

Cipagluco­sidase alfa (Pompe disease, combination with miglustat)

Resolution of: 1 February 2024
Entry into force on: 1 February 2024
Federal Gazette, BAnz AT 28.03.2024 B5

valid until: unlimited

Therapeutic indication (according to the marketing authorisation of 20 March 2023):

Pombiliti (cipagluco­sidase alfa) is a long-term enzyme replacement therapy used in combination with the enzyme stabiliser miglustat for the treatment of adults with late-onset Pompe disease (acid α -gluco­sidase [GAA] deficiency).

Therapeutic indication of the resolution (resolution of 1 February 2024):

See therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adults with late-onset Pompe disease (acid α -gluco­sidase [GAA] deficiency)

Appropriate comparator therapy:

Algluco­sidase alfa

Extent and probability of additional benefit of cipagluco­sidase alfa in combination with miglustat compared with algluco­sidase alfa:

Hint for a minor additional benefit

Study results according to endpoints:¹

Adults with late-onset Pompe disease (acid α -gluco­sidase [GAA] deficiency)

¹ Data from the dossier assessment of the IQWiG (A23-79) and from the addendum (A23-133), unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↑	Advantage in the ability to move and in the energy level.
Health-related quality of life	∅	No data available.
Side effects	↔	No relevant difference for the benefit assessment.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable		

PROPEL study: RCT, direct comparison: Cipagluco­sidase alfa + miglustat vs algluco­sidase alfa + placebo, treatment over 52 weeks

Mortality

Endpoint	Cipagluco­sidase alfa + miglustat		Algluco­sidase alfa + placebo		Cipagluco­sidase alfa + miglustat vs algluco­sidase alfa + placebo
	N	Patients with event n (%)	N	Patients with event n (%)	
Overall mortality					
	85	0 (0)	38	0 (0)	–



Morbidity

Endpoint	Cipaglusosidase alfa + miglustat		Alglucosidase alfa + placebo		Cipaglusosidase alfa + miglustat vs alglucosidase alfa + placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value ^a
R-PAct / PROMIS: deterioration in each case^b (at week52):					
Physical functioning (R-PAct)	85	1 (1)	38	0 (0)	–
Physical functioning (PROMIS Physical Function)	85	0 (0)		1 (3)	–
Fatigue (PROMIS Fatigue)	85	5 (6)	38	3 (8)	0.78 [0.18; 3.39] 0.739
Dyspnoea (PROMIS Dyspnoea Severity)	No suitable data				
Function of the upper extremities (PROMIS Upper Extremity)	85	4 (5)	38	0 (0)	1.41 [0.36; 5.54] 0.618
SGIC: Deterioration^c (at week 52):					
General physical well-being	85	15 (18)	38	11 (29)	0.65 [0.33; 1.26]; 0.199
Breathing effort	85	7 (8)	38	4 (11)	0.79 [0.23; 2.75]; 0.715
Muscle power	85	15 (18)	38	11 (29)	0.65 [0.34; 1.25]; 0.195
Muscle function	85	12 (14)	38	11 (29)	0.50 [0.25; 1.02]; 0.057
Ability to move	85	9 (11)	38	13 (34)	0.32 [0.15; 0.67]; 0.002
Activities of daily living	85	8 (9)	38	5 (13)	0.82 [0.28; 2.41]; 0.714
Energy level	85	9 (11)	38	9 (24)	0.40 [0.18; 0.88]; 0.023
Muscle pain	85	16 (19)	38	9 (24)	0.78 [0.37; 1.66]; 0.515
^a Cochran-Mantel-Haenszel (CMH) method; stratified by distance travelled in the 6MWT at start of study and enzyme replacement therapy status; endpoints collected using SGIC: missing values were replaced with the last value collected after start of study (post-baseline) (LOCF).					



