Nusinersen (exceeding € 50 million turnover limit: Spinal Muscular Atrophy)

Resolution of: 20 May 2021 Valid until: unlimited
Entry into force on: 20 May 2021
BAnz AT 24 06 2021 B6

Therapeutic indication (according to the marketing authorisation of 30 May 2017):

Spinraza is indicated for the treatment of 5q spinal muscular atrophy.

Therapeutic indication of the resolution (resolution from the 20/05/2021):

see therapeutic indication according to marketing authorisation

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

a) Patients with 5q spinal muscular atrophy (5q-SMA) type 1:

Appropriate comparator therapy:

BSC

Extent and probability of the additional benefit of nusinersen compared to BSC:

Indication of a major additional benefit

b) Patients with 5q-SMA type 2

Appropriate comparator therapy:

BSC

Extent and probability of the additional benefit of nusinersen compared to BSC:

Hint of a considerable additional benefit

c) Patients with 5q-SMA type 3 / 4

Appropriate comparator therapy:

BSC

Extent and probability of the additional benefit of nusinersen compared to BSC:

An additional benefit is not proven.

d1) Pre-symptomatic patients with 5q SMA and 2 SMN2 gene copies

Appropriate comparator therapy:

BSC

Extent and probability of the additional benefit of nusinersen compared to BSC:

Hint of a major additional benefit

d2) Pre-symptomatic patients with 5q SMA and 3 SMN2 gene copies

Appropriate comparator therapy:

BSC

Extent and probability of the additional benefit of nusinersen compared to BSC:

Hint for a non-quantifiable additional benefit

d3) Pre-symptomatic patients with 5q SMA and more than 3 SMN2 gene copies

Appropriate comparator therapy:

BSC

Extent and probability of the additional benefit of nusinersen compared to BSC:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Patients with 5q-SMA type 1:

RCT study ENDEAR: Nusinersen vs BSC

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↑↑	Advantage in overall survival
Morbidity	↑↑	Advantages in achievement of motor milestones and in permanent ventilation
Health-related quality of life	∅	No data on benefit assessment are available
Side effects	n.a.	There are no assessable data
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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

[1] Data from the dossier assessment of the IQWiG (A20-114) and from the addendum (A21-43), unless otherwise indicated.

Mortality

Endpoint Feature - Subgroup	**Nusinersen**		**BSC**		**Nusinersen vs BSC**
	N	Median time to event in weeks [95 % CI] Patients with event n (%)	N	Median time to event in weeks [95 % CI] Patients with event n (%)	HR[a] [95 % CI] p value Absolute difference (AD)[b]
Overall survival	80	n. a. 13 (16)	41	n. a. [23,1; n. c.] 16 (39)	0,37 [0,18; 0,77]; 0,008 AD = 23 %
Effect modification on the endpoint Overall survival by the characteristic Age at symptom onset					
≤ 12 weeks	72	n. a. 10 (14)	32	n. a. [13,6; n. c.] 14 (44)	0.26 [0.12; 0.59] 0,001
> 12 weeks	8	30,6 [0,9; n. c.] 3 (38)	9	n. a. [23,1: n. c.] 2 (22)	3.28 [0.50; 21.37] 0,215
Total[c]				Interaction:	0,021

Morbidity

Endpoint Feature - Subgroup	**Nusinersen**		**BSC**		**Nusinersen vs BSC**
	N	Median time to event in weeks [95 % CI] Patients with event n (%)	N	Median time to event in weeks [95 % CI] Patients with event n (%)	HR[a] [95 % CI] p value Absolute difference (AD)[b]
Death or permanent ventilation[d]	80	n. a. [36,3; n. c.] 31 (39)	41	22,6 [13,6; 31,3] 28 (68)	0,53 [0,32; 0,89]; 0,017 AD = 29%
Permanent ventilation	80	n. a. 18 (22)	41	n. a. [22,6; n. c.] 13 (32)	0,66 [0,32; 1,37]; 0,269
Effect modification for the endpoint Permanent ventilation by the characteristic Duration of disease					
≤ 12 weeks	34	n. a. 3 (9)	18	n. a. [15,0; n. c.] 6 (33)	0.12 [0.03; 0.52] 0,005
> 12 weeks	46	n. a. [36,3: n. c.] 15 (33)	23	27,1 [19,1; n. c.] 7 (30)	1.17 [0.47; 2.89] 0,739
Total[c]				Interaction:	0,004

