Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V: Satralizumab
(neuromyelitis optica spectrum disorders, anti-aquaporin-4IgG seropositive, ≥ 12 years)

of 6 January 2022

At its session on 6 January 2022, the Federal Joint Committee (G-BA) resolved to amend the 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 by the publication of the resolution of D 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 Satralizumab as follows:

Satralizumab

Resolution of: 6 January 2022
Entry into force on: 6 January 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 24 June 2021):

Enspryng is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive.

Therapeutic indication of the resolution (resolution of 6 January 2022):

see therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Satralizumab is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The Federal Joint Committee (G-BA) determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5, Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 AM-NutzenV, indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5, Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

<u>Adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive</u>

Extent of the additional benefit and significance of the evidence of Satralizumab:

Hint for a minor additional benefit

Study results according to endpoints:[1]

Adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↑	Advantages in disease relapses and disability progression.
Health-related quality of life	n.a.	There are no assessable data.
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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

SAkuraStar study: RCT; satralizumab vs placebo

SAkuraSky study: RCT; satralizumab + basic immunosuppressive therapy vs placebo + basic immunosuppressive therapy

Relevant sub-population: anti-aquaporin-4 IgG (AQP4-IgG) seropositive patients

Mortality

Endpoint, study	Satralizumab		Placebo		Satralizumab vs placebo
	N[a]	*Patients with event n (%)*	N[a]	*Patients with event n (%)*	Hazard ratio [95% CI] p value
Overall mortality					
SAkuraStar	41	0	23	0	-
SAkuraSky	27	0	28	0	-

[1] Data from the dossier assessment of the G-BA (published on the 15. Oktober 2021), unless otherwise indicated.

Morbidity

Endpoint, study	Satralizumab		Placebo		Satralizumab vs Placebo
	N[a]	Median time to event in weeks [95% CI] Patients with event n (%) Censoring n (%)	N[a]	Median time to event in weeks [95% CI] Patients with event n (%) Censoring n (%)	Hazard ratio [95% CI] p value
Disease relapses					
Time until the occurrence of a protocol-defined relapse					
SAkuraStar[b]	41	n.c. [n.c.; n.c.] 9 (22.0) 32 (78.0)	23	58.0 [11.7; n.c.] 13 (56.5) 10 (43.5)	0.26 [0.11; 0.63]; 0.0014[d]
SAkuraSky[c]	27	n.c. [n.c.; n.c.] 3 (11.1) 24 (88.9)	28	144.3 [29.4; n.c.] 12 (42.9) 16 (57.1)	0.21 [0.06; 0.75]; 0.0086[e]
Disability progression (EDSS-based)					
Time to EDSS progression					
SAkuraStar[b]	41	n.c. [121.0; n.c.] 11 (26.8) 30 (73.2)	23	47.1 [13.0; n.c.] 11 (47.8) 12 (52.2)	0.34 [0.14; 0.82]; 0.0124[b]
SAkuraSky[c]	27	n.c. [n.c.; n.c.] 5 (18.5) 22 (81.5)	28[f]	113.4 [23.1; 178.6] 11 (40.7) 16 (59.3)	0.36 [0.12; 1.06]; 0.0529[c]

Endpoint, study	Satralizumab			Placebo		
	N	Values at baseline MV (SD)	Values at week 24 MV (SD)	N	Values at baseline MV (SD)	Values at week 24 MV (SD)
Visual acuity (Snellen test)[g]						
Right eye						
SAkuraStar	41	0.58 (0.80)	0.65 (0.96)	23	0.69 (1.03)	0.61 (0.91)
SAkuraSky	27	0.32 (0.54)	0.40 (0.65)	28	0.58 (0.99)	0.61 (0.98)
Left eye						
SAkuraStar	41	0.68 (0.91)	0.68 (0.91)	23	0.55 (0.93)	0.66 (1.14)
SAkuraSky	27	0.78 (1.17)	0.85 (1.24)	28	0.40 (0.79)	0.41 (0.85)

Health-related quality of life

Change in SF-36
Data not assessable.

