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Bimekizumab (plaque psoriasis) –

Addendum to Commission A21-110[1]

Addendum

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List of abbreviations

Abbreviation	Meaning
BSA	body surface area
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IGA	Investigator's Global Assessment
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
NRI	non-responder imputation
PASI	Psoriasis Area and Severity Index
PGA	Patient Global Assessment
PSD	Patient Symptom Diary
RCT	randomized controlled trial
SMD	standardized mean difference

1 Background

On 25 January 2022, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments on Commission A21-110 (Bimekizumab – benefit assessment according to §35a Social Code Book V) [1].

The G-BA commissioned IQWiG with assessing the BE SURE and BE RADIANT studies' data on the outcome of patient-reported symptoms (Patient Global Assessment, PGA) and the missing domains of the psoriasis diary (Patient Symptom Diary, PSD) as well as with additionally presenting the inclusion criteria for the patient population of research question 1 using the analyses [2] presented by the pharmaceutical company (hereinafter "company") in the commenting procedure [2] and the subsequently submitted data [3].

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

2 Assessment

The benefit assessment of bimekizumab involved the randomized controlled trials (RCTs) BE SURE, comparing bimekizumab with adalimumab, and BE RADIANT, comparing bimekizumab with secukinumab. For research question 1 (adult patients who are not candidates for conventional treatment as part of initial systemic therapy), the assessment was based on a subpopulation of both studies which was formed by the company and includes patients who had not yet received any systemic psoriasis therapy at baseline and who, according to the company, were not candidates for conventional treatment. However, the information provided by the company fails to show whether all patients of the subpopulation were actually to be allocated to research question 1 and which specific criteria led to the selection in each case. After the oral hearing, the company submitted additional data which, in the company's view, show that the subpopulation it presented is suitable for answering research question 1. These data are discussed in Section 2.1.1.

Regarding symptoms, the company's dossier presents the results from an internally developed electronic diary used as an instrument for recording patient-relevant psoriasis symptoms. However, the presented results lacked 9 of the 14 domains surveyed in the BE SURE study. The BE SURE and BE RADIANT studies additionally surveyed the outcome of patient-reported symptoms (PGA), but Module 4 A of the company's dossier did not show any data on this outcome. As part of the commenting procedure, the company submitted analyses on the outcomes of patient-reported absence of symptoms (PSD) and patient-reported symptoms (PGA). The results relevant for research question 1 are presented in Section 2.1.2, and those for research question 2, in Section 2.2.1.

2.1 Research question 1: adult patients who are not candidates for conventional treatment as part of initial systemic therapy

2.1.1 Characterization of the study population

In the subsequently submitted documents, the company has redefined the subpopulation relevant for research question 1 based on the following criteria:

- Psoriasis Area and Severity Index (PASI) ≥ 20 or body surface area (BSA) ≥ 20% or Investigator's Global Assessment (IGA) = 4
- Dermatology Life Quality Index (DLQI) ≥ 15
- Scalp IGA ≥ 3

In the BE SURE study, 37 of the original 45 patients in the bimekizumab arm (82.2%) and 44 of the original 49 patients in the comparator arm (89.8%) meet at least 1 criterion. In the BE RADIANT study, this is the case for 52 of the original 58 patients in the bimekizumab arm (89.7%) and 89 of the original 98 patients in the comparator arm (90.8%).

For this redefined population, the company expects no adequate success of conventional therapy, concluding that the results of the originally analysed population are relevant for research question 1. The company bases its criteria on the German S3 guideline for the treatment of psoriasis vulgaris [4]. Concurring with the company, the criteria of PASI ≥ 20, BSA ≥ 20%, IGA = 4, and DLQI ≥ 15 are deemed to be thresholds for severe manifestation or severe impairment of the quality of life. In addition to said criteria, guidelines suggest the criteria of severe involvement of fingernails, scalp, or the genital area, of which the company looked only at scalp involvement, specifying a scalp IGA ≥ 3 as the threshold for severe involvement. However, severe scalp involvement is defined as a scalp IGA of 4. Therefore, this criterion inadequately reflects severe disease and hence the unsuitability of conventional systemic therapy.

The data subsequently submitted by the company do not show the number of patients included in the analysis of the redefined population or the criteria based on which they were included. The company reported only the number of patients who met at least 1 of the above criteria. Hence, it is unclear how many patients meet only the criterion of scalp IGA ≥ 3.

In summary, the company's subsequently submitted data still fail to clarify whether the patients included in the subpopulation were actually to be allocated to research question 1 and which specific criteria led to the selection in each case. There is still no information available on the physician's individual considerations and evaluations regarding the treatment decision in each case. As already discussed in the initial assessment, the described uncertainties of results were taken into account in the assessment.

2.1.2 Results on added benefit

2.1.2.1 Risk of bias

The risk of bias for the subsequently submitted results on patient-reported absence of symptoms (PSD) and patient-reported symptoms (PGA) is deemed high. For patient-reported symptoms (PGA) in either study, this is due to the high and differential percentages of patients who were disregarded in the analysis. For patient-reported absence of symptoms (PSD), the BE SURE study exhibits a high and differential percentage of patients who were replaced using non-responder imputation (NRI) (see Table 1 and compare A21-100). The subsequently submitted domains from patient-reported absence of symptoms (PSD) were not recorded in the BE RADIANT study.

Table 1: Overview of replaced values in individual outcomes of the BE SURE and BE RADIANT studies for evaluating the risk of bias on the outcome level (research question 1: initial systemic therapy)

Outcome Time point (replacement strategy)	BE SURE		BE RADIANT	
	Bimekizumab (N = 45)	Adalimumab (N = 49)	Bimekizumab (N = 58)	Secukinumab (N = 98)
PSD (all domains[c])				
N (%) in analysis (NRI)	44 (97.8)	48 (98.0)	58 (100)	98 (100)
Replaced values (NRI), n (%)	15 (33.3)	13 (26.5)	4 (6.9)	19 (19.4)
PGA				
N (%) in analysis at last time point	43 (95.6[b])	43 (87.8[b])	54 (93.1[b])	79 (80.6[b])

a. Operationalized as domain score = 0; the BE SURE study surveyed and presented the 14 domains of itching, pain, scaling, redness, burning, cracking, dryness, irritation, sensitivity, lesions, thickening, fatigue, embarrassment, and choice of clothing; the BE RADIANT study surveyed and presented only the 3 domains of itching, pain, and scaling.
b. IQWiG calculation.

