29 January 2016
EMA/COMP/794903/2015
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

[4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) for the treatment of pseudohypoaldosteronism 1B

On 14 December 2015, orphan designation (EU/3/15/1592) was granted by the European Commission to Apeptico Forschung und Entwicklung GmbH, Austria, for [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) (also known as AP318) for the treatment of pseudohypoaldosteronism 1B.

## What is pseudohypoaldosteronism 1B?

Pseudohypoaldosteronism 1B is an inherited disorder characterised by abnormal salt and water balance in the body. The disease is caused by a genetic mutation (change) leading to defects in certain proteins called sodium ion channels located in the cells of the gut, kidney and lungs. These ion channels regulate the transport of salt and water in the body. As a result of the mutation, patients have sodium loss from the body, dehydration and high blood levels of potassium and acid, which can lead to organ damage. In the lungs, fluid accumulation in the alveoli (tiny air sacs in the lungs where oxygen is absorbed) leads to cough and repeated infections.

Pseudohypoaldosteronism 1B is a long-lasting, debilitating disease and may be life threatening because of its damaging effects on the gut, lungs and kidneys.

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

At the time of designation, pseudohypoaldosteronism 1B affected approximately 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,000 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, no medicines were authorised in the EU for the treatment of pseudohypoaldosteronism 1B. Treatments were aimed at correcting salt levels, fluid balance and other symptoms of the disease rather than correcting the underlying cause of the disease.

## How is this medicine expected to work?

This medicine is intended to be given by inhalation. When inhaled, it is expected to activate sodium ion channels and facilitate the transport of sodium into the bloodstream. This is expected to help reduce the fluid in the alveoli and thereby reduce lung infections and improve cough, and also to improve the general electrolyte imbalance in patients with pseudohypoaldosteronism 1B.

## 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 medicine in patients with pseudohypoaldosteronism 1B had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for pseudohypoaldosteronism 1B 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 12 November 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:

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 | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Treatment of pseudohypoaldosteronism type 1B |
| Bulgarian | [4-аминобутаноева киселина-глицил-L-глутаминил-L-аргинил-L-.алфа.-глутамил-L-треонил-L-пролил-L-.алфа.-глутамилглицил-L-аланил-L-.алфа.-глутамил-L-аланил-L-лизил-L-пролил-L-триптофил-L-тирозил-L-аспартил](цикло 1-Дгама17) | Лечение на псевдохипоалдостеронизъм тип 1Б |
| Croatian | [4-aminobutanoatna kiselina-glicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-L-aspartil](ciklo 1-Dgama17) | Liječenje pseudohipoaldosteronizma tipa 1B |
| Czech | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Léčba pseudohypoaldosteronismus typ 1B |
| Danish | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Behandling af pseudohypoaldosteronism type 1B |
| Dutch | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Behandeling van pseudohypoaldosteronisme type 1B |
| Estonian | [4-aminobutanoiikhappe-glütsüül-L-glutaminüül-L-arginüül-L-.alfa.-glutamüül-L-threonüül-L-prolüül-L-.alfa.-glutamüülglütsüül-L-alanüül-L-.alfa.-glutamüül-L-alanüül-L-lüsüül-L-prolüül-L-trüptofüül-L-türosüül-L-aspartüül](tsüklo 1-Dgamma17) | 1B tüüpi pseudohüpoaldosteronism ravi |
| Finnish | [4-aminovoihappo-glysyyli-L-glutaminyyli-L-arginyyli-L-.alpha.-glutamyyli-L-threonyyli-L-prolyyli-L-.alpha.-glutamyyliglysyyli-L-alanyyli-L-.alpha.-glutamyyli-L-alanyyli-L-lysyyli-L-prolyyli-L-tryptofyyli-L-tyrosyyli-L-aspartyyli](syklo 1-Dgamma17) | Tyypin 1B pseudohypoaldosteronismin hoito |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| French | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Traitement du pseudohypoaldostéronisme de type 1B |
| German | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Behandlung des Pseudohypoaldosteronismus Typ 1B |
| Greek | [4-αμινοβουτανοϊκό οξύ-γλυκυλ-L-γλουταμινυλ-L-αργινυλ-L-α-γλουταμυλ-L-θρεονυλ-L-προλυλ-L-α-γλουταμυλγλυκυλ-L-αλανυλ-L-α-γλουταμυλ-L-αλανυλ-L-λυσυλ-L-προλυλ-L-τρυπτοφυλ-L-τυροσυλ-L-ασπαρτυλ](κυκλο 1-Dγ17) | Θεραπεία του ψευδοϋποαλδοστερονισμού τύπου 1Β |
| Hungarian | [4-aminobutánsav glicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-._alfa.-glutamilglicil-L-alanil-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-L-aspartil](ciklo 1-Dgamma17) | 1B-típusú pseudohypoaldosteronismus kezelése |
| Italian | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Trattamento dello pseudoipoaldosteronismo tipo 1B |
| Latvian | [4-aminosviestskābes-glicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-threonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-L-aspartil](ciklo 1-Dgamma17) | 1B tipa pseidohipoaldosteronisma ārstēšana |
| Lithuanian | [4-aminobutano rūgštis-glicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lisil-L-prolil-L-triptofil-L-tirosil-L-aspartil](ciklo 1-Dgamma17) | Pseudohipoaldosteronizmo 1B tipo gydymas |
| Maltese | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Kura ta' psewdoipoaldosteroniżmu tat-tip 1B |
| Polish | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Leczenie pseudohypoaldosteronizmu typu 1B |

