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EMA/COMP/632552/2017

# Public summary of opinion on orphan designation

## Synthetic cyclic 8 amino acid analogue of human unacylated ghrelin for the treatment of Prader-Willi syndrome

On 16 October 2017, orphan designation (EU/3/17/1932) was granted by the European Commission to Alizé Pharma, France, for synthetic cyclic 8 amino acid analogue of human unacylated ghrelin (also known as AZP-531) for the treatment of Prader-Willi syndrome.

### What is Prader-Willi syndrome?

Prader-Willi syndrome is an inherited condition caused by defects in specific regions of chromosome 15. This causes a wide range of symptoms, some of which can appear at birth, such as feeding problems, small size and reduced muscle strength. During childhood further symptoms develop, including increased appetite leading to constant eating and severe obesity, short stature, incomplete sexual development, learning difficulties and behavioural problems, such as aggression and stubbornness.

Prader-Willi syndrome is a life-long debilitating and life-threatening disease because of its serious symptoms, particularly learning difficulties, behavioural problems and obesity.

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

At the time of designation, Prader-Willi syndrome affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 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).

#### What treatments are available?

At the time of designation, growth hormone was authorised in the EU for treating Prader-Willi syndrome. In addition, symptoms were treated or managed in various ways, including supervised access to food to prevent obesity.

*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 515,700,000 (Eurostat 2017).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with Prader-Willi syndrome. Early studies show that it may reduce the excessive food intake – benefit not seen with current therapy. 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?

The medicine is thought to work by counteracting the activity of a hormone called ghrelin, which is produced mainly by the stomach. Ghrelin has an effect on appetite by regulating how fats and glucose (sugar) are used by the body. By counteracting the activity of ghrelin, this medicine is expected to reduce the patients' appetite and thus their food intake.

## 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 Prader-Willi syndrome were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for Prader-Willi syndrome 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 7 September 2017 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 | Synthetic cyclic 8 amino acid analogue of human unacylated ghrelin | Treatment of Prader-Willi syndrome |
| Bulgarian | Синтетичен цикличен 8-аминокиселинен аналог на на човешкия не-ацилиран грелин | Лечение на синдром на Прадер-Вили |
| Croatian | Sintetski ciklički 8-aminokiselinski analog humanog neaciliranog grelina | Liječenje Prader-Willijevog sindroma |
| Czech | Syntetický cyklický analog lidského neacylovaného ghrelinu složený z 8 aminokyselin | Léčba Prader-Williho syndromu |
| Danish | Syntetisk, cyklisk 8-aminosyre analog af humant ikke-acyleret ghrelin | Behandling af Prader-Willis syndrom |
| Dutch | Synthetisch cyclisch 8 aminozuuranaloog van humaan niet-geacyleerde ghreline | Behandeling van Prader-Willi syndroom |
| Estonian | Inimese atsüleerimata greliini sünteetiline tsükliline 8 aminohappe analoog | Prader-Willi sündroomi ravi |
| Finnish | Ihmisen asyloimattoman greliinin synteettinen syklinen 8 aminohapon analogi | Prader-Willin oireyhtymän hoito |
| French | Analogue d'acide aminé 8 cyclique synthétique de la ghréline humaine non acylée | Traitement du syndrome de Prader-Willi |
| German | Synthetisches zyklisches 8-Aminosäuren-Analogon des humanen nicht-acylierten Ghrelins | Behandlung des Prader-Willi-Syndroms |
| Greek | Συνθετικό κυκλικό ανάλογο 8 αμινοξέων της ανθρώπινης μη ακυλιωμένης γκρελίνης | Θεραπεία του συνδρόμου Prader-Willi |
| Hungarian | A humán nem acilált ghrelin szintetikus, ciklikus, 8 aminosavas analógja | Prader-Willi szindróma kezelése |
| Italian | Analogo sintetico ciclico a 8 amminoacidi della grelina umana non acilata | Trattamento della sindrome di Prader-Willi |
| Latvian | Cilvēka neacilētā grelīna sintētisks, ciklisks 8 aminoskābju analogs | Prader-Wili sindroma ārstēšana |
| Lithuanian | Sintetinis ciklinis neacetilinto žmogaus grelino 8 aminorūgščių analogas | *Prader-Willi* sindromo gydymas |
| Maltese | Analogu sintetiku ċikliku ta' 8 amminoaċidi tal-grelina mhux aċilat uman | Kura għal Prader-Willi Syndrome |
| Polish | Syntetyczny cykliczny analog ludzkiej nieacylowanej greliny składający się z 8 aminokwasów | Leczenie zespołu Pradera-Williego |
| Portuguese | Análogo sintético cíclico de 8 aminoácidos da grelina humana não-acilada | Tratamento da síndrome de Prader-Willi |
| Romanian | Analog sintetic ciclic al ghrelinei umane neacilate format din 8 aminoacizi | Tratamentul sindromului Prader-Willi |
| Slovak | Syntetický cyklický analóg ľudského neacylovaného grelínu z 8 aminokyselín | Liečba Praderovho-Williho syndrómu |

[1] At the time of designation

| Language | Active ingredient | Indication |
|---|---|---|
| Slovenian | Sintetični ciklični 8 aminokislinski analog humanega neaciliranega grelina | Zdravljenje Prader-Willijevega sindroma |
| Spanish | Análogo sintético cíclico de 8 aminoácidos de la ghrelina humana no acilada | Tratamiento del Síndrome de Prader-Willi |
| Swedish | Syntetisk cyklisk 8-aminosyreanalog av humant oacylerat ghrelin | Behandling av Prader Willis syndrom |
| Norwegian | Syntetisk syklisk 8 aminosyreanalog av humant ikke-acylert ghrelin | Behandling av Prader-Willis syndrom |
| Icelandic | Tilbúin 8 hringja amínósýruhliðstæða úr óasýleruðu manna ghrelíni | Meðhöndlun á Prader-Willi heilkenni |