IQWiG: Institute for Quality and Efficiency in Health Care; N: number of analysed patients; n: number of analysed patients with event; NRI: non-responder imputation; PGA: Patient Global Assessment; PSD: Patient Symptom Diary

Certainty of conclusions

As described in dossier assessment A21-110, the BE RADIANT study is used as the anchor for the qualitative summary.

Due to the high risk of bias for the results of the patient-reported symptoms (PGA) outcome, no more than hints, e.g. of added benefit, can be derived for this outcome from each of the 2 studies. On the basis of the BE SURE study, the high risk of bias for the results of the outcome of patient-reported absence of symptoms (PSD) means that, likewise, no more than hints, e.g. of added benefit, can be derived for this outcome. The BE RADIANT study did not survey the subsequently submitted domains of patient-reported absence of symptoms (PSD).

In the present research question, however, fundamental questions remained concerning the subpopulation submitted by the company on research question 1 (see Section 2.1.1). Therefore, no more than hints, e.g. of added benefit, can be derived, even if the results of both studies are statistically significant and exhibit the same direction of effect.

2.1.2.2 Results

Table 2 and Table 3 summarize the results of the outcomes of patient-reported absence of symptoms (PSD) and patient-reported symptoms (PGA) in patients with moderate to severe plaque psoriasis who are not candidates for conventional treatment as part of initial systemic therapy.

The results on the other outcomes of the symptoms category as well as on the outcomes of mortality, health-related quality of life, and side effects are presented in dossier assessment A21-110.

Table 2: Results (morbidity, dichotomous) – RCT, direct comparison: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy)

Outcome category Outcome Study	Bimekizumab		Adalimumab or secukinumab		Bimekizumab vs. adalimumab or secukinumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value[a]
Morbidity					
Patient-reported absence of symptoms (PSD)[b]					
PSD cracking					
BE SURE (Week 24)	44	17 (38.6)	48	12 (25.0)	1.72 [0.94; 3.13]; 0.078
BE RADIANT (Week 48)				Not recorded	
PSD dryness					
BE SURE (Week 24)	44	8 (18.2)	48	7 (14.6)	1.33 [0.52; 3.38]; 0.557
BE RADIANT (Week 48)				Not recorded	
PSD irritation					
BE SURE (Week 24)	44	13 (29.5)	48	8 (16.7)	1.98 [0.91; 4.27]; 0.080
BE RADIANT (Week 48)				Not recorded	
PSD sensitivity					
BE SURE (Week 24)	44	12 (27.3)	48	10 (20.8)	1.38 [0.66; 2.86]; 0.394
BE RADIANT (Week 48)				Not recorded	
PSD lesions					
BE SURE (Week 24)	44	10 (22.7)	48	8 (16.7)	1.45 [0.64; 3.28]; 0.383
BE RADIANT (Week 48)				Not recorded	
PSD thickening					
BE SURE (Week 24)	44	17 (38.6)	48	10 (20.8)	2.06 [1.07; 3.96]; 0.028
BE RADIANT (Week 48)				Not recorded	
PSD fatigue					
BE SURE (Week 24)	44	16 (36.4)	48	14 (29.2)	1.48 [0.84; 2.60]; 0.175
BE RADIANT (Week 48)				Not recorded	
PSD embarrassment					
BE SURE (Week 24)	44	17 (38.6)	48	14 (29.2)	1.39 [0.80; 2.43]; 0.251
BE RADIANT (Week 48)				Not recorded	
PSD choice of clothing					
BE SURE (Week 24)	44	15 (34.1)	48	16 (33.3)	1.10 [0.64; 1.88]; 0.747
BE RADIANT (Week 48)				Not recorded	

a. RR and CI: CMH test with region as stratification variable; p-value: CMH test for general association. Missing values for morbidity outcomes were replaced using NRI.
b. Operationalized as score = 0 for all symptoms.

CI: confidence interval; CMH: Cochran–Mantel–Haenszel; n: number of patients with (at least 1) event; N: number of analysed patients; NRI: non-responder imputation; PSD: Patient Symptom Diary; RCT: randomized controlled trial; RR: relative risk

Table 3: Results (morbidity, continuous) – RCT, direct comparison: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy)

Outcome category Outcome Study	Bimekizumab			Adalimumab or secukinumab			Bimekizumab vs. adalimumab or secukinumab
	N[a]	Values at baseline mean (SD)	Change by end of study mean[b] (SE)	N[a]	Values at baseline mean (SD)	Change by end of study mean[b] (SE)	MD [95% CI]; p-value[b]
Morbidity							
Patient-reported symptoms							
PGA							
BE SURE (Week 24)	43	3.52 (0.93)	-1.84 (0.17)	43	3.49 (0.98)	-1.25 (0.16)	-0.59 [-0.94; -0.25]; 0.001 Hedges' g -0.55 [-0.99; -0.12]
BE RADIANT (Week 48)	54	3.62 (0.97)	-2.22 (0.09)	79	3.48 (0.92)	-2.03 (0.07)	-0.19 [-0.41; 0.03]; 0.091

a. Number of patients included in the analysis for calculating the effect estimation; baseline values may be based on different patient numbers.
b. MMRM with treatment, visit, treatment*visit, region, and baseline value as fixed effects, visit as repeat measurement and patient as random effect.