Endpoint	Cipaglicosidase alfa + miglustat		Alglucosidase alfa + placebo		Cipaglicosidase alfa + miglustat vs alglucosidase alfa + placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value ^a

^b Response threshold: 15% of the respective scale range (based on the transformed values).

^c Defined as slightly deteriorated, severely deteriorated and very severely deteriorated compared to the start of study medication.

Abbreviations used:

6MWT: 6-minute walk test; CI: confidence interval; LOCF: last observation carried forward; N: number of patients evaluated; n: number of patients with (at least 1) event; PROMIS: Patient Reported Outcomes Measurement Information System; R-PAct: Rasch-built Pompe-specific Activity; RR: relative risk; SGIC: Subject's Global Impression of Change

Endpoint	Cipaglicosidase alfa + miglustat			Alglucosidase alfa + placebo			Cipaglicosidase alfa + miglustat vs alglucosidase alfa + placebo
	N ^a	Values at start of study MV (SD)	Change at week 52 MV (SE)	N ^a	Values at start of study MV (SD)	Change at week 52 MV (SE)	MD [95% CI]; p value ^b
Physical resilience							
6MWT [metres]	81	357.93 (111.84)	21.44 (5.75) ^c	37	350.14 (119.78)	16.11 (8.58) ^c	5.33 [-15.21; 25.88]; 0.608 ^c
Motor function							
GSGC total value ^d	72	14.27 (5.04)	-0.56 (0.28)	31	13.97 (4.82)	0.74 (0.43)	-1.30 [-2.34; -0.26]; 0.015 SMD [95% CI] -0.51 [-0.94; -0.08]
Walking ^e	73	2.71 (1.09)	-0.09 (0.08)	35	2.67 (1.01)	0.12 (0.12)	-0.21 [-0.50; 0.08]
Climbing stairs ^e	67	3.63 (1.77)	-0.30 (0.14)	30	3.46 (1.84)	0.25 (0.21)	-0.55 [-1.06; -0.05]
Gowers manoeuvre ^e	63	4.41 (1.66)	0.12 (0.12)	27	4.52 (1.55)	0.10 (0.18)	0.01 [-0.42; 0.45]
Getting up from the chair ^f	73	3.84 (1.61)	-0.22 (0.12)	32	3.91 (1.54)	0.09 (0.19)	-0.31 [-0.76; 0.15]
Time [seconds] required to complete the individual GSGC tests ^g (presented additionally)							



Endpoint	Cipaglicosidase alfa + miglustat			Alglucosidase alfa + placebo			Cipaglicosidase alfa + miglustat vs alglucosidase alfa + placebo
	N ^a	Values at start of study MV (SD)	Change at week 52 MV (SE)	N ^a	Values at start of study MV (SD)	Change at week 52 MV (SE)	MD [95% CI]; p value ^b
- Walking [seconds]	80	9.68 (7.63)	-0.60 (0.63)	36	9.53 (5.44)	1.96 (0.95)	-2.56 [-4.85; -0.27]
- Climbing stairs [seconds]	78	13.95 (70.97)	-6.70 (0.85)	35	7.95 (9.67)	-3.64 (1.28)	-3.06 [-6.15; 0.04]
- Gowers manoeuvre [seconds]	61	10.84 (7.45)	-0.35 (0.79)	26	15.30 (11.68)	-1.92 (1.25)	1.57 [-1.44; 4.58]
- Getting up from the chair [seconds]	77	13.58 (86.05)	-7.50 (0.41)	33	4.42 (5.19)	-6.71 (0.63)	-0.80 [-2.305; 0.711]
TUG [seconds] (presented additionally)	75	12.88 (10.14)	-0.40 (0.76)	32	11.37 (4.99)	0.03 (1.19)	-0.43 [-3.29; 2.42]; 0.763
Health status							
EQ-5D VAS ^h	84	68.86 (18.25)	0.05 (1.54)	37	71.91 (15.20)	3.87 (2.36)	-3.82 [-9.51; 1.87]; 0.187
<p>^a Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at start of study can be based on other patient numbers.</p> <p>^b Unless otherwise stated, MV and SE (mean change at week 52 per treatment group) as well as MD, CI and p value (group comparison): ANCOVA without repeated measures modelling; adjusted for value at the start of study, enzyme replacement therapy status, sex, age, weight and height</p> <p>^c MV and SE (mean change at week 52 per treatment group) as well as MD, CI and p value (group comparison): MMRM; adjusted for value at the start of study, enzyme replacement therapy status, sex, age, weight and height</p> <p>^d Lower (decreasing) values mean better motor function (scale range 4 to 27); negative effects (intervention minus comparison) mean an advantage for the intervention.</p> <p>^e Lower (decreasing) values mean better motor function (scale range 1 to 7); negative effects (intervention minus comparison) mean an advantage for the intervention.</p> <p>^f Lower (decreasing) values mean better motor function (scale range 1 to 6); negative effects (intervention minus comparison) mean an advantage for the intervention.</p> <p>^g The time required is not included in the GSGC total value.</p> <p>^h Higher (increasing) values mean better health status (scale range 0 to 100); positive effects (intervention minus control) mean an advantage for the intervention.</p>							
Abbreviations used:							



