Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Ozanimod (Relapsing Remitting Multiple Sclerosis)

of 7 January 2021

On 7 January 2021, the Federal Joint Committee (G-BA) resolved by written statement to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (Pharmaceuticals Directive, AM-RL) in the version dated 18 December 2008/22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended on DD Month YYYY (Federal Gazette, BAnz AT DD MM YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient ozanimod as follows:

Ozanimod

Resolution of: 7 January 2021
Entry into force on: 7 January 2021
Federal Gazette, BAnz AT DD MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 20 May 2020):

Zeposia is indicated for the treatment of adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease as defined by clinical or imaging features.

Therapeutic indication of the resolution (resolution of 7 January 2021):

See therapeutic indication according to marketing authorisation.

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

a) Adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease who have not previously received disease-modifying therapy or adult patients previously treated with disease-modifying therapy whose disease is not highly active.

Appropriate comparator therapy:

- Interferon beta-1a or interferon beta-1b or glatiramer acetate, taking into account the authorisation status

Extent and probability of the additional benefit of ozanimod compared to interferon beta-1a:

Indication of a minor additional benefit.

b) Adult patients with relapsing remitting multiple sclerosis (RRMS) with highly active disease in spite of prior treatment with disease-modifying therapy[1].

Appropriate comparator therapy:

- Alemtuzumab or fingolimod or natalizumab

Extent and probability of the additional benefit of ozanimod compared with the appropriate comparator therapy:

An additional benefit is not proven.

[1] Generally, (pre)-treatment should have lasted a minimum of six months. Depending on relapse frequency and the severity of progression of disability, treatment with disease-modifying therapy of less than six months is permissible, but must be justified.

a) Adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease who have not previously received disease-modifying therapy or adult patients previously treated with disease-modifying therapy whose disease is not highly active.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↔	No differences relevant for the benefit assessment.
Morbidity	↑↑	Benefit in the confirmed disease relapse endpoint
Health-related quality of life	↔	No differences relevant for the benefit assessment.
Side effects	↔	Exclusively a benefit in the specific AE influenza-like illness.

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

Study results according to endpoints:[2]

RADIANCE B study: RCT, ozanimod vs interferon beta-1a, 24 month treatment duration

SUNBEAM study: RCT, ozanimod vs interferon beta-1a, 12 month treatment duration

Meta-analytic summary of results at month 12.

Mortality

Endpoint	Ozanimod		INF-β 1a		Ozanimod vs INF-β 1a
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95 % CI]; p value[a]
Overall mortality					
RADIANCE B	371	0 (0)	366	0 (0)	-
SUNBEAM	383	0 (0)	358	0 (0)	-

Morbidity

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N	n_E	Annual relapse rate [95% CI][b]	N	n_E	Annual relapse rate [95% CI][b]	Rate proportion [95 % CI]; p value[b]
Confirmed disease relapses (EDSS based)							
Annual relapse rate (total)							
RADIANCE B	370	127	0.17 [0.13; 0.23]	367	188	0.25 [0.19; 0.33]	0.68 [0.51; 0.92]; 0.011
SUNBEAM	383	83	0.16 [0.11; 0.24]	360	139	0.29 [0.20; 0.42]	0.55 [0.41; 0.75]; < 0.001
Total							0.62 [0.50; 0.76]; no data available[c]
of which serious[d] (shown as a supplement)							
RADIANCE B	370	57	no data available	367	95	no data available	no data available
SUNBEAM	383	42	no data available	360	68	no data available	no data available
Total							no data available

[2] Data from the dossier assessment of the IQWiG (A20-59) and the addendum (A20-96) unless otherwise indicated.

Endpoint	Ozanimod		INF-β 1a		Ozanimod vs INF-β 1a
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95 % CI]; p value[e]
Confirmed disability progression (EDSS based)					
RADIANCE B	370	n.a. 30 (8.1)	367	n.a. 23 (6.3)	1.31 [0.76; 2.27]; 0.326
SUNBEAM	383	n.a. 8 (2.1)	360	n.a. 6 (1.7)	1.04 [0.33; 3.26]; 0.946
Total					1.26 [0.77; 2.06]; no data available[c]
Fatigue					
RADIANCE B	Endpoint not surveyed				
SUNBEAM	Endpoint not surveyed				

