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 Secukinumab (New Therapeutic Indication: Plaque Psoriasis, from the Age of 6 to <18 Years)

of 18 February 2021

At its session on 18 February 2021 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 amended on DD Month YYYY (Federal Gazette, BAnz AT DD MM YYYY BX), as follows:

In Annex XII, the following information shall be added after No. 12 to the information on the benefit assessment of secukinumab in accordance with the resolution of 18 February 2021:

Secukinumab

Resolution of: 18 February 2021
Entry into force on: 18 February 2021
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 23 July 2020):

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 18 February 2021):

See new therapeutic indication according to marketing authorisation

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

Children and adolescents from the age of age of 6 years and with moderate to severe plaque psoriasis who are candidates for systemic therapy

Appropriate comparator therapy:

Adalimumab or etanercept or ustekinumab

Extent and probability of the additional benefit of secukinumab compared with etanercept:

Hint for a minor additional benefit

Study results according to endpoints:[1]

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↔	No deaths occurred
Morbidity	↑	Advantage in skin symptomatology
Health-related quality of life	↔	No differences relevant for the benefit assessment
Side effects	↔	No differences relevant 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		

Results of the CAIN457A2310 study at week 24:

Mortality

Endpoint (week 24)	Secukinumab		Etanercept		Secukinumab vs etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
Overall mortality					
Main analysis[b]	*40*	*0 (0)*	*41*	*0 (0)*	-
Sensitivity analysis C[c]	31	0 (0)	26	0 (0)	-

Morbidity

Endpoint (week 24)	Secukinumab		Etanercept		Secukinumab vs etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
Remission (PASI 100)					
Main analysis[b]	*40*	*22.6 (56.5)*	*41*	*9.3 (22.6)*	*2.50 [1.32; 4.74]; 0.005*
Sensitivity analysis C[c]	31	15.6 (50.3)	26	3.2 (12.5)	4.06 [1.33; 12.38]; 0.014

[1] Data from the dossier assessment of the IQWiG (A20-78) and the addendum (A21-02) unless otherwise indicated.

Response (PASI 90)					
Main analysis[b]	*40*	*33.8 (84.4)*	*41*	*19.6 (47.7)*	*1.77 [1.24; 2.52]; 0.002*
Sensitivity analysis C[c]	31	24.8 (79.9)	26	10.5 (40.4)	1.98 [1.19; 3.29]; 0.009
Response (PASI 75)					
Main analysis[b]	*40*	*38.0 (94.9)*	*41*	*26.9 (65.6)*	*1.45 [1.14; 1.83]; 0.002*
Sensitivity analysis C[c]	31	29.0 (93.5)	26	13.8 (53.1)	1.76 [1.20; 2.58]; 0.004

Health-related quality of life

Endpoint (week 24)	**Secukinumab**		**Etanercept**		**Secukinumab vs etanercept**
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
CDLQI (0 or 1), ≤ 16 years					
Main analysis[b]	*25*	*13.6 (54.2)*	*28*	*8.6 (30.6)*	*1.77 [0.90; 3.51]; 0.100*
Sensitivity analysis C[c]	19	9.6 (50.3)	17	3.0 (17.7)	2.85 [0.92; 8.77]; 0.068
CDLQI (0 or 1), all age groups[d]					
Main analysis[b]	*40*	*21.9 (54.9)*	*41*	*18.7 (45.5)*	*1.21 [0.77; 1.88]; 0.411*
Sensitivity analysis C[c]	31	15.9 (51.4)	26	9.0 (34.5)	1.49 [0.79; 2.83]; 0.221

Side effects[e]

Endpoint (week 24)	**Secukinumab**		**Etanercept**		**Secukinumab vs etanercept**
	N[a]	Patients with event n (%)[a]	N[a]	N[a]	Patients with event n (%)[a]
Adverse events (AEs)					
Main analysis[b]	*40*	*29 (72.5)*	*41*	*30 (73.2)*	-
Sensitivity analysis C[c]	31	21 (67.7)	26	20 (76.9)	-
Serious adverse events (SAEs)					
Main analysis[b]	*40*	*2 (5.0)*	*41*	*5 (12.2)*	*0.41 [0.08; 1.99]; 0.432*
Sensitivity analysis C[c]	31	2 (6.5)	26	5 (19.2)	0.34 [0.07; 1.59]; 0.228
Discontinuation due to AEs					

