16 November 2020
EMADOC-628903358-2617

Public summary of opinion on orphan designation

C-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker for the treatment of achondroplasia

On 27 July 2020, orphan designation EU/3/20/2299 was granted by the European Commission to Ascendis Pharma Growth Disorders A/S, Denmark, for c-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker for the treatment of achondroplasia.

What is achondroplasia?

Achondroplasia represents the most common form of short-limb dwarfism, a condition where the bones in the arms and legs do not form properly and are shorter than normal. Patients with achondroplasia have a short stature, an enlarged head with a prominent forehead, bowed legs, ear problems, compression of the spinal cord, as well as short fingers, toes, lower legs and upper arms.

Achondroplasia is an inherited disease caused by a mutation (change) in a gene responsible for making a protein called fibroblast growth-factor receptor 3 (*FGFR3*). Patients who have inherited the defective gene from both parents are the most severely affected and normally die around birth or a few months afterwards. In patients with only one defective *FGFR3* gene, achondroplasia causes long-term disability and may result in a shorter life span.

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

At the time of designation, achondroplasia affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 30,000 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, no satisfactory methods were authorised in the EU for the treatment of achondroplasia. Patients were given supportive care, as well as surgery to extend limb length, to correct spinal compression or to correct bowed legs.

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

How is this medicine expected to work?

The exact way the medicine works is not clear. However early studies indicate that it may inhibit the action of the defective *FGFR3* gene, thereby relieving symptoms of the disease.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with achondroplasia were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of achondroplasia. Orphan designation had been granted in the United States for the condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 18 June 2020, 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

Contact details of the current sponsor for this orphan designation can be found on EMA website.

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	C-type natriuretic peptide conjugated to multi-arm polyethylene glycol carrier through a cleavable linker	Treatment of achondroplasia
Bulgarian	С-тип натриуретичен пептид конюгиран чрез нестабилна връзка с многораменен полиетилен гликол носител	Лечение на ахондроплазия
Croatian	Natriuretski peptid tipa C konjugiran na nosač polietilen glikola višestrukih krakova kroz povezivač koji se može odcijepiti	Liječenje ahondroplazije
Czech	Natriuretický peptid typu C konjugovaný s multiramenným polyethylenglykolovým nosičem prostřednictvím štěpitelné spojky	Léčba achondroplazie
Danish	C-type natriuretisk peptid konjugeret med et flergrenet polyethylenglycolsubstrat via et led, der kan spaltes	Behandling af akondroplasi
Dutch	C-type natriuretisch peptide geconjugeerd aan multi-arm polyethyleneglycol drager door een afkliefbare linker	Behandeling van achondroplasie
Estonian	C-tüüpi natriureetiline peptiid, mis on lõigatava linkeriga konjugeeritud mitme õlaga polüetüleenglükool-kandjaga	Akondroplaasia ravi
Finnish	C-tyypin natriureettinen peptidi, joka on konjugoitu moniketjulliseen polyetyleeniglykolikantajaan katkaistavan linkkerin kautta	Akondroplasian hoito
French	Peptide natriurétique de type C conjugué à un transporteur en polyéthylène glycol à bras multiples par l'intermédiaire d'un lien clivable	Traitement de l’achondroplasie
German	Natriuretisches Peptid Typ C konjugiert an einen Multi-Arm Polyethylen Glycol Träger über eine spaltbare Verbindung	Behandlung der Achondroplasie
Greek	Νατριουρητικό πεπτίδιο τύπου C προσδεμένο σε ένα φορέα πολυκλαδικής πολυεθυλενογλυκόλης μέσω ενός αποκόψιμου προσδέματος	Θεραπεία της Αχονδροπλασίας

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	Hasítható linkeren keresztül többkarú polietilénglikol hordozóhoz konjugált C-típusú natriuretikus peptid	Achondroplasia (chondrodystrophia) kezelése
Italian	Peptide natruiretico tipo C coniugato con un carrier di glicole etilenico multi-braccio attraverso un legame scindibile	Trattamento dell'acondroplasia
Latvian	C-tipa nātriurētisks peptīds, kas kojugēts ar daudz-zaru polietilēna glikola nesēju caur skaldāmu savienotāju	Ahondroplāzijas ārstēšana
Lithuanian	C-tipo natriuretinis peptidas, per skaldomą jungtį sujungtas su daugiašakiu polietilenglikolio nešikliu	Achondroplazijos gydymas
Maltese	Peptide natrijuretiku tat-tip Ċ konjugat ma' portatur polietilenglikol multi-arm permezz ta' linker li jista' jinqasam	Kura tal-akondroplasija
Polish	Natriuretyczny peptyd typu C skonjugowany z wieloramiennym nośnikiem w postaci glikolu polietylenowego, za pomocą rozcinalnego łącznika	Leczenie achondroplazji
Portuguese	Peptídeo natriurético do tipo C conjugado com um transportador de polietileno glicol de vários braços através de um ligante clivável	Tratamento da acondroplasia
Romanian	Peptidul natriuretic de typ C conjugat cu un transportor din polietilenglicol cu brațe multiple prin intermediul unui agent de legatură scindabil	Tratamentul acondroplaziei
Slovak	C-type nátriuretického peptidu konjugovaný na multi-ramenný polyetylén glykolový nosič cez štiepitelný linker	Liečba achondroplázie
Slovenian	Natriuretični peptid tipa-C, konjugiran na polietilenski glikolni nosilec z razgradljivo povezavo	Zdravljenje ahondroplazije
Spanish	Peptide naturetico tipo-c conjugada a un transportador en glicol de polietilena a un brazo multiple por medio de un vinculo escindible	Tratamiento de la acondroplasia
Swedish	natriuretisk peptid typ C konjugerad till en multi-arm polyetylenglykolbärare med en delbar linker	Behandling av akondroplasi
Norwegian	C-type natriuretisk peptid konjugert til multiarm polyetylenglykol-bærer gjennom en kløyvbar linker	Behandling av akondroplasi
Icelandic	Natríumræsihormón af C-gerð sem tengt er fjölarma pólýetýlenglýkólbera með rjúfanlegu tengi	Meðferð við brjóskkröm (e. achondroplasia)