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	MD [95% CI]; p value[h]
Severity of disability							
MSFC-z score[i]							
RADIANCE B	370	0.03 (0.68)	-0.10 (0.03)	367	0.05 (0.67)	-0.09 (0.03)	-0.01 [-0.06; 0.04]; 0.739
SUNBEAM[j]	383	0.09 (0.67)	-0.02 (0.03)	360	0.01 (0.69)	-0.06 (0.03)	0.04 [-0.01; 0.09]; 0.158
Overall[k]							0.02 [-0.02; 0.05][k]; 0.406[k]
Walking ability (T25-FW (seconds)[l])							
RADIANCE B	350	5.8 (2.2)	0.7 (0.2)	342	5.7 (2.7)	0.6 (0.2)	0.05 [-0.21; 0.30]; 0.739
SUNBEAM	365	5.9 (2.2)	0.4 (0.2)	342	6.1 (2.9)	0.4 (0.2)	-0.00 [-0.27; 0.27]; 0.158
Total							0.03 [-0.16; 0.21][k]
Coordination (9-HPT (seconds)[l])							
RADIANCE B	351	22.4 (6.7)	0.6 (0.3)	344	21.8 (5.5)	0.6 (0.3)	0.05 [-0.42; 0.52]

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	MD [95% CI]; p value[h]
SUNBEAM	365	22.6 (6.4)	-0.6 (0.3)	342	23.3 (6.6)	-0.4 (0.3)	-0.15 [-0.66; 0.37]
Total							-0.04 [-0.39; 0.31][k]
Cognition (PASAT-3 (correct answers)[i])							
RADIANCE B	351	48.0 (11.4)	0.1 (0.5)	344	48.2 (10.4)	0.2 (0.5)	-0.10 [-0.99; 0.80]
SUNBEAM	Instrument not employed						
Cognition (SDMT (correct answers)[i])							
RADIANCE B	Instrument not employed						
SUNBEAM	364	48.1 (13.8)	0.6 (0.7)	342	47.9 (13.3)	-1.0 (0.7)	1.61 [0.51; 2.72]
Visual acuity (LCLA contrast 100 % (correctly recognized letters)[i])							
RADIANCE B	348	53.6 (8.6)	-0.5 (0.5)	339	53.4 (8.2)	-0.3 (0.5)	-0.19 [-1.06; 0.67]; 0.660
SUNBEAM	364	52.9 (8.2)	-0.3 (0.4)	341	51.8 (10.2)	-0.4 (0.5)	0.10 [-0.61; 0.80]; 0.791
Total							-0.02 [-0.56; 0.53][k]; 0.955[k]

Health-related quality of life

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	MD [95% CI]; p value[h]
MSQoL-54[l]							
Total score PHCS[m]							
RADIANCE B	370	69.2 (18.0)	-0.6 (0.9)	367	72.0 (16.4)	-2.4 (0.9)	1.82 [0.21; 3.43]; 0.027
SUNBEAM	380	68.6 (18.5)	-0.1 (1.1)	357	70.1 (18.6)	-1.6 (1.1)	1.59 [-0.10; 3.28]; 0.066
Total							1.71 [0.54; 2.88][k]; 0.004[k] SMD: 0.15 [0.05; 0.25]
Total score MHCS[n]							

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	MD [95% CI]; p value[h]
RADIANCE B	370	73.0 (17.7)	-1.8 (1.1)	367	73.4 (17.6)	-2.4 (1.1)	0.64 [-1.37; 2.65]; 0.535
SUNBEAM	382	71.2 (19.1)	-1.1 (1.3)	360	71.7 (18.6)	-1.6 (1.4)	0.47 [-1.65; 2.59]; 0.662
Total							0.56 [-0.90; 2.02][k]; 0.452[k]
Physical health							
RADIANCE B	370	73.5 (24.3)	-1.7 (1.2)	367	77.7 (22.8)	-3.6 (1.2)	1.90 [-0.22; 4.01]
SUNBEAM	382	74.4 (24.3)	-1.3 (1.4)	360	74.6 (25.8)	-2.3 (1.4)	0.96 [-1.19; 3.11]
Total							1.44 [-0.07; 2.95][k]
Role limitations due to physical problems							
RADIANCE B	370	63.6 (41.7)	-5.9 (2.4)	367	68.0 (39.4)	-8.1 (2.4)	2.17 [-2.21; 6.55]
SUNBEAM	382	59.0 (41.5)	-1.6 (2.9)	360	61.9 (41.8)	-0.4 (3.0)	2.03 [−2.61; 6.66]
Total							2.10 [-1.08; 5.29][k]
Role limitations due to emotional problems							
RADIANCE B	370	79.1 (35.4)	-7.6 (2.6)	367	77.9 (36.1)	-8.5 (2.6)	0.96 [−3.76; 5.68]
SUNBEAM	382	73.2 (37.8)	-3.4 (3.0)	360	72.5 (38.1)	-3.5 (3.1)	0.08 [-4.80; 4.96]
Total							0.53 [-2.86; 3.93][k]
Pain							
RADIANCE B	370	79.3 (21.6)	-3.6 (1.3)	367	80.0 (20.7)	-4.6 (1.3)	0.95 [-1.42; 3.32]
SUNBEAM	382	77.7 (23.1)	-1.6 (1.5)	360	81.4 (21.6)	-3.2 (1.5)	1.63 [−0.70; 3.96]
Total							1.30 [-0.37; 2.96][k]
Emotional well-being							

