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Secukinumab (plaque psoriasis in children and adolescents) –

Addendum to Commission A20-78[1]

Addendum

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Abbreviation	Meaning
ACT	appropriate comparator therapy
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
PASI	Psoriasis Area and Severity Index
RCT	randomized controlled trial
SPC	Summary of Product Characteristics

1 Background

On 12 January 2021, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A20-78 (Secukinumab – Benefit assessment according to §35a Social Code Book V) [1].

In its dossier [2], the pharmaceutical company (hereinafter referred to as "the company") presented analyses of the CAIN457A2310 study [3,4] on various patient populations (main analysis and sensitivity analyses A to C) at week 52 for the benefit assessment of secukinumab in comparison with the appropriate comparator therapy (ACT) in children and adolescents from the age of 6 years with moderate to severe plaque psoriasis who are candidates for systemic therapy.

Dossier assessment A20-78 on secukinumab concluded that the data presented were not suitable for the assessment of the added benefit of secukinumab in comparison with the ACT etanercept. This is particularly due to the fact that in the study presented, a relevant proportion of included patients in the etanercept arm did not receive optimal treatment in the case of non-response to treatment, or the etanercept treatment was not in compliance with the requirements of the Summary of Product Characteristics (SPC) [1].

In its comments on the benefit assessment [5], the company presented further analyses of the CAIN457A2310 study at week 24 and week 52. The G-BA commissioned IQWiG to assess the following data submitted subsequently in the commenting procedure or available in the dossier of the company:

- Analyses of the CAIN457A2310 study at week 24
  - total population (main analysis)
  - sensitivity analysis C
- Analyses of the CAIN457A2310 study at week 52
  - total population (main analysis)
  - sensitivity analysis C

The responsibility for the present assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

The CAIN457A2310 study is a randomized controlled trial (RCT) comparing 2 different dosages of secukinumab (low dose, high dose) with etanercept and placebo. The study included 162 children and adolescents aged 6 to < 18 years with severe plaque psoriasis. The investigator had to consider systemic therapy to be indicated, either because the patients had not responded adequately to topical therapies, systemic therapies or phototherapy, or because they had not tolerated systemic therapies or phototherapy. Detailed characteristics of the CAIN457A2310 study can be found in dossier assessment A20-78 [1]. Information on the only partial representation of the therapeutic indications of secukinumab and etanercept by the included study population is also available there. Furthermore, the dossier assessment contains information on the approval-compliant use of the secukinumab dosage, which only in the "low"-dose secukinumab arm largely complies with the recommendations in the SPC.

The lack of suitability of the data available in the company's dossier for the CAIN457A2310 study was justified in dossier assessment A20-78 on secukinumab [1]. For example, the data presented are not suitable for the assessment because the etanercept treatment in the comparator arm of the CAIN457A2310 study was not in compliance with the requirements of the SPC. On the one hand, according to the SPC, treatment should be discontinued in patients who show no response after 12 weeks. As shown in the dossier assessment, approximately 1 third of the children and adolescents in the etanercept arm (total population) did not achieve a response according to the Psoriasis Area and Severity Index (PASI) 75 at week 12, but 40 out of 41 patients continued treatment with etanercept after completion of the induction phase after 12 weeks. Thus, the children and adolescents without response continued treatment with etanercept beyond week 12, instead of switching to another, possibly more effective therapy. For this reason alone, the available data from the CAIN457A2310 study are not suitable for answering the present research question of the benefit assessment. On the other hand, the children and adolescents in the comparator arm received etanercept for 52 weeks, although, according to the SPC, the treatment should be given for a maximum of 24 weeks [6].

Other limitations of the study include, as explained in the dossier assessment, a dosing error in the primary secukinumab arms in weeks 13, 14 and 15.

Available analyses at week 24 and week 52

The analyses for week 52, available in the dossier and subsequently submitted by the company in the commenting procedure, are not suitable for the benefit assessment due to the limitation of the treatment duration of etanercept to 24 weeks described in the SPC. Furthermore, the company presented analyses of the CAIN457A2310 study for week 24 in its comments. These data are also not usable for the assessment. At this time, the etanercept treatment of the patients was in compliance with the requirements of the SPC with regard to duration. However, these analyses did not resolve the problem of continued treatment with etanercept after an inadequate response at week 12 in a relevant proportion of the included patients. For this reason alone, the

available data from the CAIN457A2310 study, both at week 24 and at week 52, are overall not suitable for answering the present research question of the benefit assessment.

