Ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1) deficiency is an inherited disorder in which the body does not produce the enzyme ENPP1. The enzyme is important for preventing harmful calcification (build-up of calcium) in soft tissues and for controlling mineralisation (take up of minerals) in bones. ENPP1 deficiency can lead either to a problem called generalised arterial calcification of infancy (GACI) or to autosomal recessive hypophosphataemic rickets (ARHR).

GACI starts in very young babies whose arteries become narrower and stiffer, increasing the heart's workload. Patients develop very high blood pressure, heart failure (when the heart no longer works as well as it should), breathing difficulty, oedema (build-up of fluid in body tissues) and skin and lips becoming blue. ARHR, which starts appearing in early childhood, results in slow or reduced growth, bone abnormalities and pain which get worse with time. Adults develop osteomalacia (bones becoming soft and weak).

ENPP1 deficiency is a long-term debilitating and life-threatening disease that can lead to death in infancy.

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

At the time of designation, ENPP1 deficiency affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 people[*], and is below the ceiling for

[*]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 517,400,000 (Eurostat 2018).

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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?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of ENPP1 deficiency. Treatment was mainly supportive to manage symptoms of the condition.

How is this medicine expected to work?

The medicine consists of a synthetic form of the enzyme ENPP1. The enzyme is attached to a protein called Fc fragment to help it stay in the body for longer. By replacing the missing enzyme in patients with ENPP1 deficiency, the medicine is expected to reduce symptoms of the condition.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with ENPP1 deficiency had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for ENPP1 deficiency 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 21 June 2018 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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 ectonucleotide pyrophosphatase/phosphodiesterase 1 fused to the Fc fragment of IgG1	Treatment of ectonucleotide pyrophosphatase/phosphodiesterase 1 deficiency
Bulgarian	Рекомбинантна човешка ектонуклеотидна пирофосфатаза/фосфодиестераза 1 свързана с Fc фрагмента на имуноглобулин G1	Лечение на недостатъчност на ектонуклеотидна пирофосфатаза/фосфодистераза 1
Croatian	Rekombinantna ljudska ektonukleotid pirofosfataza/fosfodiesteraza 1 vezana za Fc fragment IgG1	Liječenje nedostatka ektonukleotid pirofosfataze/fosfodiesteraze 1
Czech	Rekombinantní lidská pyrofosfátáza/fosfodiesteráza 1 fúzovaná na Fc fragment IgG1	Léčba deficience ektonukleotidu pyrofosfatázy/fosfodiesterázy 1
Danish	Rekombinant human ectonukleotid pyrophosphatase/phosphodiesterase 1 fusioneret til Fc-fragmentet af IgG1	Behandling af ectonucleotid-pyrofosfatase-/fosfodiesterase-1-mangel
Dutch	Recombinant humaan ectonucleotide pyrofosfatase/fosfodiësterase 1, gekoppeld aan het Fc-fragment van IgG1	Behandeling van ectonucleotide pyrofosfatase/fosfodiësterase 1-deficiëntie
Estonian	Rekombinantne inimese ektonukleotiidpürofosfataas/fosfodiesteraas 1, mis on liidetud IgG1 Fc fragmendiga	Ektonukleotiidpürofosfataasi/fosfodiesteraas 1 vaeguse ravi
Finnish	IgG1:n Fc-fragmenttiin fuusioitu, rekombinantti ihmisen ektonukleotidipyrofosfataasi/fosfodiesteraasi 1	Ektonukleotidipyrofosfataasin/fosfodiesteraasi 1:n puutoksen hoito
French	Ectonucléotide pyrophosphatase/phosphodiestérase humaine recombinante de type 1 fusionnée au fragment Fc d'IgG1	Traitement du déficit en ectonucléotide pyrophosphatase/phosphodiestérase 1
German	Rekombinante menschliche Ectonukleotid-Pyrophosphatase/Phosphodiesterase 1 verbunden an dem Fc-Fragment von IgG1	Behandlung des Ektonukleotid-Pyrophosphatase/Phosphodiesterase 1-Mangels
Greek	Ανασυνδυασμένη ανθρώπινη πυροφωσφατάση/φωσφοδιεστεράση 1 εξωνουκλεοτιδίου, συντηγμένη με το τμήμα Fc της ανοσοσφαιρίνης IgG1	Θεραπεία ανεπάρκειας πυροφωσφατάσης/φωσφοδιεστεράσης 1 εξωνουκλεοτιδίου
Hungarian	Rekombináns humán ektonukleotid-pirofoszfatáz/-foszfodiészteráz-1, IgG1 Fc fragmentjéhez kapcsolva	Az ektonukleotid pirofoszfatáz/foszfodiészteráz 1 hiány kezelése