CI: confidence interval; MD: mean difference; MMRM: mixed effect model repeated measurement; N: number of analysed patients; PGA: Patient Global Assessment; RCT: randomized controlled trial; SD: standard deviation; SE: standard error

As described in Section 2.1.2.1, on the basis of the available information, the overall analysis of the BE RADIANT and BE SURE studies can derive no more than hints, e.g. of added benefit.

Morbidity

Patient-reported absence of symptoms

PSD thickening

For the outcome of PSD thickening, the BE SURE study shows a statistically significant difference in favour of bimekizumab in comparison with secukinumab. This difference is no more than marginal, however. The outcome was not recorded in the BE RADIANT study. This results in no hint of added benefit of bimekizumab in comparison with the ACT; an added benefit is therefore not proven.

PSD – further domains

For the outcome of patient-reported absence of symptoms (PSD – further domains), the BE SURE study shows no statistically significant difference between treatment arms. These outcomes were not recorded in the BE RADIANT study. This results in no hint of added benefit of bimekizumab in comparison with the ACT; an added benefit is therefore not proven.

Patient-reported symptoms (Patient Global Assessment)

For the outcome of patient-reported symptoms (PGA), the BE SURE study shows a statistically significant difference between treatment arms in favour of bimekizumab versus adalimumab. However, the 95% CI of the standardized mean difference (SMD) (Hedges' g) was not fully outside the irrelevance range of -0.2 to 0.2. The observed can therefore not be inferred to be relevant. No statistically significant difference between treatment arms was found for the determinative BE RADIANT study. This results in no hint of added benefit of bimekizumab in comparison with the ACT; an added benefit is therefore not proven.

2.1.3 Probability and extent of added benefit

For research question 1 (adult patients who are not candidates for conventional treatment as part of initial systemic therapy), the probability and extent of added benefit are derived at outcome level below. The various outcome categories and the effect sizes have been taken into account. The methods used for this purpose are explained in the IQWiG General Methods [5].

The approach for deriving an overall conclusion on any added benefit by aggregating the conclusions reached at outcome level is a proposal by IQWiG. The G-BA decides on the added benefit.

2.1.3.1 Assessment of added benefit at outcome level

On the basis of the results presented in Section 2.1.2 and the results of dossier assessment A21-110, the extent of the respective added benefit was estimated at outcome level (see Table 4).

Determination of the outcome category for the outcome of thickening from patient-reported absence of symptoms (PSD thickening)

Insufficient information is available for categorizing the severity of the outcome of thickening from the patient-reported absence of symptoms (PSD thickening). Concurring with the company, this outcome is assigned to the category of non-serious/non-severe symptoms / late complications.

Determination of the outcome category for the outcome of patient-reported symptoms (Patient Global Assessment)

Insufficient information is available for categorizing the severity of the outcome of patient-reported symptoms (PGA). Therefore, the outcome is assigned to the category of non-serious/non-severe symptoms / late complications.

Table 4: Extent of added benefit on outcome level: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy) (multipage table)

Outcome category **Outcome** **Study**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
Mortality		
All-cause mortality		
BE SURE	0% vs. 0% RR: –	Lesser/added benefit not proven
BE RADIANT		
Morbidity		
Remission (PASI 100)		
BE SURE	57.8% vs. 14.3% RR: 4.01 [1.91; 8.41] RR: 0.25 [0.12; 0.52][c] p < 0.001	Outcome category: non-serious/non-severe symptoms / late complications $CI_u < 0.90$ Added benefit; extent: minor
BE RADIANT	74.1% vs. 44.9% RR: 1.58 [1.21; 2.06] RR: 0.63 [0.49; 0.83][c] p = 0.001	
	probability: hint[d]	
Absence of symptoms on the scalp (scalp IGA)		
BE SURE	79.1% vs. 45.0% RR: 1.70 [1.18; 2.44] RR: 0.59 [0.41; 0.85][c] p = 0.002	Lesser/added benefit not proven
BE RADIANT	83.3% vs. 69.7% RR: 1.16 [0.97; 1.39] p = 0.125	
Absence of symptoms on the palms and soles (ppIGA)		
BE SURE	No usable data	Lesser/added benefit not proven
BE RADIANT		
Absence of symptoms on fingernails (mNAPSI 100)		
BE SURE	No usable data	Lesser/added benefit not proven
BE RADIANT		
PSD itching		
BE SURE	25.0% vs. 16.7% RR: 1.60 [0.69; 3.75] p = 0.270	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[e]
BE RADIANT	75.9% vs. 52.0% RR: 1.38 [1.10; 1.74] RR: 0.72 [0.75; 0.91][c] p = 0.010	

Table 4: Extent of added benefit on outcome level: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy) (multipage table)

Outcome category **Outcome** **Study**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
PSD pain		
BE SURE	34.1% vs. 29.2% RR: 1.31 [0.74; 2.33] p = 0.358	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[e]
BE RADIANT	87.9% vs. 67.3% RR: 1.27 [1.07; 1.49] RR: 0.79 [0.67; 0.93][c] p = 0.010	
PSD scaling		
BE SURE	31.8% vs. 16.7% RR: 1.97 [0.91; 4.25] p = 0.080	Outcome category: non-serious/non-severe symptoms / late complications $CI_u < 0.90$ Added benefit; extent: minor
BE RADIANT	77.6% vs. 46.9% RR: 1.54 [1.21; 1.96] RR: 0.65 [0.51; 0.83][c] p < 0.001	
	Probability: hint	
PSD redness		
BE SURE	25.0% vs. 18.8% RR: 1.38 [0.64; 2.97] p = 0.416	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD burning		
BE SURE	34.1% vs. 25.0% RR: 1.48 [0.81; 2.74] p = 0.212	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD cracking		
BE SURE	38.6% vs. 25.0% RR: 1.72 [0.94; 3.13] p = 0.078	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD dryness		
BE SURE	18.2% vs. 14.6% RR: 1.33 [0.52; 3.38] p = 0.557	Lesser/added benefit not proven
BE RADIANT	Not recorded	