Endpoint Feature - Subgroup	**Nusinersen**		**BSC**		**Nusinersen vs BSC**
	N	Median time to event in weeks [95 % CI] Patients with event n (%)	N	Median time to event in weeks [95 % CI] Patients with event n (%)	HR[a] [95 % CI] p value Absolute difference (AD)[b]
Achievement of motor milestones (HINE - subscale 2)[e]	80	26,1 [25,1; 29,1] 49 (61)	41	n. a. 8 (20)	3,22 [1,50; 6,90]; 0,003 AD = 41%
Effect modification on the endpoint Achievement of motor milestones by the characteristic Duration of disease					
≤ 12 weeks	34	25,3 [10,1; 27,0] 27 (79)	18	n. a. 2 (11)	9.03 [2.09; 39.04] 0,003
> 12 weeks	46	43,1 [25,1; 57,1] 22 (48)	23	n. a. [10,1; n. c.] 6 (26)	1.53 [0.62; 3.78] 0,362
Total[c]				Interaction:	0,004
	N	Adjusted annual rate [95% CI] Number of events	N	Adjusted annual rate [95% CI] Number of events	Rate ratio [95 % CI]; p value Absolute difference (AD)[b]
Severe respiratory events[g]	80	4.41 [3.43; 5.66] 238	41	5.43 [3.80; 7.77] 117	0,81 [0,53; 1,25]; 0,346 [f]
Hospitalisations[h]	80	4.33 [3.61; 5.19] 264	41	5.70 [4.39; 7.41] 119	0,76 [0,55; 1,05][i]; 0,097

	N[j]	Values at start of study MV (SD)	Change to day 394 MV[k] (SE)	N[j]	Values at start of study MV (SD)	Change to day 394 MV[k] (SE)	MD [95 %- CI]; p value[e] Absolute difference (AD)[b]
motor function (CHOP INTEND)[l]	26	27.3 (7.9)	13.55 (1.59)	11	29.0 (7.9)	-10.90 (2.53)	2.45 [1.82; 3.07]; < 0.001 AD = 24,45 Hedges' g: 2.91 [1.92; 3.91]

Health-related quality of life

No data on health-related quality of life were assessed.

Side effects

Endpoint	Nusinersen		BSC		Nusinersen vs BSC
	N	Median time to event in weeks [95 % CI] Patients with event n (%)	N	Median time to event in weeks [95 % CI] Patients with event n (%)	HR[a] [95 % CI] p value Absolute difference (AD)[b]
Total adverse events (*presented additionally*)					
	80	2,40 [1,3; 3,1] 77 (96)	41	1,6 [0,9; 3,1] 40 (98)	-
Serious adverse events (SAE)					
	80	no usable data available[m]	41	no usable data available[m]	
Therapy discontinuation because of adverse events					
	80	no usable data available[m]	41	no usable data available[m]	

a. Cox proportional hazards regression with treatment and duration of disease at start of study as independent variables
b. Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
c. For time-to-event analysis, the p values for the interaction test were calculated with a Cox regression
d. Combined endpoint consisting of the individual components of death and permanent ventilation, which was defined as ventilation ≥ 16 hours per day continuously for > 21 days in the absence of acute reversible events or tracheostomy
e. predefined response criterion based on 7 of the 8 milestone categories of HINE subscale 2 excluding the conscious grasping category; defined as (1) improvement of at least 2 points or reaching the maximum value (touching toes) in the "kicking" category or improvement of at least 1 point in the category of head control, turning, sitting, robbing/crawling, standing, or walking, and (2) more categories with improvement than categories with deterioration. For the category "kicking", deterioration was defined analogously to improvement as a decrease of at least 2 points or reaching the lowest value (no kicking)
f. Negative binomial regression with treatment, age at symptom onset and duration of illness at start of study as independent variable
g. Summary of SAEs classified in SOC respiratory, thoracic, and mediastinal disorders as a primary SOC or secondary SOC
h. The frequency of hospitalisations for monitoring for general observation due to symptoms after dosing/sham intervention under BSC, serious adverse events or additional investigations (e.g. planned intervention such as placement of a stomach tube for preventive reasons) was recorded.
i. Negative binomial regression with treatment and age at symptom onset and duration of illness at screening as independent variables
j. Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at start of study (possibly at other times) can be based on other patient numbers
k. Linear models with the covariates Duration of illness at screening and Age at symptom onset
l. Higher (increasing) values mean better symptomatology; positive effects (intervention minus control) mean an advantage for the intervention.
m. High proportion of events of the underlying disease or events that can be both side effects and symptomatology of the underlying disease (e.g. SOC respiratory, thoracic and mediastinal disorders)