[1] At the time of designation

Italian	Ectonucleotide pirofosfatasi/fosfodiesterasi 1 ricombinante umano fuso al frammento Fc di IgG1	Trattamento della carenza di ectonucleotide pirofosfatasi/fosfodiesterasi 1
Latvian	Rekombinanta cilvēka ektonukleotīda pirofosfatāze/ fosfodiesterāze 1, kas sapludināta ar IgG1 Fc fragmentu	Ektonukleotīda pirofosfatāzes/fosfodiesterāzes 1 nepietiekamības ārstēšana
Lithuanian	Rekombinantinė žmogaus ektonukleotido pirofosfatazė/fosfodiesterazė 1 sulietos su IgG1 Fc fragmentufragment	Ektonukleotidų pirofosfatazės/fosfodiesterazės 1 stokos gydymas
Maltese	Ektonukleotid pirofosfataži/fosfodiesteraži 1 uman rikombinanti mwaħħla mal-framment Fc ta' IgG1	Trattament ta' defiċjenza ta' ektonukleotid pirofosfataži/fosfodiesteraži 1
Polish	Rekombinowana ludzka pirofosfataza ektonukleotydowa /fosfodiesteraza 1 zespolona z fragmentem Fc IgG1	Leczenie niedoboru pirofosfatazy ektonukleotydowej /fosfodiesterazy 1
Portuguese	Ectonucleotídeo pirofosfatase/fosfodiesterase 1 humano recombinante fundido com o fragmento Fc da IgG1	Tratamento de deficiência de ectonucleotido pirofosfatase/fosfodiesterase 1
Romanian	Ectonucleotid pirofosfatază/fosfodiesterază 1 recombinantă umană atașat la fragmentul Fc al IgG1	Tratamentul deficitului de ectonucleotid pirofosfatază/fosfodiesterază 1
Slovak	Rekombinantná ľudská ektonukleotidová pyrofosfatáza/fosfodiesteráza 1 fúzovaná s Fc fragmentom IgG1	Liečba deficiencie ektonukleotidovej pyrofosfatázy/fosfodiesterázy 1
Slovenian	Rekombinantna humana ektonukleotidna pirofosfataza/fosfodiesteraza 1, spojena s Fc fragmentom IgG1	Zdravljenje pomanjkanja ekto-nukleotid pirofosfataze/fosfodiesteraze 1
Spanish	Ectonucleótido pirofosfatasa/fosfodiesterasa 1 recombinante humano unido al fragmento Fc de IgG1	Tratamiento de la deficiencia de ectonucleótido pirofosfatasa/fosfodiesterasa 1
Swedish	Rekombinant humant ektonukleotid pyrofosfatas/fosfodiesteras 1 fuserat med Fc-fragmentet av IgG1	Behandling av ektonukleotidpyrofosfatas/fosfodiesteras 1-brist
Norwegian	Rekombinant human ektonukleotid pyrofosfatase/fosfodiesterase 1 fusjonert med Fc-fragmentet av IgG1	Behandling av ektonukleotid pyrofosfatase/fosfodiesterase 1-mangel
Icelandic	Raðbrigða ektónúkleótíð pýrófosfatasi/fosfódíesterasi 1 bundinn við Fc-hluta G-ónæmisglóbúlíns (IgG1)	Meðferð við skorti á ektónúkleótíð pýrófosfatasa/fosfódíesterasa 1