Main analysis[b]	*40*	*0 (0)*	*41*	*1 (2.4)*	*0.34 [0.01; 8.14]; > 0.999*
Sensitivity analysis C[c]	31	0 (0)	26	1 (3.8)	0.28 [0.01; 6.63]; 0.456
Infections[f] (SOC, AEs)					
Main analysis[b]	*40*	*24 (60.0)*	*41*	*20 (48.8)*	*1.23 [0.82; 1.84]; 0.375*
Sensitivity analysis C[c]	31	17 (54.8)	26	15 (57.7)	0.95 [0.60; 1.50]; > 0.999
Infections[f] (SOC, SAEs)					
Main analysis[b]	*40*	*1 (2.5)*	*41*	*0 (0)*	*3.07 [0.13; 73.28]; 0.494*
Sensitivity analysis C[c]	31	1 (3.2)	26	0 (0)	2.53 [0.11; 59.63]; > 0.999
Neoplasms[g] (SMQ, AEs)					
Main analysis[b]	*40*	*0 (0)*	*41*	*0 (0)*	-
Sensitivity analysis C[c]	31	0 (0)	26	0 (0)	-

a. In the analysis of the results of the PASI and CDLQI instruments, missing values were replaced using multiple imputation; due to the many imputations of missing values, the number of responders is usually not a whole number. Number (percentage %) of replaced values per treatment arm (secukinumab vs etanercept) for
   - PASI
     - Main analysis: 1 (2.5 %) vs 4 (9.8 %)
     - Sensitivity analysis C: 1 (3.2 %) vs 3 (11.5 %)
   - CDLQI
     - Main analysis, ≤ 16 years: 1 (4.0 %) vs 1 (3.5 %)
     - Sensitivity analysis C, ≤ 16 years: 1 (5.3 %) vs 0 (0 %)
     - Main analysis: 2 (5.0 %) vs 2 (4.9 %)
     - Sensitivity analysis C: 2 (6.5 %) vs 1 (3.8 %)

b. Primary secukinumab treatment arm (dosage according to the product information: < 50 kg BW: 75 mg; ≥ 50 kg BW: 150 mg) vs etanercept arm

c. Primary secukinumab treatment arm (dosage according to the product information: < 50 kg BW: 75 mg; ≥ 50 kg BW: 150 mg) vs etanercept arm, of which exclusively patients for whom etanercept is approved as a result of their prior treatment.

d. CDLQI has only been validated for children and adolescents up to 16 years of age. Analyses that include data on 16–18 year olds are presented as a supplement.

e. The pharmaceutical company has presented results on adverse event endpoints, including and excluding disease-specific events. The events that the pharmaceutical company considers to be disease-specific are presented in Module 4 of its dossier. The results including and excluding disease-specific events are identical.

f. The following events are considered (coded as per MedDRA): Infections and infestations (SOC, AEs).

g. The following events are considered (coded as per MedDRA): Neoplasms malignant and unspecified (SMQ, AEs).

Abbreviations used:
CDLQI: Children's Dermatology Life Quality Index; BW: body weight; CI: confidence interval; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with (at least 1) event; N: number of patients evaluated; PASI: Psoriasis Area and Severity Index; RCT: randomised controlled study; RR: relative risk; SOC: system organ class; SAE: serious adverse event; SMQ: standardised MedDRA questionnaire; AE: adverse event

Supplementary presented study results of the CAIN457A2310 study Week 52:

Mortality

Endpoint (week 52)	Secukinumab		Etanercept		Secukinumab vs etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
Overall mortality					
Main analysis[b]	*40*	*0 (0)*	*41*	*0 (0)*	-
Sensitivity analysis C[c]	*31*	*0 (0)*	*26*	*0 (0)*	-

Morbidity

Endpoint (week 52)	Secukinumab		Etanercept		Secukinumab vs etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
Remission (PASI 100)					
Main analysis[b]	*40*	*16.3 (40.7)*	*41*	*9.5 (23.2)*	*1.76 [0.88; 3.49]; 0.108*
Sensitivity analysis C[c]	*31*	*11.3 (36.4)*	*26*	*4.3 (16.5)*	*2.22 [0.81; 6.13]; 0.123*
Response (PASI 90)					
Main analysis[b]	*40*	*30.6 (76.5)*	*41*	*21.9 (53.5)*	*1.43 [1.02; 2.02]; 0.041*
Sensitivity analysis C[c]	*31*	*23.6 (76.2)*	*26*	*13.5 (52.0)*	*1.47 [0.95; 2.26]; 0.082*
Response (PASI 75)					
Main analysis[b]	*40*	*35.9 (89.8)*	*41*	*30.0 (73.1)*	*1.23 [0.98; 1.54]; 0.074*
Sensitivity analysis C[c]	*31*	*26.9 (86.8)*	*26*	*17.2 (66.3)*	*1.31 [0.95; 1.82]; 0.103*