Table 4: Extent of added benefit on outcome level: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy) (multipage table)

Outcome category **Outcome** **Study**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
PSD irritation		
BE SURE	29.5% vs. 16.7% RR: 1.98 [0.91; 4.27] p = 0.080	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD sensitivity		
BE SURE	27.3% vs. 20.8% RR: 1.38 [0.66; 2.86] p = 0.394	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD lesions		
BE SURE	22.7% vs. 16.7% RR: 1.45 [0.64; 3.28] p = 0.383	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD thickening		
BE SURE	38.6% vs. 20.8% RR: 2.06 [1.07; 3.96] RR: 0.49 [0.25; 0.93][c] p = 0.028	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD fatigue		
BE SURE	36.4% vs. 29.2% RR: 1.48 [0.84; 2.60] p =0.175	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD embarrassment		
BE SURE	38.6% vs. 29.2% RR: 1.39 [0.80; 2.43] p = 0.251	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD choice of clothing		
BE SURE	34.1% vs. 33.3% RR: 1.10 [0.64; 1.88] p = 0.747	Lesser/added benefit not proven
BE RADIANT	Not recorded	

Table 4: Extent of added benefit on outcome level: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy) (multipage table)

Outcome category **Outcome** **Study**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
Patient-reported symptoms (PGA)		
BE SURE	-1.84 vs. -1.25 MD: -0.59 [-0.94; -0.25] p = 0.001 Hedges' g: -0.55 [-0.99; -0.12][f]	Lesser/added benefit not proven
BE RADIANT	-2.22 vs. -2.03 MD: -0.19 [-0.41; 0.03] p = 0.091	
Health status (EQ-5D VAS)		
BE SURE	9.8 vs. 3.8 MD: 6.02 [0.73; 11.31] p = 0.026 Hedges' g: 0.47 [0.05; 0.90][f]	Lesser/added benefit not proven
BE RADIANT	8.2 vs. 7.2 MD: 0.93 [-3.54; 5.40] p = 0.682	
Health-related quality of life		
DLQI ≤ 1		
BE SURE	64.4% vs. 36.7% RR: 1.78 [1.15; 2.76] RR: 0.56 [0.36; 0.87][c] p = 0.007	Lesser/added benefit not proven
BE RADIANT	84.5% vs. 71.4% RR: 1.13 [0.97; 1.33] p = 0.153	
SF-36 PCS		
BE SURE	5.6 vs. 5.3 MD: 0.35 [-1.82; 2.52] p = 0.750	Lesser/added benefit not proven
BE RADIANT	Outcome not surveyed	
SF-36 MCS		
BE SURE	2.3 vs. 2.5 MD: -0.21 [-2.66; 2.25] p = 0.868	Lesser/added benefit not proven
BE RADIANT	Outcome not surveyed	

Table 4: Extent of added benefit on outcome level: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy) (multipage table)

Outcome category **Outcome** **Study**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
Side effects		
SAEs		
BE SURE	0% vs. 0% RR: –	Outcome category: serious/severe side effects greater harm; extent: non-quantifiable
BE RADIANT	6.9% vs. 0% RR: NC p = 0.003	
	Probability: hint	
Discontinuation due to AEs		
BE SURE	2.3% vs. 4.1% RR: 0.58 [0.04; 7.75] p = 0.682	Greater/lesser harm not proven
BE RADIANT	0% vs. 3.1% RR: NC p = 0.234	
Infections and infestations (AE)		
BE SURE	48.8% vs. 46.9% RR: 1.04 [0.68; 1.58] p = 0.865	Greater/lesser harm not proven
BE RADIANT	62.1% vs. 44.9% RR: 1.34 [1.00; 1.80] p = 0.058	
Fungal infectious disorders (AE)		
BE SURE	16.3% vs. 2.0% RR: 7.05 [0.97; 51.04] RR: 0.14 [0.02; 1.03][c] p = 0.019	Outcome category: non-serious/non-severe side effects $0.90 \leq CI_u < 1.00$ Greater/lesser harm not proven[c]
BE RADIANT	22.4% vs. 9.2% RR: 2.33 [1.04; 5.19] RR: 0.43 [0.19; 0.96][c] p = 0.035	

Table 4: Extent of added benefit on outcome level: bimekizumab vs. adalimumab or secukinumab (research question 1: initial systemic therapy) (multipage table)

Outcome category **Outcome** **Study**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
a. Probability given if statistically significant differences are present. b. Estimations of effect size are made depending on the outcome category, with different limits according to the upper limit of the confidence interval (CI_u). c. IQWiG calculation; reversed direction of effect to enable use of limits to derive the extent of added benefit. d. Uncertainties in the formation of the subpopulation led to reduced certainty of conclusions (see Sections 2.1.1 and 2.1.2.1). e. The extent of the effect in this non-serious/non-severe outcome was no more than marginal. f. If the CI for Hedges' g is fully outside the irrelevance range [-0.2; 0.2], this is interpreted to be a relevant effect. In other cases, the presence of a relevant effect cannot be inferred. AE: adverse event; CI: confidence interval; CI_u: upper limit of the confidence interval; DLQI: Dermatology Life Quality Index; IQWiG: Institute for Quality and Efficiency in Health Care; MCS: Mental Component Summary; MD: mean difference; mNAPSI: modified Nail Psoriasis Area and Severity Index; NC: not calculable; PASI: Psoriasis Area and Severity Index; PCS: Physical Component Summary; PGA: patient global assessment; ppIGA: palmoplantar IGA; PSD: Patient Symptom Diary; RR: relative risk; SAE: serious adverse event; SF-36: Short Form 36-Item Health Survey; VAS: visual analogue scale		

2.1.3.2 Overall conclusion on added benefit

Table 5 summarizes the results included in the overall conclusion on the extent of added benefit.