In accordance with the commission, the results of the main analysis and of sensitivity analysis C of the CAIN457A2310 study at weeks 24 and 52 and corresponding patient characteristics are presented in Appendix A. The presented analyses are based on the populations mentioned below and the comparison of the study arms mentioned:

- Main analysis: total population of the respective study arms; primary secukinumab arm with the (low) dosage according to the SPC versus etanercept arm
- Sensitivity analysis C: in each case, population for which etanercept is approved due to the pretreatment; primary secukinumab arm with the (low) dosage according to the SPC versus etanercept arm

The company referred to the intervention arms of the CAIN457A2310 study in which secukinumab was administered from the start of the study as "primary secukinumab arms". The populations included in the analyses presented are described in detail in dossier assessment A20-78 on secukinumab [1].

2.1 Summary

In the CAIN457A2310 study presented by the company, a relevant proportion of included patients in the etanercept arm did not receive optimal treatment in the case of non-response to treatment, or the etanercept treatment was not in compliance with the requirements of the SPC [1]. The data presented by the company for the CAIN457A2310 study are therefore not suitable for drawing conclusions on the added benefit of secukinumab in comparison with the ACT. The conclusion on the added benefit of secukinumab from dossier assessment A20-78 is therefore not changed by the present addendum.

The following Table 1 shows the result of the benefit assessment of secukinumab under consideration of dossier assessment A20-78 and the present addendum.

Table 1: Secukinumab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Children and adolescents from the age of 6 years with moderate to severe plaque psoriasis who are candidates for systemic therapy	Adalimumab or **etanercept** or ustekinumab[b]	Added benefit not proven

a. Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.
b. The respective approval of the drugs is to be considered.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

3 References

The reference list contains citations provided by the company in which bibliographical information may be missing.

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6. Pfizer. Enbrel 25 mg [online]. 2020 [Accessed: 02.11.2020]. URL: https://www.fachinfo.de.

Appendix A – Main analysis and sensitivity analysis C of study CAIN457A2310 at weeks 24 and 52

Table 2: Characteristics of the study population – RCT, direct comparison: secukinumab vs. etanercept (multipage table)

Study Characteristic Category	Main analysis[a]		Sensitivity analysis C[b]	
	Secukinumab N[c] = 40	Etanercept N[c] = 41	Secukinumab N[c] = 31	Etanercept N[c] = 26
CAIN457A2310				
Age [years], mean (SD)	13.7 (2.9)	13.5 (2.9)	13.5 (3.2)	13.5 (2.9)
Age group [years], n (%)				
< 12	8 (20)	10 (24)	8 (26)	6 (23)
≥ 12	32 (80)	31 (76)	23 (74)	20 (77)
Sex [F/M], %	68/33	61/39	71/29	62/38
Weight category [kg], n (%)				
< 25	2 (5)	4 (10)	2 (7)	3 (12)
≥ 25 to < 50	17 (43)	16 (39)	13 (42)	8 (31)
≥ 50	21 (53)	21 (51)	16 (52)	15 (58)
Family origin, n (%)				
Caucasian	34 (85)	30 (73)	27 (87)	20 (77)
Black	1 (3)	0 (0)	1 (3)	0 (0)
Asian	1 (3)	3 (7)	1 (3)	2 (8)
Native Americans	3 (8)	8 (20)	1 (3)	4 (15)
Other	1 (3)	0 (0)	1 (3)	0 (0)
Region, n (%)				
Africa	1 (3)	4 (10)	1 (3)	3 (12)
America	4 (10)	8 (20)	2 (7)	4 (15)
Asia	7 (18)	5 (12)	7 (23)	3 (12)
Europe	28 (70)	24 (59)	21 (68)	16 (62)
Time since first diagnosis of plaque psoriasis [years]				
Mean (SD)	4.8 (4.3)	4.5 (3.7)	5.7 (4.4)	5.2 (4.3)
Median [min; max]	3.8 [0.3; 17.0]	3.9 [0.3; 14.0]	4.8 [0.3; 17.0]	4.0 [0.5; 14.0]
PASI at baseline				
Mean (SD)	27.6 (6.9)	28.4 (9.1)	28.1 (7.5)	29.3 (10.4)
Median [min; max]	25.6 [20.2; 48.0]	24.8 [20.1; 59.8]	25.2 [20.2; 48]	25.3 [20.1; 59.8]
BSA at baseline				
Mean (SD)	37.6 (13.9)	43.1 (19.6)	37.7 (15.1)	44.2 (23.0)
Median [min; max]	36.7 [12.0; 72.5]	37.7 [13.1; 90.5]	36.8 [12; 72.5]	34.0 [13.1; 90.5]
IGA mod 2011 at baseline, n (%)				
3 (moderate disease)	0 (0)	0 (0)	0 (0)	0 (0)
4 (severe disease)	40 (100)	41 (100)	31 (100)	26 (100)