Health-related quality of life

Endpoint (week 52)	Secukinumab		Etanercept		Secukinumab vs etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
CDLQI (0 or 1), ≤ 16 years					
Main analysis[b]	*25*	*17.1 (68.6)*	*28*	*14.3 (51.0)*	*1.35 [0.84; 2.15]; 0.215*

Sensitivity analysis C[c]	*19*	*12.1 (63.9)*	*17*	*6.6 (38.8)*	*1.65 [0.81; 3.39]; 0.170*
CDLQI (0 or 1), all age groups[d]					
Main analysis[b]	*40*	*21.8 (54.6)*	*41*	*21.8 (53.3)*	*1.02 [0.68; 1.55]; 0.908*
Sensitivity analysis C[c]	*31*	*16.8 (54.3)*	*26*	*10.4 (40.0)*	*1.36 [0.75; 2.45]; 0.309*

Side effects[e]

Endpoint (week 52)	**Secukinumab**		**Etanercept**		**Secukinumab vs etanercept**
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95 % CI]; p value
Adverse events (AE)					
Main analysis[b]	*40*	*34 (85.0)*	*41*	*34 (82.9)*	-
Sensitivity analysis C[c]	*31*	*25 (80.6)*	*26*	*24 (92.3)*	-
Serious adverse events (SAE)					
Main analysis[b]	*40*	*3 (7.5)*	*41*	*5 (12.2)*	*0.62 [0.16; 2.40]; 0.712*
Sensitivity analysis C[c]	*31*	*3 (9.7)*	*26*	*5 (19.2)*	*0.50 [0.13; 1.91]; 0.448*
Discontinuation due to AEs					
Main analysis[b]	*40*	*1 (2.5)*	*41*	*1 (2.4)*	*1.03 [0.07; 15.83]; > 0.999*
Sensitivity analysis C[c]	*31*	*1 (3.2)*	*26*	*1 (3.8)*	*0.84 [0.06; 12.76]; > 0.999*
Infections[f] (SOC, AEs)					
Main analysis[b]	*40*	*30 (75.0)*	*41*	*27 (65.9)*	*1.14 [0.86; 1.51]; 0.467*
Sensitivity analysis C[c]	*31*	*21 (67.7)*	*26*	*19 (73.1)*	*0.93 [0.66; 1.30]; 0.774*
Infections[f] (SOC, SAEs)					
Main analysis[b]	*40*	*1 (2.5)*	*41*	*0 (0)*	*3.07 [0.13; 73.28]; 0.494*
Sensitivity analysis C[c]	*31*	*1 (3.2)*	*26*	*0 (0)*	*2.53 [0.11; 59.63]; > 0.999*
Neoplasms[g] (SMQ, AEs)					
Main analysis[b]	*40*	*0 (0)*	*41*	*0 (0)*	-
Sensitivity analysis C[c]	*31*	*0 (0)*	*26*	*0 (0)*	-

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

Children and adolescents from the age of age of 6 years and with moderate to severe plaque psoriasis who are candidates for systemic therapy

approx. 270–2035 patients

15. 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 Cosentyx (active ingredient: secukinumab) at the following publicly accessible link (last accessed: 26 January 2021):

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

In patients who have not responded to therapy in up to 16 weeks of treatment, the discontinuation of treatment should be considered. Some patients with an initially partial response improve over time if treatment is continued beyond 16 weeks.

16. Treatment costs

Annual treatment costs:

Children and adolescents from the age of age of 6 years and with moderate to severe plaque psoriasis who are candidates for systemic therapy

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Secukinumab	€ 10,343.44–20,686.88
Appropriate comparator therapy:	
Adalimumab Additionally required SHI services Total	€ 6,280.18–11,510.06 € 180.64 € 6,460.82–11,690.70
Etanercept Additionally required SHI services Total	€ 3,943.31–7,778.20 € 180.64 € 4,123.95–7,958.84
Ustekinumab Additionally required SHI services Total	€ 21,326.37 € 74.24 € 21,400.61

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

I. 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 18 February 2021.

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

Berlin, 18 February 2021

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

Prof. Hecken