Table 5: Favourable and unfavourable effects from the assessment of bimekizumab in comparison with adalimumab or secukinumab (research question 1: initial systemic therapy)

Favourable effects	**Unfavourable effects**
Non-serious/non-severe symptoms / late complications ▪ Remission (PASI 100): hint of an added benefit – extent: minor ▪ PSD scaling: hint of an added benefit – extent: minor	
	Serious/severe side effects ▪ SAEs: hint of greater harm – extent: non-quantifiable
PASI: Psoriasis Area and Severity Index; PSD: Patient Symptom Diary; SAE: serious adverse event	

Overall, there are no differences concerning favourable and unfavourable effects when compared with dossier assessment A21-110. In summary, for adult patients who are not candidates for conventional therapy as part of initial systemic therapy (research question 1), there is a hint of minor added benefit of bimekizumab in comparison with the ACT.

2.2 Research question 2: adult patients with inadequate response or intolerance to prior systemic therapy

2.2.1 Results on added benefit

2.2.1.1 Risk of bias

The risk of bias of the subsequently submitted results on patient-reported absence of symptoms (PSD) is deemed high in the BE SURE study. This is due to the high percentage of NRI-replaced values (see A21-110). The BE RADIANT study did not survey the subsequently submitted domains of patient-reported absence of symptoms (PSD). For the results on the outcome of patient-reported symptoms (PGA), the risk of bias is rated as high for the BE RADIANT study as well. This is due to the high percentage of patients who were disregarded in the analysis (see Table 6). For the results of the outcome of patient-reported symptoms (PGA), the risk of bias of the BE SURE study is rated as low.

Table 6: Overview of replaced values in individual outcomes of the BE SURE and BE RADIANT studies for evaluating the risk of bias on the outcome level (research question 2: inadequate response or intolerance to prior therapy)

Outcome Time point (replacement strategy)	BE SURE		BE RADIANT	
	Bimekizumab (N = 87)	Adalimumab (N = 84)	Bimekizumab (N = 128)	Secukinumab (N = 228)
PSD (all domains[c]) N (%) in analysis (NRI) Replaced values (NRI), n (%)	 86 (98.9) 26 (29.9)	 81 (96.4) 24 (28.6)	 128 (100) 12 (9.4)	 228 (100) 28 (12.3)
PGA N (%) in analysis at last time point	79 (90.8[b])	78 (92.9[b])	115 (89.9[b])	200 (87.7[b])

a. Operationalized as domain score = 0; the BE SURE study surveyed and presented the 14 domains of itching, pain, scaling, redness, burning, cracking, dryness, irritation, sensitivity, lesions, thickening, fatigue, embarrassment, and choice of clothing; the BE RADIANT study surveyed and presented only the 3 domains of itching, pain, and scaling.
b. IQWiG calculation.

IQWiG: Institute for Quality and Efficiency in Health Care; N: number of analysed patients; n: number of analysed patients with event; NRI: non-responder imputation; PGA: Patient Global Assessment; PSD: Patient Symptom Diary

Certainty of conclusions

As described in Section 2.1.2.1 and in dossier assessment A21-110, the BE RADIANT study is used as the anchor for the qualitative summary.

On the basis of the subsequently submitted information, no more than hints, e.g. of added benefit, can be derived for the BE RADIANT study due to the high risk of bias of the results of the outcome of patient-reported symptoms (PGA), while from the BE SURE study, indications can be derived due to low risk of bias. If the results of both studies point in the same direction and are statistically significant, the certainty of the BE SURE study's results can be upgraded

here as well, allowing indications to be derived for these outcomes in the overall analysis of both studies.

The subsequently submitted domains of the outcome of patient-reported absence of symptoms (PSD) were surveyed only in the BE SURE study. The risk of bias for the outcome of patient-reported absence of symptoms was high; therefore, no more than hints, e.g. of added benefit, can be derived for this outcome.

2.2.1.2 Results

Table 7 and Table 8 summarize the results of the outcomes of patient-reported absence of symptoms (PSD) and patient-reported symptoms (PGA) in patients with moderate to severe plaque psoriasis with inadequate response or intolerance to prior systemic therapy.

The results on the other outcomes of the symptoms category as well as on the outcomes of mortality, health-related quality of life, and side effects are presented in dossier assessment A21-110.

Table 7: Results (morbidity, dichotomous) – RCT, direct comparison: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response or intolerance to prior treatment)

Outcome category Outcome Study	Bimekizumab		Adalimumab or secukinumab		Bimekizumab vs. adalimumab or secukinumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value[a]
Morbidity					
Patient-reported absence of symptoms (PSD)[b]					
PSD cracking					
BE SURE (Week 24)	86	40 (46.5)	81	30 (37.0)	1.25 [0.87; 1.81]; 0.219
BE RADIANT (Week 48)				Not recorded	
PSD dryness					
BE SURE (Week 24)	86	21 (24.4)	81	14 (17.3)	1.32 [0.71; 2.44]; 0.370
BE RADIANT (Week 48)				Not recorded	
PSD irritation					
BE SURE (Week 24)	86	35 (40.7)	81	24 (29.6)	1.37 [0.89; 2.10]; 0.142
BE RADIANT (Week 48)				Not recorded	
PSD sensitivity					
BE SURE (Week 24)	86	35 (40.7)	81	25 (30.9)	1.30 [0.85; 1.98]; 0.221
BE RADIANT (Week 48)				Not recorded	
PSD lesions					
BE SURE (Week 24)	86	32 (37.2)	81	19 (23.5)	1.67 [1.01; 2.74]; 0.039
BE RADIANT (Week 48)				Not recorded	
PSD thickening					
BE SURE (Week 24)	86	42 (48.8)	81	27 (33.3)	1.48 [1.01; 2.16]; 0.039
BE RADIANT (Week 48)				Not recorded	
PSD fatigue					
BE SURE (Week 24)	86	34 (39.5)	81	28 (34.6)	1.14 [0.76; 1.70]; 0.528
BE RADIANT (Week 48)				Not recorded	
PSD embarrassment					
BE SURE (Week 24)	86	44 (51.2)	81	28 (34.6)	1.50 [1.04; 2.16]; 0.027
BE RADIANT (Week 48)				Not recorded	
PSD choice of clothing					
BE SURE (Week 24)	86	42 (48.8)	81	30 (37.0)	1.33 [0.93; 1.90]; 0.119
BE RADIANT (Week 48)				Not recorded	

a. RR and CI: CMH test with region as stratification variable; p-value: CMH test for general association. Missing values for morbidity outcomes were replaced using NRI.
b. Operationalized as score = 0 for all symptoms.