Table 2: Characteristics of the study population – RCT, direct comparison: secukinumab vs. etanercept (multipage table)

Study Characteristic Category	Main analysis[a]		Sensitivity analysis C[b]	
	Secukinumab N[c] = 40	Etanercept N[c] = 41	Secukinumab N[c] = 31	Etanercept N[c] = 26
Diagnosis of psoriatic arthritis, n (%)	5 (13)	3 (7)	4 (13)	3 (12)
Prior psoriasis treatment, n (%)	40 (100)	41 (100)	31 (100)	26 (100)
Prior systemic therapy, n (%)	26 (65)	19 (46)	25 (81)	16 (62)
Prior phototherapy or photochemotherapy, n (%)	17 (43)	21 (51)	16 (52)	19 (73)
Prior topical therapy, n (%)	32 (80)	38 (93)	23 (74)	23 (88)
Treatment failure with ≥ 1 systemic therapy or phototherapy or photochemotherapy, n (%)	31 (78)	26 (63)	31 (100)	26 (100)
Treatment discontinuation, n (%)				
During induction phase				
From week 0 to week 12	1 (3)	1 (2)	1 (3)	0 (0)
During maintenance phase				
From week 12 to week 24	0 (0)	4 (10)	0 (0)	3 (12)
From week 12 to week 52	1 (3)	6 (15)	1 (3)	5 (19)
Study discontinuation, n (%)				
During induction phase				
From week 0 to week 12	1 (3)	0 (0)	1 (3)	0 (0)
During maintenance phase				
From week 12 to week 24	0 (0)	1 (2)	0 (0)	0 (0)
From week 12 to week 52	0 (0)	2 (5)	0 (0)	1 (4)

a. Primary secukinumab arm (dosage according to SPC: < 50 kg body weight: 75 mg; ≥ 50 kg body weight: 150 mg) vs. etanercept arm (total population).
b. Primary secukinumab treatment arm (dosage according to SPC: < 50 kg body weight: 75 mg; ≥ 50 kg body weight: 150 mg) vs. etanercept arm, of which in each case exclusively patients for whom etanercept is approved due to their pretreatment.

BSA: body surface area; F: female; IGA mod: Investigator Global Assessment modified; M: male, n: number of patients in the category; N: number of randomized patients; PASI: Psoriasis Area and Severity Index; RCT: randomized controlled trial; SD: standard deviation; SPC: Summary of Product Characteristics; vs.: versus

Table 3: Results (mortality, morbidity, health-related quality of life and side effects) – RCT, direct comparison: secukinumab vs. etanercept, week 24 (multipage table)

Study (time point) Outcome category Outcome Analysis	Secukinumab		Etanercept		Secukinumab vs. etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95% CI]; p-value
CAIN457A2310 (week 24)					
Mortality					
All-cause mortality					
Main analysis[b]	40	0 (0)	41	0 (0)	–
Sensitivity analysis C[c]	31	0 (0)	26	0 (0)	–
Morbidity					
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
Supplementary information					
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*
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					
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
Supplementary information					
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*

Table 3: Results (mortality, morbidity, health-related quality of life and side effects) – RCT, direct comparison: secukinumab vs. etanercept, week 24 (multipage table)

Study (time point) Outcome category Outcome Analysis	Secukinumab		Etanercept		Secukinumab vs. etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95% CI]; p-value
Side effects[e]					
AEs (supplementary information)					
Main analysis[b]	40	29 (72.5)	41	30 (73.2)	–
Sensitivity analysis C[c]	31	21 (67.7)	26	20 (76.9)	–
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
Tumours[g] (SMQ, AEs)					
Main analysis[b]	40	0 (0)	41	0 (0)	–
Sensitivity analysis C[c]	31	0 (0)	26	0 (0)	–