Side effects

Endpoint, study	Satralizumab		Placebo		Satralizumab vs Placebo
	N[h]	Patients with event n (%)	N[h]	Patients with event n (%)	Hazard ratio [95% CI] p value[i]
Adverse events (AEs) of any severity					
SAkuraStar	41	36 (87.8)	23	16 (69.6)	-
SAkuraSky	28	25 (89.3)	28	27 (96.4)	-
Severe adverse events (severe AEs)					
SAkuraStar	41	11 (26.8)	23	2 (8.7)	1.87 [0.41; 8.54]; 0.4119
SAkuraSky	28	5 (17.9)	28	4 (14.3)	not calculated
Serious adverse events (SAE)					
SAkuraStar	41	7 (17.1)	23	3 (13.0)	0.72 [0.18; 2.83]; 0.6368
SAkuraSky	28	9 (32.1)	28	7 (25.0)	1.08 [0.40; 2.92]; 0.8790
Therapy discontinuation due to adverse events[j]					
SAkuraStar	41	0	23	1 (4.3)	not calculated
SAkuraSky	28	3 (10.7)	28	4 (14.3)	not calculated
Adverse events of special interest					
Increased ALT or AST (> 3× ULN) in combination with either increased bilirubin (> 2× upper ULN) or clinical evidence of icterus					
SAkuraStar	41	0	23	0	-
SAkuraSky	28	0	28	0	-
Suspicion of transmission of an infectious agent via the study medication					
SAkuraStar	41	0	23	0	-
SAkuraSky	28	0	28	0	-
Infections that required intravenous treatment with antibiotics, antivirals or antifungals					
SAkuraStar	41	6 (14.6)	23	0	-

SAkuraSky	28	2 (7.1)	28	3 (10.7)	-
Infections with opportunistic pathogens that required oral treatment with antibiotics, antivirals or antifungals					
SAkuraStar	41	2 (4.9)	23	4 (17.4)	-
SAkuraSky	28	1 (3.6)	28	5 (17.6)	
Infusion-related reaction					
SAkuraStar	41	4 (9.8)	23	3 (13.0)	-
SAkuraSky	28	2 (7.1)	28	1 (3.6)	-

a) ITT population of assessment-relevant AQP4-Ab-positive patients.
b) The median duration of observation for the SAkuraStar study was 96.7 weeks in the satralizumab arm and 60.1 weeks in the placebo arm.
c) The median duration of observation for the SAkuraSky study was 139.4 weeks in the satralizumab arm and 40.2 weeks in the placebo arm.
d) Stratified analysis in Cox proportional hazards model with previous therapy to prevent relapse (B-cell depletion; immunosuppressants/other) and last relapse in year before baseline (first relapse; recurrent relapse) as stratifying factors; p value: log-rank test.
e) Stratified analysis in Cox proportional hazards model with annual relapse rate (1; > 1) and region (Asia; Europe/Other) as stratifying factors; p value: log-rank test.
f) Only 27 of the 28 patients were included in the analysis.
g) Lower values mean better visual acuity.
h) Safety population of assessment-relevant AQP4-Ab-positive patients.
i) Hazard ratio based on unstratified Cox regression model; p value: log-rank test.
j) Discontinuation of study medication after a protocol-defined relapse (in the SAkuraSky study, also after a relapse, treated with emergency therapy) represents a competing event, which is why the certainty of results and interpretability are limited.

Abbreviations used:
ALT: alanine aminotransferase; AQP4-Ab: aquaporin-4 antibody; AST: aspartate aminotransferase; EDSS = expanded disability status scale; FSS = functional system score; ITT = intention-to-treat; CI = confidence interval; MV = mean value; N = number of patients evaluated; n = number of patients with (at least 1) event; n.c. = not calculable; SD = standard deviation; SF-36 = short form (36) health questionnaire; ULN: upper limit of normal; vs = versus

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

Adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive

approx. 460 – 5,050 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 Enspryng (active ingredient: satralizumab) at the following publicly accessible link (last access: 18 November 2021): https://www.ema.europa.eu/en/documents/product-information/enspryng-epar-product-information_en.pdf

Treatment with satralizumab should be initiated and monitored by a specialist in neurology or by a specialist in neurology and psychiatry or by a specialist in paediatrics and adolescent medicine with specialisation in neuropaediatrics and experience in the treatment of neuromyelitis optica spectrum disorders.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide a patient identification card. This contains, in particular, information and warnings about the risk of infections.

4. Treatment costs

Annual treatment costs:

Adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Satralizumab	€ 121,936.19
Possibly in combination with:	
Prednisolone	€ 103.37
Azathioprine	€ 323.35 - € 477.53
Mycophenolate mofetil	€ 3,748.05

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 December 2021)

Costs for additionally required SHI services: not applicable

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 6 January 2022.

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

Berlin, 6 January 2022

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken