Report Xenpozyme® - Olipudase alfa

Product & Mechanism of action

Substance: Olipudase alfa

Brand Name: Xenpozyme

Originator/licensee: Genzyme Europe BV

Classification: NCE

ATC code: A16AB25

Orphan Status:
Eu: Yes
Us: No

Mechanism of action:
Olipudase alfa is a recombinant human acid sphingomyelinase, which is an enzyme replacement therapy that provides an exogenous source of acid sphingomyelinase [1].

ABBREVIATIONS:
ASMD: Acid Sphingomyelinase deficiency
CHMP: Committee for Medicinal Products for Human Use
CNS: Central Nervous System
IAR: infusion-associated reaction
M.A.: Marketing Authorization
PBO: placebo
Peds: pediatrics
P.O.: Positive Opinion
PPH: postpartum haemorrhage
Pts: patients
SAE: serious adverse event
SOC: standard of care
TEAE: treatment-emergent adverse event
URTI: upper respiratory tract infection
Wk: week

Authorized indications Licensing status

Authorized Indication:
EMA: Olipudase alfa is indicated as an enzyme replacement therapy for the treatment of non-CNS manifestations of ASMD in paediatric and adult pts with type A/B or type B. [1].

Route of administration: IV

Licensing status
EU CHMP P.O. date:
19/05/2022
FDA M.A. date:
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EU Speed Approval Pathway:
No
FDA Speed Approval Pathway:
No

References:

[1]. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/xenpozyme
[2]. https://www.sciencedirect.com/science/article/pii/S109836002200716X?via%3Dihub
[3]. https://www.sciencedirect.com/science/article/pii/S1098360021050620?via%3Dihub
[4]. https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=11105&Disease%20name=Niemann-Pick-disease-type-A&search=Disease_Search_Simple&title=Niemann-Pick%20disease%20type%20A#:~:text=Epidemiology,%2F167%2C000%2D250%2C000%20in%20Europe.

Essential therapeutic features

Summary of clinical EFFICACY:
(NCT02004691): ASCEND is a phase II/III, 52 wk, international, randomized, double-blind, PBO-controlled trial that enrolled 36 adults with ASMD. Pts were randomized 1:1 to reiceve PBO (0,9% saline) or olipudase alfa via iv infusion once every two wk with intrapatient dose escalation to 3 mg/kg. Primary efficacy endpoints were percent change from baseline to wk 52 in percent predicted diffusing capacity of the lung for carbon monoxide and spleen volume. Least square mean percent change from baseline to week 52 favored olipudase alfa over placebo for percent predicted diffusing capacity of the lung for carbon monoxide (22% vs 3.0% increases, P = 0.0004), spleen volume (39% decrease vs 0.5 increase, P < 0.0001), and liver volume (28% vs 1.5% decreases, P < 0.0001). Splenomegaly-related score decreased in both groups (P = 0.64) [2].
(NCT02292654): ASCEND-Peds is a phase I/II, international, multicenter, single arm, open-label trial that enrolled 20 pts: four adolescent (12-17 years), nine children (6-11 years) and seven infants/early child (1-5 years). Olipudase alfa were administered iv every two wk with intrapatient dose escalation to 3 mg/kg. Primary outcome was safety through wk 64 [3].

Summary of clinical SAFETY:
(NCT02004691): All pts experienced at least 1 AE, and numbers were similar in the olipudase alfa (242) and PBO (267) groups. No event led to permanent treatment discontinuation or study withdrawal and none that were SAE were considered potentially related to the study. [2].

Any TEAEs	Mild	Serious	Potentially related to study drug		IARs*[c]
Placebo	76%	22%*[a]	33%		28%
Olipudase alfa	79%	17%*[b]	67%		45%
Most Common TEAEs	Headache	Nasopharyngitis	Athralgia	URTI	Cough
Placebo	44%	33%	17%	22%	11%
Olipudase alfa	67%	44%	22%	33%	28%

*[a] in the PBO group, there were 3 events of epistaxis and single events of liver abcess, appendicitis, peritonitis, anemia, syncope, hemorrhagic shock, and pleural effusion.
*[b] in the olipudase alfa group, there were some events of cellulitis, viral gastritis, transient ischemic attack, and lower limb fracture.
*[c] The most frequent IAR in the olipudase alfa group was headache (11% vs 28% of placebo and olipudase alfa respectively) and none of wich were categorized as severe or serious

(NCT02292654): All pts experienced at least one event (798).

Any TEAEs (798)	Mild (705)	Serious*[a] (12)	Potentially related to study drug (136)	IARs*[c] (102)
Olipudase alfa overall	88% (705/798)	25%*[b] (12/136)	17% (136/798)	75% (102/136)

Most Common TEAEs	Pyrexia	Cough	Vomiting	Nasopharyn-gitis	Diarrhea	Headache	Nausea	Rhinitis	Oropharyn-geal	Ear pain	Rhinnorhea
Olipudase alfa overall	56	31	38	28	22	38	11	13	10	6	11

*[a] all resolved
*[b] SAEs related to treatment 42% (5/12): one event was a serious anaphylactic reaction in a 17-month-old pts. The four addictional serious events considered drug-related were two transient asymptomatic ALT increases in one pts and one case each of urticaria and rash in another patient.
*[c] The majority of IARs were urticaria (24%), pyrexia (23%) and vomiting (16%) and one severe IAR event was associated with anaphylactic reaction.

Ongoing studies:
- ***For the same indication:*** Yes
- ***For other indications:*** No

Discontinued studies (for the same indication): No

NHS impact

Cost of therapy:
Price not available.

Epidemiology:
The estimated birth prevalence of acid sphingomyelinase deficiency (both NPD types A and B combinated) is between 1/167,000 – 250,000 in Europe [4].

POSSIBLE PLACE IN THERAPY
Olipudase alfa is the first therapy to treat two types of Niemann-Pick disease, a rare genetic metabolic disorder [1].

OTHER INDICATIONS IN DEVELOPMENT:
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SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: /

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: /

*Service reorganization: No
*Possible off label use: Yes

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