| Language | Active ingredient | Indication |
|---|---|---|
| Portuguese | [ácido glicil-L-glutaminil-L-arginil-L-alpha-glutamil-L-treonil-L-prolil-L-alpha-glutamilglicil-L-alanil-L-alpha-glutamil-L-alanil-L-lisil-L-prolil-L-triptofill-L-tirosil-L-aspartil-4-aminobutanóico](cyclo 1-Dgama17) | Tratamento de pseudohipoaldosteronismo tipo 1B |
| Romanian | [acid-glicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofil-L-tirozil-L-aspartil-4 aminobutanoic](ciclo 1-Dgama17) | Tratamentul pseudohipoaldosteronismului de tip 1B |
| Slovak | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Liečba pseudohypoaldosteronizmu typ 1B |
| Slovenian | [4-aminobutanojska kislina-glicil-L-glutaminil-L-arginil-L-.alfa.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alfa.-glutamil-L-alanil-L-lizil-L-prolil-L-triptofill-L-tirozil-L-aspartil](ciklo 1-Dgama17) | Zdravljenje psevdohipoaldosteronizma 1B |
| Spanish | [4-aminobutanoic acid-glicil-L-glutaminil-L-arginil-L-.alpha.-glutamil-L-treonil-L-prolil-L-.alfa.-glutamilglicil-L-alanil-L-.alpha.-glutamil-L-alanil-L-lysil-L-prolil-L-triptofil-L-tirosil-L-aspartil](ciclo 1-Dgamma17) | Tratamiento del pseudohipoaldosteronismo tipo 1B |
| Swedish | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Behandling av pseudohypoaldosteronism typ 1B |
| Norwegian | [4-aminobutanoic acid-glycyl-L-glutaminyl-L-arginyl-L-.alpha.-glutamyl-L-threonyl-L-prolyl-L-.alpha.-glutamylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl-L-lysyl-L-prolyl-L-tryptophyl-L-tyrosyl-L-aspartyl](cyclo 1-Dgamma17) | Behandling av pseudohypoaldosteronism type 1B |
| Icelandic | [4-amínóbútanóic sýru-glýcýl-L-glútamínýl-L-arginýl-L-.alfa.-glútamýl-L-threónýl-L-prólýl-L-.alfa.-glútamýlglýcýl-L-alanýl-L-.alfa.-glútamýl-L-alanýl-L-lýsýl-L-prólýl-L-trýptóphýl-L-týrósýl-L-aspartýl](cýcló 1-Dgamma17) | Meðferð við pseudóhýpóaldósterónisma gerð 1B |