

26 February 2013
EMA/COMP/39571/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys for the treatment of high altitude pulmonary oedema

On 8 February 2013, orphan designation (EU/3/13/1102) was granted by the European Commission to Apeptico Forschung und Entwicklung GmbH, Austria, for Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys for the treatment of high altitude pulmonary oedema.

What is high altitude pulmonary oedema?

High altitude pulmonary oedema (HAPE) is a condition that occurs at high altitude in otherwise healthy people in which the alveoli (structures at the end of the airways in the lungs where the oxygen is absorbed) fill up with fluid. This results in difficulty breathing, chest tightness, cyanosis (bluish coloration of the skin and mucous membranes due to low oxygen levels in the blood), tachypnoea (rapid breathing) and tachycardia (rapid heartbeat).

HAPE is caused by the way the body reacts to the lack of oxygen at high altitude. It usually occurs after rapid ascent to altitudes of 3,000 m and higher. It usually happens in people who are not acclimatised to such altitudes but the reasons why only some people develop it are not known.

HAPE is a life-threatening medical emergency with a death rate of between 24 and 44% because the symptoms get rapidly worse if left untreated.

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

At the time of designation, HAPE affected less than 0.03 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 1,500 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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).

What treatments are available?

At the time of designation, there were no satisfactory treatments for HAPE. The best option was to bring the patients down to a lower altitude as quickly as possible while administering oxygen. Some medicines including nifedipine, steroids, beta-agonists, phosphodiesterase 5 inhibitors and diuretics were also used, although they were not authorised for treating this condition.

How is this medicine expected to work?

The medicine is designed to attach to and 'open' sodium channels (called ENaC) in the cells of the alveoli. Opening the sodium channels leads to the movement of sodium and water out of the alveoli, helping to clear the build-up of fluid. This medicine is therefore expected to improve absorption of oxygen and reduce the life-threatening symptoms of the condition, thereby improving the chances of survival.

The medicine is expected to be taken by inhalation.

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, no clinical trials with the medicinal product in patients had been started.

At the time of submission, the medicinal product was not authorised anywhere in the EU for HAPE 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 2013 recommending the granting of this designation.

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:

APEPTICO Forschung und Entwicklung GmbH
Mariahilfer Straße 136, Top 1.15
1150 Vienna
Austria
Telephone: +43 664 1432 919
Telefax: +43 125 3303 37795
E-mail: b.fischer@apeptico.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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Treatment of high altitude pulmonary oedema
Bulgarian	Цикло-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Лечение на височинен белодробен оток
Czech	Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Léčba výškového plicního edému
Danish	Cyclo- Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Behandling af højde-lungeødem
Dutch	Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Behandeling van hoogte longoedeem
Estonian	Tsüklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Kõrgaltituudist tingitud kopsuturse ravi
Finnish	Syklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Vuoristotautiin liittyvän keuhkoedeeman hoito
French	Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Traitement de l'oedème pulmonaire de haute altitude
German	Zyklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Behandlung des Höhenlungenödems
Greek	Κυκλο-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Θεραπεία του πνευμονικού οιδήματος της νόσου των ορέων.
Hungarian	Ciklo Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Nagy magasságban kialakuló tüdő oedema kezelése
Italian	Ciclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Trattamento dell' Edema Polmonare da alta quota
Latvian	Ciklo-Cis-Gli-Gln-Arg-Glu-Thr-Pro-Glu-Gli-Ala-Glu-Ala-Liz-Pro-Trp-Tir-Cis	Augstuma izraisītas plaušu tūskas ārstēšana
Lithuanian	Ciklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Aukštikalnių sukeltos plaučių edemos gydymas
Maltese	Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Kura tal-edema pulmonari ta' altitudni għolja
Polish	Cyklo Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Leczenie wysokościowego obrzęku płuc
Portuguese	Ciclo-Cis-Gli-Gln-Arg-Glu-Tre-Pro-Glu-Gli-Ala-Glu-Ala-Lis-Pro-Trp-Tir-Cis	Tratamento do edema pulmonar de alta altitude
Romanian	Ciclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Tratamentul edemului pulmonar de mare altitudine
Slovak	Cyklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Liečba pľúcneho edému spôsobeného vysokou nadmorskou výškou
Slovenian	Ciklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Zdravljenje pljučnega edema pri višinski bolezni

¹ At the time of designation

Language	Active ingredient	Indication
Spanish	Ciclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Tratamiento del edema pulmonar por altitud
Swedish	Cyclo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Behandling av höghöjdslungödem
Norwegian	Syklo-Cys-Gly-Gln-Arg-Glu-Thr-Pro-Glu-Gly-Ala-Glu-Ala-Lys-Pro-Trp-Tyr-Cys	Behandling av høyde-lungeødem
Icelandic	Cýkló-Cys-Glý-Gln-Arg-Glú-Thr-Pró-Glú-Glý-Ala-Glú-Ala-Lýs-Pró-Trp-Týr-Cys	Meðferð við háfjallalungnabjúg