Table 3: Results (mortality, morbidity, health-related quality of life and side effects) – RCT, direct comparison: secukinumab vs. etanercept, week 24 (multipage table)

Study (time point) Outcome category	Secukinumab		Etanercept		Secukinumab vs. etanercept
Outcome Analysis	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95% CI]; p-value

a. In the analysis of the instruments PASI and CDLQI, missing values were imputed using multiple imputation; due to the multiple imputation of missing values, there is usually no whole number of responders. Number (proportion %) of imputed 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 SPC: < 50 kg body weight: 75 mg; ≥ 50 kg body weight: 150 mg) vs. etanercept arm.
c. Primary secukinumab treatment arm (dosage according to SPC: < 50 kg body weight: 75 mg; ≥ 50 kg body weight: 150 mg) vs. etanercept arm, of which exclusively patients for whom etanercept is approved due to their pretreatment.
d. The CDLQI is only validated for children and adolescents up to 16 years of age. Analyses that include data of the 16- to 18-year-olds are presented as supplementary information.
e. The company presented results on side effect outcomes including and excluding disease-specific events. Module 4 of its dossier shows which events the company considered to be disease-specific. The results including and excluding the disease-specific events are identical.
f. The following events (MedDRA coding) are considered: infections and infestations (SOC, AEs).
g. The following events are considered (MedDRA coding): malignant or unspecified tumours (SMQ, AEs).

AE: adverse event; CDLQI: Children's Dermatology Life Quality Index; CI: confidence interval; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with (at least one) event; N: number of analysed patients; PASI: Psoriasis Area and Severity Index; RCT: randomized controlled trial; RR: relative risk; SAE: serious adverse event; SMQ: Standardized MedDRA Query; SOC: System Organ Class; SPC: Summary of Product Characteristics; vs.: versus

Table 4: Results (mortality, morbidity, health-related quality of life and side effects) – RCT, direct comparison: secukinumab vs. etanercept, week 52 (multipage table)

Study (time point) Outcome category Outcome Analysis	Secukinumab		Etanercept		Secukinumab vs. etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95% CI]; p-value
CAIN457A2310 (week 52)					
Mortality					
All-cause mortality					
Main analysis[b]	40	0 (0)	41	0 (0)	–
Sensitivity analysis C[c]	31	0 (0)	26	0 (0)	–
Morbidity					
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
Supplementary information					
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*
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					
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
Supplementary information					
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*

Table 4: Results (mortality, morbidity, health-related quality of life and side effects) – RCT, direct comparison: secukinumab vs. etanercept, week 52 (multipage table)

Study (time point) Outcome category Outcome Analysis	Secukinumab		Etanercept		Secukinumab vs. etanercept
	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95% CI]; p-value
Side effects					
AEs[e] (supplementary information)					
Main analysis[b]	40	34 (85.0)	41	34 (82.9)	–
Sensitivity analysis C[c]	31	25 (80.6)	26	24 (92.3)	–
SAEs[e]					
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
Tumours[g] (SMQ, AEs)					
Main analysis[b]	40	0 (0)	41	0 (0)	–
Sensitivity analysis C[c]	31	0 (0)	26	0 (0)	–

Table 4: Results (mortality, morbidity, health-related quality of life and side effects) – RCT, direct comparison: secukinumab vs. etanercept, week 52 (multipage table)

Study (time point) Outcome category	Secukinumab		Etanercept		Secukinumab vs. etanercept
Outcome Analysis	N[a]	Patients with event n (%)[a]	N[a]	Patients with event n (%)[a]	RR [95% CI]; p-value

a. In the analysis of the instruments PASI and CDLQI, missing values were imputed using multiple imputation; due to the multiple imputation of missing values, there is usually no whole number of responders. Number (proportion) of imputed values per treatment arm (secukinumab vs. etanercept) for
- PASI
  - main analysis: 1 (2.5%) vs. 7 (17.1%)
  - sensitivity analysis C: 1 (3.2%) vs. 5 (19.2%)
- CDLQI
  - main analysis, ≤ 16 years: 1 (4.0%) vs. 4 (14.3%)
  - sensitivity analysis C, ≤ 16 years: 1 (5.3%) vs. 3 (17.6%)
  - main analysis: 3 (7.5%) vs. 6 (14.6%)
  - sensitivity analysis C: 3 (9.7%) vs. 4 (15.4%)

b. Primary secukinumab treatment arm (dosage according to SPC: < 50 kg body weight: 75 mg; ≥ 50 kg body weight: 150 mg) vs. etanercept arm.
c. Primary secukinumab treatment arm (dosage according to SPC: < 50 kg body weight: 75 mg; ≥ 50 kg body weight: 150 mg) vs. etanercept arm, of which exclusively patients for whom etanercept is approved due to their pretreatment.
d. The CDLQI is only validated for children and adolescents up to 16 years of age. Analyses that include data of the 16- to 18-year-olds are presented as supplementary information.
e. The company presented results on side effect outcomes including and excluding disease-specific events. Module 4 of its dossier shows which events the company considered to be disease-specific. The results including and excluding the disease-specific events are identical.
f. The following events (MedDRA coding) are considered: infections and infestations (SOC, AEs).
g. The following events are considered (MedDRA coding): malignant or unspecified tumours (SMQ, AEs).

AE: adverse event; CDLQI: Children's Dermatology Life Quality Index; CI: confidence interval; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with (at least one) event; N: number of analysed patients; PASI: Psoriasis Area and Severity Index; RCT: randomized controlled trial; RR: relative risk; SAE: serious adverse event; SMQ: Standardized MedDRA Query; SOC: System Organ Class; SPC: Summary of Product Characteristics; vs.: versus

Table 5: Common AEs[a] – RCT, direct comparison: secukinumab vs. etanercept, sensitivity analysis C, week 24

Study	Patients with event n (%)	
SOC[b] PT[b]	Secukinumab N = 31	Etanercept N = 26
CAIN457A2310		
Sensitivity analysis C (week 24)		
Overall AE rate	21 (67.7)	20 (76.9)
Infections and infestations	17 (54.8)	15 (57.7)
Nasopharyngitis	6 (19.4)	5 (19.2)
Pharyngitis	1 (3.2)	3 (11.5)
Oral herpes	1 (3.2)	3 (11.5)
Skin and subcutaneous tissue disorders	9 (29.0)	4 (15.4)
Gastrointestinal disorders	6 (19.4)	8 (30.8)
Abdominal pain	2 (6.5)	4 (15.4)
General disorders and administration site conditions	5 (16.1)	5 (19.2)
Investigations	3 (9.7)	5 (19.2)
Blood and lymphatic system disorders	4 (12.9)	0 (0)
Nervous system disorders	4 (12.9)	1 (3.8)
Headache	4 (12.9)	1 (3.8)

a. Events that occurred in ≥ 10% of the patients in at least one study arm.
b. MedDRA version 23.1; SOC and PT notation taken from MedDRA without adaptation.

AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; SOC: System Organ Class; vs: versus

Table 6: Common SAEs[a] – RCT, direct comparison: secukinumab vs. etanercept, sensitivity analysis C, week 24

Study	Patients with event n (%)	
SOC[b]	Secukinumab N = 31	Etanercept N = 26
CAIN457A2310		
Sensitivity analysis C (week 24)		
Overall SAE rate	2 (6.5)	5 (19.2)
Gastrointestinal disorders	0 (0)	3 (11.5)

a. Events that occurred in ≥ 5% of the patients in at least one study arm.
b. MedDRA version 23.1; SOC notation taken from MedDRA without adaptation.

MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; RCT: randomized controlled trial; SAE: serious adverse event; SOC: System Organ Class; vs.: versus

Table 7: Common discontinuations due to AEs – RCT, direct comparison: secukinumab vs. etanercept, sensitivity analysis C, week 24

Study	Patients with event n (%)	
SOC[a] PT[a]	Secukinumab N = 31	Etanercept N = 26
CAIN457A2310		
Sensitivity analysis C (week 24)		
Overall rate of discontinuations due to AEs	0 (0)	1 (3.8)
Investigations	0 (0)	1 (3.8)
Hepatic enzyme increased	0 (0)	1 (3.8)

a. MedDRA version 23.1; SOC notation taken from MedDRA without adaptation.

AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with at least one event; N: number of analysed patients; PT: Preferred Term; RCT: randomized controlled trial; SOC: System Organ Class; vs.: versus