CI: confidence interval; CMH: Cochran-Mantel-Haenszel; n: number of patients with (at least 1) event; N: number of analysed patients; NRI: non-responder imputation; PSD: Patient Symptom Diary; RCT: randomized controlled trial; RR: relative risk

Table 8: Results (morbidity, continuous) – RCT, direct comparison: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response or intolerance to prior treatment)

Outcome category Outcome Study	Bimekizumab			Adalimumab or secukinumab			Bimekizumab vs. adalimumab or secukinumab
	N[a]	Values at baseline mean (SD)	Change by end of study mean[b] (SE)	N[a]	Values at baseline mean (SD)	Change by end of study mean[b] (SE)	MD [95% CI]; p-value[b]
Morbidity							
Patient-reported symptoms							
PGA							
BE SURE (Week 24)	79	3.87 (0.76)	-2.34 (0.08)	78	3.77 (0.83)	-1.69 (0.08)	-0.65 [-0.88; -0.43]; < 0.001 Hedges' g: -0.88 [-1.21; -0.55]
BE RADIANT (Week 48)	115	3.67 (0.87)	-2.32 (0.07)	200	3.77 (0.87)	-2.05 (0.05)	-0.26 [-0.42; -0.10]; 0.001 Hedges' g: -0.37 [-0.60; -0.14]

a. Number of patients included in the analysis for calculating the effect estimation; baseline values may be based on different patient numbers.
b. MMRM with treatment, visit, treatment*visit, region, and baseline value as fixed effects, visit as repeat measurement and patient as random effect.

CI: confidence interval; MD: mean difference; MMRM: mixed effect model repeated measurement; N: number of analysed patients; PGA: Patient Global Assessment; RCT: randomized controlled trial; SD: standard deviation; SE: standard error

As described in Section 2.2.1.1 and given that no further aspects reduce the certainty of conclusions in the present research question 2, the available information in the overall analysis of the BE RADIANT and BE SURE studies can be used to derive at most indications, e.g. of added benefit, for the outcome of patient-reported symptoms (PGA). For the outcome of patient-reported absence of symptoms (PSD), no more than hints, e.g. of added benefit, can be derived.

Morbidity

Patient-reported absence of symptoms

PSD lesions, PSD thickening, and PSD embarrassment

For each of the outcomes of PSD lesions, PSD thickening, and PSD embarrassment, the BE SURE study shows a statistically significant difference in favour of bimekizumab in comparison with secukinumab. In each case, this difference is no more than marginal, however. These outcomes were not recorded in the BE RADIANT study. This results in no hint of added benefit of bimekizumab in comparison with the ACT; an added benefit is therefore not proven.

PSD – further domains

For the outcome of patient-reported absence of symptoms (PSD – further domains), the BE SURE study shows no statistically significant difference between treatment arms. These outcomes were not recorded in the BE RADIANT study. This results in no hint of added benefit of bimekizumab in comparison with the ACT; an added benefit is therefore not proven.

Patient-reported symptoms (Patient Global Assessment)

For the outcome of patient-reported symptoms (PGA), the BE SURE study as well as the BE RADIANT study show a statistically significant difference between treatment arms in favour of bimekizumab versus adalimumab. For the determinative BE RADIANT study, however, the 95% CI of the SMD (Hedges' g) was not completely outside the irrelevance range of -0.2 to 0.2. It can therefore not be inferred that the observed effect is relevant. This results in no hint of added benefit of bimekizumab in comparison with the ACT; an added benefit is therefore not proven.

2.2.2 Probability and extent of added benefit

For research question 2 (patients with inadequately response or intolerance to prior systemic therapy), the probability and extent of added benefit are derived below at the outcome level. The various outcome categories and the effect sizes have been taken into account. The methods used for this purpose are explained in the IQWiG General Methods [5].

The approach for deriving an overall conclusion on any added benefit by aggregating the conclusions reached at outcome level is a proposal by IQWiG. The G-BA decides on the added benefit.

2.2.2.1 Assessment of added benefit at outcome level

On the basis of the results presented in Section 2.2.1 and the results of dossier assessment A21-110, the extent of the respective added benefit was estimated at outcome level (see Table 9).

Determination of the outcome category for the outcomes of lesions, thickening, and embarrassment from patient-reported absence of symptoms (PSD)

Insufficient information is available for categorizing the severity of the outcomes of lesions, thickening, and embarrassment from patient-reported absence of symptoms (PSD). Concurring with the company, these outcomes are assigned to the category of non-serious/non-severe symptoms / late complications.

Determination of the outcome category for the outcome of patient-reported symptoms (Patient Global Assessment)

Insufficient information is available for categorizing the severity of the outcome of patient-reported symptoms (PGA). Therefore, the outcome is assigned to the category of non-serious/non-severe symptoms / late complications.