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	MD [95% CI]; p value[h]
RADIANCE B	370	70.5 (17.1)	-1.3 (1.1)	367	70.3 (16.1)	-1.5 (1.1)	0.22 [-1.77; 2.21]
SUNBEAM	382	69.3 (18.1)	-0.5 (1.3)	360	69.0 (18.6)	-1.3 (1.3)	0.78 [-1.32; 2.88]
Total							0.48 [-0.96; 1.93][k]
Energy							
RADIANCE B	370	59.1 (19.7)	-0.5 (1.1)	367	59.6 (19.2)	-2.1 (1.1)	1.59 [-0.43; 3.60]
SUNBEAM	382	58.1 (19.6)	-3.1 (1.4)	360	59.9 (20.0)	-3.6 (1.4)	0.52 [-1.69; 2.73]
Total							1.10 [-0.38; 2.59][k]
Health perceptions							
RADIANCE B	370	56.3 (19.0)	-0.8 (1.2)	367	58.1 (18.4)	-2.2 (1.2)	1.38 [-0.77; 3.53]
SUNBEAM	382	56.0 (19.4)	-0.9 (1.3)	360	57.2 (20.4)	-2.0 (1.4)	1.08 [-1.04; 3.21]
Total							1.23 [-0.28; 2.74][k]
Social function							
RADIANCE B	370	80.2 (19.6)	-3.7 (1.1)	367	82.4 (18.1)	-4.7 (1.1)	1.01 [-1.05; 3.06]
SUNBEAM	382	79.4 (19.4)	-1.2 (1.4)	360	80.4 (19.3)	-3.2 (1.4)	1.99 [-0.20; 4.19]
Total							1.47 [-0.03; 2.97][k]
Cognitive function							
RADIANCE B	370	76.1 (21.8)	-0.0 (1.1)	367	79.0 (20.3)	-0.1 (1.1)	0.09 [-1.99; 2.16]
SUNBEAM	382	76.8 (22.9)	-1.7 (1.3)	360	79.0 (20.2)	-1.5 (1.4)	-0.26 [-2.47; 1.96]
Total							-0.07 [-1.59; 1.44][k]
Health distress							
RADIANCE B	370	67.9 (22.7)	1.9 (1.2)	367	70.7 (21.3)	0.3 (1.2)	1.63 [-0.62; 3.88]

Endpoint	Ozanimod			INF-β 1a			Ozanimod vs INF-β 1a
	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	N[g]	Values at start of study MV (SD)	Change at Month 12 MV[h] (SE)	MD [95% CI]; p value[h]
SUNBEAM	382	68.4 (21.7)	1.6 (1.5)	360	69.5 (23.6)	0.6 (1.6)	1.02 [-1.41; 3.46]
Total							1.35 [-0.30; 3.00][k]
Quality of life							
RADIANCE B	370	70.4 (14.9)	-1.3 (1.0)	367	69.9 (16.0)	-2.0 (1.0)	0.70 [-1.07; 2.47]
SUNBEAM	382	68.9 (17.3)	-0.0 (1.2)	360	70.5 (17.1)	-0.8 (1.2)	0.80 [-1.08; 2.68]
Total							0.75 [-0.54; 2.04][k]
Sexual function							
RADIANCE B	370	82.7 (24.2)	-1.6 (1.3)	367	85.2 (22.5)	-2.3 (1.3)	0.73 [-1.68; 3.13]
SUNBEAM	380	84.4 (23.0)	-1.0 (1.5)	357	84.2 (21.5)	-2.1 (1.6)	1.13 [-1.30; 3.55]
Total							0.93 [-0.78; 2.64][k]
Satisfaction with sexual function (shown as a supplement)[o]							
RADIANCE B	370	70.7 (28.9)	-0.5 (1.8)	367	72.2 (27.7)	-2.0 (1.8)	1.52 [-1.73; 4.76]
SUNBEAM	380	71.4 (28.8)	-1.0 (2.0)	358	73.3 (27.4)	-3.6 (2.1)	2.66 [-0.58; 5.91]
Total							2.09 [-0.20; 4.38][k]
Change in health (shown as a supplement)[o]							
RADIANCE B	370	43.6 (23.5)	10.9 (1.8)	367	46.8 (23.4)	8.9 (1.8)	1.97 [-1.29; 5.22]
SUNBEAM	382	42.3 (22.8)	15.1 (2.0)	360	44.1 (24.6)	9.7 (2.1)	5.35 [2.08; 8.63]
Total							3.65 [1.34; 5.96][k]