Endpoint	Cipaglucosidase alfa + miglustat			Alglucosidase alfa + placebo			Cipaglucosidase alfa + miglustat vs alglucosidase alfa + placebo
	N ^a	Values at start of study MV (SD)	Change at week 52 MV (SE)	N ^a	Values at start of study MV (SD)	Change at week 52 MV (SE)	MD [95% CI]; p value ^b
6MWT: 6-minute walk test; ANCOVA: analysis of covariance; GSGC: Gait, Stairs, Gowers Manoeuvre, Chair; CI: confidence interval; MD: mean difference; MV: mean value; n: number of patients with (at least 1) event; N: number of patients evaluated; RR: relative risk; SD: standard deviation; SE: standard error; SMD: standardised mean difference; VAS: visual analogue scale							

Health-related quality of life

No data available.

Side effects

Endpoint	Cipaglucosidase alfa + miglustat		Alglucosidase alfa + placebo		Cipaglucosidase alfa + miglustat vs alglucosidase alfa + placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value
AEs (presented additionally)	85	81 (95)	38	37 (97)	–
SAEs	85	8 (9)	38	1 (3)	3.58 [0.50; 25.61]; 0.205
Discontinuation due to AEs	85	2 (2)	38	1 (3)	0.86 [0.09; 8.63]; 0.898
Abbreviations used: n: number of patients with (at least 1) event; N: number of patients evaluated; SAE: serious adverse event; AE: adverse event;					

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with late-onset Pompe disease (acid α -glucosidase [GAA] deficiency)

approx. 170 – 1,760 patients



3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Pombiliti (active ingredient: cipagluco­sidase alfa) at the following publicly accessible link (last access: 12 December 2023):

https://www.ema.europa.eu/en/documents/product-information/pombiliti-epar-product-information_en.pdf

Treatment with cipagluco­sidase alfa should only be initiated and monitored by doctors experienced in treating patients with Pompe disease or other congenital metabolic diseases or neuromuscular diseases.

4. Treatment costs

Annual treatment costs:

Adults with late-onset Pompe disease (acid α -glucosidase [GAA] deficiency)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Cipagluco­sidase alfa	€ 624,935.79
Miglustat	€ 5,794.81
Total:	€ 630,730.60
Appropriate comparator therapy:	
Alglucosidase alfa	€ 616,383.28

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 January 2024)

Costs for additionally required SHI services: not applicable

5. Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with cipagluco­sidase alfa

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with cipagluco­sidase alfa for the treatment of adults with late-onset Pompe disease (acid α -glucosidase [GAA] deficiency):

Adults with late-onset Pompe disease (acid α -glucosidase [GAA] deficiency)

- No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.