Table 9: Extent of added benefit at outcome level: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response / intolerance to prior treatment) (multipage table)

Outcome category **Outcome**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
Mortality		
All-cause mortality		
BE SURE	0% vs. 0% RR: –	Lesser/added benefit not proven
BE RADIANT	0.8% vs. 0.4% RR: 1.54 [0.13; 18.63] p = 0.733	
Morbidity		
Remission (PASI 100)		
BE SURE	67.8% vs. 39.3% RR: 1.69 [1.24; 2.30] RR: 0.59 [0.43; 0.81][c] p < 0.001	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[d]
BE RADIANT	61.7% vs. 47.8% RR: 1.29 [1.07; 1.56] RR: 0.78 [0.64; 0.93][c] p = 0.010	
Absence of symptoms on the scalp (scalp IGA)		
BE SURE	84.5% vs. 66.7% RR: 1.28 [1.05; 1.55] RR: 0.78 [0.65; 0.95][c] p = 0.008	Lesser/added benefit not proven
BE RADIANT	77.7% vs. 73.9% RR: 1.05 [0.92; 1.19] p = 0.493	
Absence of symptoms on the palms and soles (ppIGA)		
BE SURE	No usable data	Lesser/added benefit not proven
BE RADIANT		
Absence of symptoms on fingernails (mNAPSI 100)		
BE SURE	No usable data	Lesser/added benefit not proven
BE RADIANT		

Table 9: Extent of added benefit at outcome level: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response / intolerance to prior treatment) (multipage table)

Outcome category **Outcome**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
PSD itching		
BE SURE	34.9% vs. 22.2% RR: 1.57 [0.95; 2.60] p = 0.076	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[d]
BE RADIANT	60.2% vs. 46.5% RR: 1.28 [1.05; 1.57] RR: 0.78 [0.64; 0.95][c] p = 0.018	
PSD pain		
BE SURE	51.2% vs. 34.6% RR: 1.44 [1.00; 2.08] RR: 0.69 [0.48; 1.00][c] p = 0.041	Lesser/added benefit not proven
BE RADIANT	81.3% vs. 71.9% RR: 1.12 [1.00; 1.25] p = 0.070	
PSD scaling		
BE SURE	43.0% vs. 23.5% RR: 1.86 [1.15; 2.99] RR: 0.54 [0.33; 0.87][c] p = 0.007	Outcome category: non-serious/non-severe symptoms / late complications $0.80 \leq CI_u < 0.90$ Added benefit; extent: minor
BE RADIANT	70.3% vs. 51.3% RR: 1.36 [1.15; 1.61] RR: 0.74 [0.62; 0.87][c] p < 0.001	
	Probability: proof	
PSD redness		
BE SURE	41.9% vs. 21.0% RR: 2.06 [1.25; 3.40] RR: 0.49 [0.29; 0.80][c] p = 0.003	Outcome category: non-serious/non-severe symptoms / late complications $0.80 \leq CI_u < 0.90$ Added benefit; extent: minor
BE RADIANT	Not recorded	
	Probability: hint[e]	

Table 9: Extent of added benefit at outcome level: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response / intolerance to prior treatment) (multipage table)

Outcome category **Outcome**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
PSD burning		
BE SURE	45.3% vs. 34.6% RR: 1.29 [0.88; 1.89] p = 0.178	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD cracking		
BE SURE	46.5% vs. 37.0% RR: 1.25 [0.87; 1.81] p = 0.219	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD dryness		
BE SURE	24.4% vs. 17.3% RR: 1.32 [0.71; 2.44] p = 0.370	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD irritation		
BE SURE	40.7% vs. 29.6% RR: 1.37 [0.89; 2.10] p = 0.142	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD sensitivity		
BE SURE	40.7% vs. 30.9% RR: 1.30 [0.85; 1.98] p = 0.221	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD lesions		
BE SURE	37.2% vs. 23.5% RR: 1.67 [1.01; 2.74] RR: 0.60 [0.36; 0.99][c] p = 0.039	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[d]
BE RADIANT	Not recorded	

Table 9: Extent of added benefit at outcome level: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response / intolerance to prior treatment) (multipage table)

Outcome category **Outcome**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
PSD thickening		
BE SURE	48.8% vs. 33.3% RR: 1.48 [1.01; 2.16] RR: 0.68 [0.46; 0.99][c] p = 0.039	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[d]
BE RADIANT	Not recorded	
PSD fatigue		
BE SURE	39.5% vs. 34.6% RR: 1.14 [0.76; 1.70] p = 0.528	Lesser/added benefit not proven
BE RADIANT	Not recorded	
PSD embarrassment		
BE SURE	51.2% vs. 34.6% RR: 1.50 [1.04; 2.16] RR: 0.67 [0.46; 0.96][c] p= 0.027	Outcome category: non-serious/non-severe symptoms / late complications $0.90 \leq CI_u < 1.00$ Lesser/added benefit not proven[d]
BE RADIANT	Not recorded	
PSD choice of clothing		
BE SURE	48.8% vs. 37.0% 1.33 [0.93; 1.90] p = 0.119	Lesser/added benefit not proven
BE RADIANT	Not recorded	
Patient-reported symptoms (PGA)		
BE SURE	-2.34 vs. -1.69 MD: -0.65 [-0.88; -0.43] p < 0.001 Hedges' g: -0.88 [-1.21; -0.55][f]	Lesser/added benefit not proven
BE RADIANT	-2.32 vs. -2.05 MD: -0.26 [-0.42; -0.10] p = 0.001 Hedges' g: -0.37 [-0.60; -0.14][f]	

Table 9: Extent of added benefit at outcome level: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response / intolerance to prior treatment) (multipage table)

Outcome category **Outcome**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
Health status (EQ-5D VAS)		
BE SURE	12.0 vs. 8.4 MD: 3.55 [-0.64; 7.74] p = 0.096	Lesser/added benefit not proven
BE RADIANT	12.6 vs. 11.0 MD: 1.59 [-1.71; 4.88] p = 0.344	
Health-related quality of life		
Response DLQI ≤ 1		
BE SURE	67.8% vs. 52.4% RR: 1.29 [1.01; 1.65] RR: 0.78 [0.61; 0.99][c] p = 0.042	Lesser/added benefit not proven
BE RADIANT	78.9% vs. 68.9% RR: 1.13 [1.00; 1.29] p = 0.060	
SF-36 PCS		
BE SURE	5.5 vs. 4.4 MD: 1.02 [-0.71; 2.75] p = 0.246	Lesser/added benefit not proven
BE RADIANT	Outcome not surveyed	
SF-36 MCS		
BE SURE	4.1 vs. 2.2 MD: 1.93 [0.20; 3.67] p = 0.029 Hedges' g: 0.35 [0.03; 0.67][f]	Lesser/added benefit not proven
BE RADIANT	Outcome not surveyed	
Side effects		
SAEs		
BE SURE	1.2% vs. 4.8% RR: 0.26 [0.03; 2.64] p = 0.206	Greater/lesser harm not proven
BE RADIANT	6.3% vs. 8.3% RR: 0.74 [0.33; 1.65] p = 0.455	