Abbreviations used:
AD: Absolute difference: BSC: Best supportive care; CHOP INTEND: Children's Hospital of Philadelphia Infant Test for Neuromuscular Disease; HINE: Hammersmith Infant Neurological Examination; HR: Hazard ratio; CI: Confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; n. c. = not

calculable; n.a. = not achieved; SOC: system organ class; AE: adverse event; SAE: serious adverse event; vs: versus

b) Patients with 5q-SMA type 2

RCT study CHERISH: Nusinersen vs BSC

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↔	No relevant difference
Morbidity	↑	Benefits in motor function (HFMSE and RULM) and disease-related hospitalisations based on SAE
Health-related quality of life	↔	No relevant difference
Side effects	n.a.	Disadvantages for specific AE, but overall there are no assessable data available
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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

Mortality

Endpoint	Nusinersen[a]		BSC[a]		Nusinersen[a] vs BSC[a]
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value Absolute difference (AD)[b]
Total mortality	84	0 (0)	42	0 (0)	–

Morbidity

Endpoint	Nusinersen[a]			BSC[a]			Nusinersen[a] vs BSC[a]
	N	Adjusted annual rate [95 % CI][c] Number of events		N	Adjusted annual rate [95 % CI][c] Number of events		Rate ratio [95% CI] p value Absolute difference (AD)[b]
Frequency of serious respiratory events[d]	84	0.11 [0.05; 0.22] 11		42	0.25 [0.11; 0.55] 14		0,43 [0,15; 1,25]; 0,123
Disease-related hospitalizations based on SAEs[e]	84	0.11 [0.06; 0.21] 11		42	0.28 [0.14; 0.54] 16		0,39 [0,15; 0,97]; 0,043
	N[f]	Values at start of study MV (SD)	Change to day 456 MV[g] (SE)	N[f]	Values at start of study MV (SD)	Change to day 456 MV[g] (SE)	MD [95 %- CI]; p value[g]
Achievement of motor milestones (HFSME)[h]	84	22.4 (8.3)	3.9 (0.5)	42	19.9 (7.2)	-1.0 (0.7)	4,92 [3,29; 6,56]; < 0,001 Hedges' g: 0.95 [0.56; 1.34]
Motor function of the upper extremities (RULM) [h]	84	19.4 (6.2)	4.2 (0.4)	42	18.4 (5.7)	0.5 (0.5)	3,68 [2,39; 4,98]; < 0,001 Hedges' g: 0.67 [0.29; 1.06]

Health-related quality of life

Endpoint	Nusinersen[a]			BSC[a]			Nusinersen[a] vs BSC[a]
	N[f]	Values at start of study MV (SD)	Change to day 456 MV[g] (SE)	N[f]	Values at start of study MV (SD)	Change to day 456 MV[g] (SE)	MD [95 %- CI]; p value[g] Absolute difference (AD)[b]
PedsQL 4.0 (patient assessment[i])[h,]							
Total score	21	60.6 (12.0)	4.5 (4.0)	8	69.3 (15.1)	-2.3 (6.3)	6.79 [-7.97; 21.54] 0.384
PedsQL 3.0 (patient assessment[j])[h]							
Neuromuscular disease	21	75.0 (13.4)	-2.2 (4.4)	8	69.0 (18.9)	0.8 (7.1)	−3,01 [−19,99; 13,97]; 0,734

Side effects

Endpoint	Nusinersen[a]		BSC[a]		Nusinersen[a] vs BSC[a]
	N	Patients with event n (%)	N	Patients with event n (%)	HR[a] [95 % CI] p value Absolute difference (AD)[b]
Total adverse events (*presented additionally*)					
	84	78 (93)	42	42 (100)	-
Serious adverse events (SAE)					
	84	no usable data available[j]	42	no usable data available[j]	-
Therapy discontinuation because of adverse events					
	84	no usable data available[j]	42	no usable data available[j]	-
Specific adverse events, PT					
Vomiting	84	24 (29)	42	5 (12)	2,40 [0,99; 5,84]; 0,037[k]
Headaches	84	24 (29)	42	3 (7)	4.00 [1.28; 12.53]; 0,006[k]
Back pain	84	21 (25)	42	0 (0)	21,75 [1,35; 350,55] < 0,001[k]

a. Treatment should be given against a background of supportive concomitant therapy. There is insufficient information on the implementation in the study, so that there are remaining uncertainties regarding an adequate implementation of BSCs
b. Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
c. Negative binomial regression with treatment and age after start of study as independent variables
d. Summary of SAEs classified as primary SOC or secondary SOC in the SOC "Respiratory, thoracic, and mediastinal disorders"
e. SAEs that required inpatient hospitalisation or for which hospitalisation was prolonged; classification of disease-related hospitalisation was by a blinded committee
f. Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at the start of the study (possibly at other times) can be based on other patient numbers.
g. Adjusted mean value changes were calculated using linear models with treatment (sham intervention, nusinersen) as fixed effect and adjusted for age at start of study and value at start of study. In case of missing values, multiple imputation was performed using ANCOVA with treatment (sham intervention, nusinersen) as fixed effect and covariates age at start of study and value at start of study. The effect measure Hedges' g is the difference in mean value divided by the pooled standard deviation.
h. Higher (increasing) values mean better motor function and health-related quality of life; positive effects (intervention minus control) mean an advantage for the intervention.
i. completed by patients ≥ 5 years of age
j high proportion of events of the underlying disease or events that can be both a side effects and symptomatology of the underlying disease (e.g. SOC Respiratory, thoracic and mediastinal disorders)
k. Own calculation, unconditional exact test (CSZ method according to Martín Andrés & Silva Mato,1994)

Abbreviations used:
ANCOVA: Analysis of covariance; HFMSE: Hammersmith Functional Motor Scale - Expanded; CI: Confidence interval; MD: mean difference; MV: mean value; n: number of patients with (at least 1) event; N: number of patients evaluated; PedsQL: Pediatric Quality of Life Inventory; PT: Preferred Term; RR: relative risk; RULM: Upper Limb Module Test (revised version); SD: Standard deviation; SE: Standard error; SAE: serious adverse event; AE: adverse event

c) Patients with 5q-SMA type 3 / 4

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	n.a.	There are no assessable data
Morbidity	n.a.	There are no assessable data
Health-related quality of life	n.a.	There are no assessable data
Side effects	n.a.	There are no assessable data

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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

d1) Pre-symptomatic patients with 5q SMA and 2 SMN2 gene copies

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↑	Advantage under transfer of evidence of results from patients with 5q-SMA type 1 and 2 SMN2 gene copies
Morbidity	↑	Advantage under transfer of evidence of results from patients with 5q-SMA type 1 and 2 SMN2 gene copies
Health-related quality of life	∅	No data on benefit assessment are available
Side effects	n.a.	There are no assessable data

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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

Juxtaposition: NURTURE study (open-label, single-arm study of pre-symptomatic SMA patients, patients with 2 SMN2 gene copies) versus intervention arm from the ENDEAR RCT study (early symptomatic onset of therapy, [duration of disease ≤ 12 weeks])

Endpoint category **Endpoint**	**Nusinersen study NURTURE (pre-symptomatic, 2 SMN2 gene copies)**		**Nusinersen study ENDEAR (early symptomatic start of therapy [duration of disease ≤ 12 weeks])**	
	N[a]	Median time to event in months [95 % CI] Patients with event n (%)	N[a]	Median time to event in months [95 % CI] Patients with event n (%)
Mortality				
Overall survival	15	– 0 (0)	34	n. a. 3 (9)
Morbidity				
Death or permanent ventilation[b]	15	– 0 (0)	34	n. a. 6 (18)
Permanent ventilation	15	– 0 (0)	34	n. a. 3 (9)
Achievement of motor milestones (HINE subscale 2)[c]	15	n. d.[d] 15 (100)	34	25,3 [10,1; 27,0] 27 (79)
Side effects				
SAEs	no usable data available[e]			
Discontinuation because of AEs	no usable data available[e]			

