REPORT Lonapegsomatropin Ascendis Pharma®- lonapegsomatropin

Product & Mechanism of action

Substance: lonapegsomatropin

Brand Name: Lonapegsoma-tropinAscendis Pharma

Originator/licensee: Ascendis Pharma Endocrinology Division A/S

Classification: NCE

ATC code: H01AC

Orphan Status:
Eu: Yes
Us: Yes

Mechanism of action:
Lonapegsomatropin is a hGH prodrug consisting of rhGH that is transiently conjugated to a mPEG carrier via a TransCon® linker, that slowly releases the active molecule hGH viahydrolysis. hGH acts directly via stimulation of GH-receptor and indirectly via IGF-1 primarilyproduced in the liver. GH via its action on GH-receptors present on multiple tissues results ingrowth stimulation, change in body composition and stimulation of metabolic actions [1].

Authorized indications Licensing status

Authorized Indication:
EMA: Growth failure in children and adolescents aged from 3 years up to 18 years due to insufficient endogenous growth hormone secretion (GHD) [2].

FDA: lonapegsomatropin is indicated for the treatment ofpediatric pts 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous GH[3]

Route of administration:SC

Licensing status
EU CHMP P.O. date: 11/11/2021
FDA M.A. date: 25/08/2021

EU Speed Approval Pathway:-
FDA Speed Approval Pathway:
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ABBREVIATIONS:
AE: adverse events
AHV: annualized height velocity
BL: baseline
CHMP: Committee for Medicinal Products for Human Use
hGH: humangrowth hormone
GH: growth hormone
GHD: growth hormone deficiency
GHR: growth hormone receptor
IGF-1: insulin-like growth factor-1
LSM: least squares mean
mPEG: methoxypolyethylene glycol
M.A.: Marketing Authorization
p: p-Value
P.O.: Positive Opinion
Pts: patients
rhGH: recombinant human growth hormone
SAE: Serious Adverse Events
SC: subcutaneous
SDS: standard deviation score
SIEDP: Società Italianadi Endocrinologiae Diabetologia Pediatrica
wk: weeky

Essential therapeutic features

Summary of clinical EFFICACY:

Trial	Treatment Arms	Primary Endpoint	Results
heiGHttrial (NCT02781727) phase 3 randomized, open-label, active-controlled trial. Pts enrolled were at Tanner stage 1 with GHD. The pts aged from 3 to 13 years.	-lonapegsomatropin (0.24 mg hGH/kg/wk) once-weekly, SC (n=105, group A) - somatropin (0.034 mg hGH/kg/day) daily; SC (n=56, group B)	AHV (cm/year) after 52 weeks	At 52 weeks, LSM for AHV was 11.2 (±0.2) cm/year for pts in lonapegsomatropin arm vs 10.3 (±0.3) cm/year for pts in somatropin arm (p=0.009) [1,3-5]
Supportive trial:			
fliGHttrial (NCT03305016) multicenter, phase 3, open-label, single-arm, in children aged 6 months to 17 years old with open epiphysis and in Tanner stage <5	lonapegsomatropin (0.24 mg hGH/kg/wk) once-weekly, SC (n=146, group C)	AHV (cm/year) after 26 weeks	The LSM for AHV was 8.72 cm/year (95% CI: 8.55-9.77) at week 26[1,4,6].
enlighten trial (NCT03344458) a phase 3, ongoing, multicenter, open-label extension trial of lonapegsomatropin administered once-weekly inpediatric pts with GHD who previously participated in heiGHtor fliGHt trials.	lonapegsomatropin (0.24 mg hGH/kg/wk) once-weekly, SC (n=103 from group A; n=55 from group B; n=140 from group C)	AHV (cm/year) after four years (192 weeks)	**Partial results:** The treatment difference in LSM height SDS (A vs B) at the end of heiGHt trial was sustained through week 104 (1.61 vs 1.49; p=0.158). For group C, height SDS improved from −1.42 at fliGHttrial BL to −0.69 at week 78. [1,4,7]

Summary of clinical SAFETY:
In heiGHttrial the incidence of SAEs was low in both groups. A total of two SAEs occurred in two pts, one in each treatment group (one appendicitis in group A and one concussion in group B). No serious AEs occurred in 77.1% of pts ingroup A vs. 69.6% of pts in group B, the most common AEs were (in group A vs. B, respectively): viral infection (15% vs. 11%), pyrexia (15% vs.9%), cough (11% vs. 7%), nausea and vomiting (11% vs. 7%), hemorrhage (7% vs. 2%), diarrhea (6% vs. 5%), arthralgia and arthritis (6% vs.2%)[1,3].
In fliGHt trialSAEs occurred in 0.7% (1/146) of pts and included atrioventricular block, which was likely not related to the study drug. In enlighten trial SAEs occurred in 1,7% (5/296) of pts and included: gastrointestinal viral infection, pyrexia, epilepsy, vomiting, rash (all with an incidence of 0.3%). There were no discontinuations due to AEs during the three phase 3 trials of lonapegsomatropin [1].

Ongoing studies:
- ***For the same indication:***Yes
- ***For other indications:***No**Discontinued studies (for the same indication):**No

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References:
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6. https://adisinsight.springer.com/trials/700288036?query
7. Maniatis, Aristides K et al. "Efficacy and Safety of up to 2 Years of Treatment With TransConhGH (Lonapegsomatropin) in Treatment-Naïve and Treatment-Experienced Children With Growth Hormone Deficiency." Journal of the Endocrine Society vol. 5,Suppl 1 A676. 3 May. 2021, doi:10.1210/jendso/bvab048.1378
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NHS impact

Cost of therapy:
In the USA, lonapegsomatropin is available in different dosages:
-4 prefilled SC injections3 mg cost $2,747
-4 prefilled SC injections of 3,6 mg cost $3,294.34
-4 prefilled SC injectionsof 4,3 mg cost $3,933.06
-4 prefilled SC injections of 5,2 mg cost $4,754.27
-4 prefilled SC injections of 6,3 mg cost $5,757.97
-4 prefilled SC injectionsof 7,6 mg cost $6,944.17
-4 prefilled SC injectionsof 9,1 mg cost $8,312.85
-4 prefilled SC injectionsof 11 mg cost $10,046.52
-4 prefilled SC injectionsof 13,3 mg cost $12,145.16 [8]
The recommended dose is 0.24 mg/kg body weight once-weekly [3]; one pack of 4 prefilled SC injection covers onemonth therapy, for any dosage chosen.

Epidemiology:
In Europe, at January 2021 the prevalence of GHD was 0.3/100,000 [9]

POSSIBLE PLACE IN THERAPY
According to SIEDP the primary treatment for GHD is replacement therapy with a synthetic form of GH. [10]

OTHER INDICATIONS IN DEVELOPMENT: -

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:-

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: Somatrogon, Eutropin, Albusomatropin [11].

*Service reorganization No
*Possible off label use No

Issued on: November 2021