Side effects

Endpoint	Ozanimod		INF-β 1a		Ozanimod vs INF-β 1a
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95 % CI]; p value[a]
AEs (additionally shown)					
RADIANCE B	371	228 (61.5)	366	280 (76.5)	-
SUNBEAM	383	215 (56.1)	358	263 (73.5)	-
SAEs					
RADIANCE B	371	15 (4.0)	366	12 (3.3)	1.23 [0.59; 2.60]; 0.581
SUNBEAM	383	10 (2.6)	358	8 (2.2)	1.17 [0.47; 2.93]; 0.740
Total					1.21 [0.68; 2.15]; no data available[c]
Specific AEs					
Infections and infestations (SOC, AEs)					
RADIANCE B	371	108 (29.1)	366	121 (33.1)	0.88 [0.71; 1.09]; 0.247
SUNBEAM	383	100 (26.1)	358	77 (21.5)	1.21 [0.94; 1.57]; 0.142
Total					1.01 [0.86; 1.19]; no data available
Psychiatric disorders (SOC, AEs)					
RADIANCE B	371	29 (7.8)	366	28 (7.6)	1.02 [0.62; 1.68]; 0.933
SUNBEAM	383	23 (6.0)	358	21 (5.9)	1.02 [0.58; 1.82]; 0.936
Total[c]					1.02 [0.70; 1.49]; no data available
Influenza-like illness (PT, AEs)					
RADIANCE B	371	21 (5.7)	366	191 (52.2)	0.11 [0.07; 0.17]; < 0.001
SUNBEAM	383	16 (4.2)	358	188 (52.5)	0.08 [0.05; 0.13]; < 0.001
Total					0.09 [0.07; 0.13]; no data available
Bradycardia (PT, AEs)					
RADIANCE B	371	no data available [p]	366	no data available [p]	no data available [p]
SUNBEAM	383	no data available	358	no data available	no data available
Total					no data available
Discontinuation due to AEs					

Endpoint	Ozanimod		INF-β 1a		Ozanimod vs INF-β 1a
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95 % CI]; p value[a]
RADIANCE B	371	8 (2.2)	366	11 (3.0)	0.72 [0.29; 1.76]; 0.467
SUNBEAM	383	10 (2.6)	358	12 (3.4)	0.78 [0.34; 1.78]; 0.553
Total					0.75 [0.41; 1.38]; no data available[c]

[a] RR and CI: according to the pharmaceutical company, "stratified logistic regression", although the pharmaceutical company does not specify the factors employed; p-value: Cochran-Mantel-Haenszel test.
[b] Adjusted annual relapse rate and CI (per treatment arm) as well as rate ratio with CI and p value (group comparison): Negative binomial model, adjusted for region, age and number of Gd-enriching lesions at baseline; log observation time as offset variable
[c] Meta-analysis with fixed effect (inverse variance)
[d] Relapses requiring hospitalisation.
[e] HR, CI and p-value from Cox proportional hazards model stratified by region, age and EDSS at baseline.
[f] Defined as an EDSS increase ≥ 1 point compared to baseline, confirmation after 6 months (or at the time of premature discontinuation).
[g] Number of patients who were taken into account in the evaluation for the calculation of the estimation of the effect; the values at the start of study can be based on other patient numbers.
[h] MV and SE (change per treatment group) as well as MD, CI, and p value (group comparison): from ANCOVA with treatment arm and value at baseline as covariates as well as "stratification factors if applicable", although the pharmaceutical company provides no information on the factors employed.
[i] A positive change from start of study to end of study means an improvement; a positive effect estimate means an advantage for ozanimod.
[j] In calculating the z-score, results from the SDMT were taken into account rather than from the PASAT-3.
Calculation by the IQWiG, meta-analysis with fixed effect (inverse variance).
[l] A negative change from start of study to end of study means an improvement; a negative effect estimate means an advantage for ozanimod.
[m] The following sub-scales are combined in this sum score: physical health, role limitations due to physical problems, pain, energy, health perceptions, social function, health distress, sexual function.
[n] The following sub-scales are combined in this sum score: role limitations due to emotional problems, emotional well-being, cognitive function, health distress, quality of life.
[o] This item is not included in any of the total scores.
[p] For the superordinate SOC cardiac disorders, the RADIANCE B trial revealed no statistically significant difference between treatment arms (12 (3.2%) patients in the ozanimod arm vs 9 (2.5%) patients in the IFN-β arm).