Table 9: Extent of added benefit at outcome level: bimekizumab vs. adalimumab or secukinumab (research question 2: inadequate response / intolerance to prior treatment) (multipage table)

Outcome category **Outcome**	**Bimekizumab vs. adalimumab or secukinumab** **Event rate (%) or MD** **Effect estimation [95% CI]** **p-value** **Probability**[a]	**Derivation of extent**[b]
Discontinuation due to AEs		
BE SURE	1.2% vs. 2.4% RR: 0.41 [0.04; 4.54] p = 0.459	Greater/lesser harm not proven
BE RADIANT	1.6% vs. 2.6% RR: 0.59 [0.12; 2.78] p = 0.498	
Infections and infestations (AE)		
BE SURE	56.6% vs. 50.0% RR: 1.13 [0.85; 1.49] p = 0.401	Greater/lesser harm not proven
BE RADIANT	69.5% vs. 59.2% RR: 1.15 [0.99; 1.35] p = 0.076	
Fungal infectious disorders (AE)		
BE SURE	15.7% vs. 0% RR: 27.32 [1.65; 452.23] RR: 0.04 [0.002; 0.61][c] p < 0.001	Outcome category: non-serious/non-severe side effects CI_u < 0.80 Greater harm; extent: considerable
BE RADIANT	39.1% vs. 9.6% RR: 3.83 [2.47; 5.96] RR: 0.26 [0.17; 0.40][c] p < 0.001	
	Probability: proof	

a. Probability given if statistically significant differences are present.
b. Estimations of effect size are made depending on the outcome category, with different limits according to the upper limit of the confidence interval (CI_u).
c. IQWiG calculation; reversed direction of effect to enable use of limits to derive the extent of added benefit.
d. The extent of the effect in this non-serious/non-severe outcome was no more than marginal.
e. Results for this outcome are available only from the BE SURE study. Due to the high risk of bias, at most a hint can be derived for this outcome (see Section 2.2.1.1).
f. If the CI for Hedges' g is fully outside the irrelevance range [-0.2; 0.2], this is interpreted to be a relevant effect. In other cases, the presence of a relevant effect cannot be concluded.

AE: adverse event; CI: confidence interval; CI_u: upper limit of the confidence interval; DLQI: Dermatology Life Quality Index; MCS: Mental Component Summary; MD: mean difference; mNAPSI: modified Nail Psoriasis Area and Severity Index; PASI: Psoriasis Area and Severity Index; PCS: Physical Component Summary; PGA: Patient Global Assessment; ppIGA: palmoplantar IGA; PSD: Patient Symptom Diary; RR: relative risk; SAE: serious adverse event; SF-36: Short Form 36-Item Health Survey; VAS: visual analogue scale

2.2.2.2 Overall conclusion on added benefit

Table 10 summarizes the results included in the overall conclusion on the extent of added benefit.

Table 10: Favourable and unfavourable effects from the assessment of bimekizumab in comparison with adalimumab or secukinumab (research question 2: inadequate response or intolerance to prior treatment)

Favourable effects	Unfavourable effects
Non-serious/non-severe symptoms / late complications ▪ PSD scaling: proof of added benefit – extent: minor ▪ PSD redness: hint of added benefit – extent: minor	Non-serious/non-severe side effects ▪ Fungal infectious disorders: proof of greater harm – extent: considerable
PASI: Psoriasis Area and Severity Index; PSD: Patient Symptom Diary	

As described in dossier assessment A21-110, the overall analysis reveals both favourable effects in the outcome category of non-serious/non-severe symptoms / late complications and an unfavourable effect in the outcome category of non-serious/non-severe side effects.

Compared to dossier assessment A21-110, the subsequently submitted data eliminated uncertainties regarding the results of the other PSD domains. For the other PSD domains, no favourable or unfavourable effects were found. In summary, for patients with moderate to severe plaque psoriasis with inadequate response or intolerance to prior systemic therapy (research question 2), there is proof of minor added benefit of bimekizumab in comparison with the ACT.

2.3 Summary

The data subsequently submitted by the company in the commenting procedure change the conclusion on added benefit of bimekizumab drawn in dossier assessment A21-110 for research question 2: For patients with moderate to severe plaque psoriasis with inadequate response or intolerance to systemic therapy, taking into account the subsequently submitted data, results in proof of minor added benefit of bimekizumab in comparison with the ACT. In dossier assessment A21-110, there was no hint of added benefit for this research question, in part because of uncertainties regarding the selective presentation of the PSD domains.

For research question 1, there is no change in comparison with dossier assessment A21-110.

Table 11: Bimekizumab – probability and extent of added benefit

Research question	**Therapeutic indication**	**ACT[a]**	**Probability and extent of added benefit**
1	Adult patients with moderate to severe plaque psoriasis who are not candidates for conventional treatment as part of initial systemic therapy	**Adalimumab** or guselkumab or ixekizumab or **secukinumab**	Hint of minor added benefit
2	Adult patients with moderate to severe plaque psoriasis with inadequate response or intolerance to prior systemic therapy	**Adalimumab** or brodalumab or guselkumab or infliximab or ixekizumab or risankizumab or **secukinumab** or ustekinumab	Proof of minor added benefit

a. Presented is the respective ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in bold.

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

The G-BA decides on the added benefit.

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