a. Number of patients in the evaluation
b. Combined endpoint consisting of the individual components of death and permanent ventilation, which was defined as ventilation ≥ 16 hours per day continuously for > 21 days in the absence of acute reversible events or tracheostomy
c. predefined response criterion based on 7 of the 8 milestone categories of HINE subscale 2 excluding the conscious grasping category; defined as (1) improvement of at least 2 points or reaching the maximum value (touching toes) in the "kicking" category or improvement of at least 1 point in the category of head control, turning, sitting, robbing/crawling, standing, or walking, and (2) more categories with improvement than categories with deterioration. For the category "kicking", deterioration was defined analogously to improvement as a decrease of at least 2 points or reaching the lowest value (no kicking).
d. After 26 weeks (day 183), the proportion of patients with event was 100%, so the median time to event is ≤ 26 weeks.
e. High proportion of events of the underlying disease or events that can be both side effects and symptomatology of the underlying disease (e.g. SOC respiratory, thoracic and mediastinal disorders).

Abbreviations:
BSC: Best supportive care; HINE: Hammersmith Infant Neurological Examination; n. d.: no data; CI: Confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; n. a.: not achieved; SMN: Survival of Motor Neuron; SOC: System organ class; SAE: serious adverse event; AE: adverse event

d2) Pre-symptomatic patients with 5q SMA and 3 SMN2 gene copies

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	∅	No data on benefit assessment are available
Morbidity	↑	Signs of improved development with regard to the achievement of motor milestones taking into account the G-BA resolution on the inclusion of 5q-associated SMA in the Expanded Newborn Screening and the written statement procedure
Health-related quality of life	∅	No data on benefit assessment are available
Side effects	∅	No data on benefit assessment are available
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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

d3) Pre-symptomatic patients with 5q SMA and more than 3 SMN2 gene copies

There are no data in comparison with the appropriate comparator therapy.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	∅	No data on benefit assessment are available
Morbidity	∅	No data on benefit assessment are available
Health-related quality of life	∅	No data on benefit assessment are available
Side effects	∅	No data on benefit assessment are available
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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

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

a) Patients with 5q-SMA type 1

approx. 130 to 300 patients

b) Patients with 5q-SMA type 2 and
c) Patients with 5q-SMA type 3 / 4

approx. 880 to 900 patients

d) Pre-symptomatic patients with 5q-SMA

No specification possible

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 Spinraza (active ingredient: nusinersen) at the following publicly accessible link (last access: 16 February 2021):

https://www.ema.europa.eu/documents/product-information/spinraza-epar-product-information_de.pdf

The initiation and monitoring of treatment with nusinersen should only be carried out by specialists in paediatrics and adolescent medicine with a focus on neuropaediatrics or neurology who are experienced in the treatment of patients with spinal muscular atrophy (SMA). Since nusinersen is intended for intrathecal use, it should be administered only by physicians experienced in performing lumbar punctures.

Molecular genetic diagnostics regarding deletion or mutation of the SMN1 gene including determination of the SMN2 gene copy number for the presence of SMA should be performed.

4. Treatment costs

Annual treatment costs:

a) Patients with 5q-SMA type 1:

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Nusinersen 1st year	€ 566,745.01
Nusinersen Subsequent years	€ 261,574.62
Best supportive care	varies patient-individual
Appropriate comparator therapy:	

Designation of the therapy	Annual treatment costs/patient
Best supportive care	varies patient-individual

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 01 May 2021)

Costs for additionally required SHI services: non-quantifiable

b) Patients with 5q-SMA type 2

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Nusinersen 1st year	€ 566,745.01
Nusinersen Subsequent years	€ 261,574.62
Best supportive care	varies patient-individual
Appropriate comparator therapy:	
Best supportive care	varies patient-individual

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 01 May 2021)

Costs for additionally required SHI services: non-quantifiable

c) Patients with 5q-SMA type 3 / 4

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Nusinersen 1st year	€ 566,745.01
Nusinersen Subsequent years	€ 261,574.62
Best supportive care	varies patient-individual
Appropriate comparator therapy:	
Best supportive care	varies patient-individual

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 01 May 2021)

Costs for additionally required SHI services: non-quantifiable

d) Pre-symptomatic patients with 5q-SMA

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Nusinersen 1st year	€ 566,745.01

Designation of the therapy	Annual treatment costs/patient
Nusinersen Subsequent years	€ 261,574.62
Best supportive care	varies patient-individual
Appropriate comparator therapy:	
Best supportive care	varies patient-individual

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 01 May 2021)

Costs for additionally required SHI services: non-quantifiable