9-HPT: Nine Hole Peg Test, ANCOVA: analysis of covariance, EDSS: Expanded Disability Status Scale, Gd: gadolinium, HR: Hazard Ratio, IFN-β: interferon beta, CI: confidence interval, LCLA: low-contrast letter acuity, MD: mean difference, MHCS: Mental Health Composite Score, MSFC: Multiple Sclerosis Functional Composite, MSIS -54: Multiple Sclerosis Quality of Life 54, MV: mean value; n: number of patients with (at least 1) event, N: number of patients evaluated, n_E: number of events, n.a. not achieved, PASAT: Paced Auditory Serial Addition Test-3, PHCS: Physical Health Composite Score, PT: preferred term, RCT: randomised controlled trial, RR: relative risk, RRMS: relapsing remitting multiple sclerosis, SD: standard deviation, SDMT: Symbol Digit Modalities Test, SE: standard error; SMD: standardised mean difference (according to pharmaceutical company according to Hedges' g), SOC: System organ class, SAE: serious adverse event, T25-FW: timed 25-foot walk; AE: adverse event

b) Adult patients with relapsing remitting multiple sclerosis (RRMS) with highly active disease in spite of prior treatment with disease-modifying therapy.

Summary of results for relevant clinical endpoints

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

Study results according to endpoints:

The data available are not assessable for the benefit assessment

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

a) Adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease who have not previously received disease-modifying therapy or adult patients previously treated with disease-modifying therapy whose disease is not highly active.

approx. 134,000–149,000 patients

b) Adult patients with relapsing remitting multiple sclerosis (RRMS) with highly active disease in spite of prior treatment with disease-modifying therapy.

approx. 15,500–17,000 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 Zeposia (active ingredient: ozanimod) at the following publicly accessible link (last access: 6 October 2020):

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

Treatment with ozanimod should only be initiated and monitored by specialists in neurology who are experienced in the treatment of multiple sclerosis.

In accordance with the specifications of the European Medicines Agency (EMA) regarding additional measures for risk minimisation, the pharmaceutical company must provide a check-list for physicians, a guideline for patients and caregivers and a patient reminder card. The training and information material shall include, in particular, instructions on how to deal with the potential side effects of ozanimod and on embryo-foetal toxicity.

4. Treatment costs

Annual treatment costs:

a) Adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease who have not previously received disease-modifying therapy or adult patients previously treated with disease-modifying therapy whose disease is not highly active.

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Ozanimod	€ 24,391.01
Appropriate comparator therapy:	
Interferon beta-1a	€ 19,666.84
Interferon beta-1b	€ 16,338.40
Glatiramer acetate	€ 10,993.44
Ocrelizumab Additionally required SHI services: Total:	€ 24,601.74 € 142.28 € 24,744.02

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 December 2020

Costs for other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Ocrelizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	2	€ 142

b) <u>Adult patients with relapsing remitting multiple sclerosis (RRMS) with highly active disease in spite of prior treatment with disease-modifying therapy</u>.

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Ozanimod	€ 24,391.01
Appropriate comparator therapy:	
Alemtuzumab Additionally required SHI services: Total:	51,211.20 € (year 1) 30,726.72 € (year 2) €58.00 51,269.20 € (year 1) 30,784.72 € (year 2)
Fingolimod	€ 21,545.47
Natalizumab	€ 28,986.75

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 December 2020

Costs for other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Alemtuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	5 (year 1) 3 (year 2)	5 (year 1) 3 (year 2)	€ 355.00 € 213.00
Natalizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	13	€ 923.00

II. Entry into force

1. **The resolution will enter into force with effect from the day of its publication on the internet on the website of the G-BA on 7 January 2021.**

2. **The period of validity for patient population b) of the resolution is limited to 1 July 2021.**

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 7 January 2021

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken