Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Bimekizumab (plaque psoriasis)

of 3 March 2022

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the first placing on the (German) market of the active ingredient bimekizumab in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 September 2021. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 25 August 2021.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de) on 15 December 2021, thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of bimekizumab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addendum to the

benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of bimekizumab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

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

2.1.1 Approved therapeutic indication of Bimekizumab (Bimzelx) according to product information

Bimzelx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 3 March 2022):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with moderate to severe plaque psoriasis for whom conventional therapy is not an option in the context of first-time systemic therapy

- Adalimumab or guselkumab or ixekizumab or secukinumab

b) Adults with moderate to severe plaque psoriasis who have responded inadequately to, or have not tolerated systemic therapy

- Adalimumab or brodalumab or guselkumab or infliximab or ixekizumab or risankizumab or secukinumab or ustekinumab

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the Federal Joint Committee has already determined the patient-relevant benefit shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. Patient population a)

In addition to bimekizumab, the biologics adalimumab, brodalumab, guselkumab, ixekizumab, certolizumab pegol, secukinumab, tildrakizumab and risankizumab are generally approved for the treatment of adult patients with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy.

Patient population b)

For the treatment of adult patients with moderate to severe plaque psoriasis who have responded inadequately to systemic therapy, the *TNF-alpha inhibitors* adalimumab, infliximab, certolizumab pegol and etanercept, the interleukin antagonists brodalumab, guselkumab, ixekizumab, secukinumab, ustekinumab, tildrakizumab and risankizumab, the *phosphodiesterase inhibitor* apremilast and the active ingredient dimethyl fumarate are basically approved in addition to bimekizumab.

on 2. In the present therapeutic indication, no non-medicinal therapies can be considered.

on 3. In the therapeutic indication under consideration here, the following resolutions of the G-BA are available:

- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient apremilast dated 6 August 2015.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient secukinumab dated 27 November 2015.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient secukinumab dated 17 August 2017.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient ixekizumab dated 17 August 2017.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient brodalumab dated 1 March 2018.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient dimethyl fumarate dated 16 March 2018.

- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient guselkumab dated 17 May 2018.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient tildrakizumab dated 2 May 2019.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient risankizumab dated 22 November 2019.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a paragraph 7 SGB V.

According to the marketing authorisation, those patients are included in the therapeutic indication who are eligible for a systemic therapy.

The approved therapeutic indication for bimekizumab is therefore divided into two patient groups: Patient group a) includes adult patients with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy. Patient group b) includes adult patients with moderate to severe plaque psoriasis who have inadequately responded to, or have not tolerated systemic therapy.

Patient population a)

The German guideline for the treatment of plaque psoriasis[2] recommends treatment with the TNF-alpha inhibitors adalimumab or certolizumab or the interleukin inhibitors brodalumab, guselkumab, ixekizumab, risankizumab, secukinumab or tildrakizumab for patients in systemic first-line therapy for whom conventional first-line therapies (e.g. fumaric acid esters, methotrexate, ciclosporin) are not expected to be successful.

The interleukin inhibitors brodalumab, guselkumab, ixekizumab, risankizumab, secukinumab and tildrakizumab were assessed in the benefit assessment according to Section 35a SGB V in the partial therapeutic indication of systemic first-line therapy. Guselkumab, ixekizumab and secukinumab were able to show a considerable additional benefit compared to fumaric acid esters. Accordingly, the biologics mentioned are to be considered appropriate for patients who are not candidates for a conventional therapy in the context of a first-time systemic therapy. Thus, in addition to adalimumab and secukinumab, guselkumab and ixekizumab are also part of the appropriate comparator therapy.

In contrast, the interleukin antagonists brodalumab, tildrakizumab and risankizumab could not show any additional benefit compared to the active ingredients of the appropriate comparator therapy in the benefit assessment according to Section 35a of

[2] German Dermatological Society (DDG). Therapy of psoriasis vulgaris; S3 guideline; long version [online]. AWMF register number 013-001. Berlin (GER): Association of the Scientific-Medical Societies; 2021. [Accessed: 21.01.2022]. URL: https://www.awmf.org/uploads/tx_szleitlinien/013-001l_S3_Therapie-Psoriasis-vulgaris_2021-07.pdf

the German Social Code, Book V, so that they are not considered to be equally appropriate alternative treatments.

The TNF-alpha inhibitor certolizumab has had marketing authorisation for the indication plaque psoriasis since 2018. No comparative data are available for the active ingredient compared with the appropriate comparator therapy. Certolizumab is therefore not part of the appropriate comparator therapy.

Against the background of the available evidence, the biologics adalimumab, guselkumab, ixekizumab and secukinumab are therefore determined as equally appropriate comparator therapies for patients who are not candidates for a conventional therapy in the context of a first-time systemic therapy. It must be taken into account that the continuation of an inadequate therapy does not correspond to the implementation of the appropriate comparator therapy.

Patient population b)

Patient group b) includes patients who have responded inadequately to, or have not tolerated systemic therapy. This refers to both conventional active ingredients and biologics.

According to the German guideline for the treatment of plaque psoriasis[2], the biologics adalimumab, brodalumab, certolizumab, guselkumab, ixekizumab, infliximab, risankizumab, secukinumab, tildrakizumab and ustekinumab, as well as the non-biologic apremilast, are recommended for patients who have responded inadequately to, or have not tolerated systemic therapy.

The interleukin antagonists brodalumab, guselkumab, ixekizumab, risankizumab and secukinumab, which showed additional benefit in the benefit assessment according to Section 35a SGB V for the treatment of patients, who have responded inadequately to, or have not tolerated systemic therapy, are now established in healthcare. Therefore, they are part of the appropriate comparator therapy. For the interleukin antagonist tildrakizumab, no additional benefit compared to the appropriate comparator therapy could be shown in the benefit assessment according to Section 35a SGB V for patients who have responded inadequately to systemic therapy or have not tolerated it. The TNF-alpha inhibitor certolizumab has a marketing authorisation for the indication plaque psoriasis since 2018. No comparative data are available for the active ingredient compared with the appropriate comparator therapy. Certolizumab is therefore not part of the appropriate comparator therapy.

For the use of apremilast, etanercept, infliximab and ustekinumab, there is only a lower-ranking, weaker recommendation. However, patient group b) also includes patients for whom the preferred options are not (or no longer) suitable, which is why ustekinumab and infliximab are part of the appropriate comparator therapy. The available evidence shows that etanercept is less effective than the other biologics approved for this therapeutic indication. Against the background of the availability of more effective alternatives with a good body of evidence, etanercept is not considered to be an appropriate comparator therapy in the therapeutic indication under consideration. No additional benefit of the phosphodiesterase inhibitor apremilast compared to the biologics, defined as appropriate comparator therapy, could be determined in the benefit assessment according to Section 35a SGB V, as no comparator study was submitted. Apremilast is therefore not included in the appropriate comparator therapy.

Against the background of the available evidence, the biologics adalimumab, brodalumab, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab and

ustekinumab are therefore determined to be equally appropriate comparator therapies for patients who have responded inadequately to, or have not tolerated systemic therapy. It must be taken into account that the continuation of an inadequate therapy does not correspond to the implementation of the appropriate comparator therapy.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of bimekizumab is assessed as follows:

a) For adult patients with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy, there is an indication of a minor additional benefit of bimekizumab compared to the appropriate comparator therapy secukinumab or adalimumab.

b) For adult patients with moderate to severe plaque psoriasis who have responded inadequately to systemic therapy, or have not tolerated it, there is an indication of a minor additional benefit of bimekizumab compared to the appropriate comparator therapy secukinumab or adalimumab.

Justification:

The pharmaceutical company submitted the results of both BE SURE and BE RADIANT studies to prove the additional benefit of bimekizumab.

The BE SURE and BE RADIANT studies are randomised, active-controlled, double-blind studies comparing 2 different dosing intervals of bimekizumab with adalimumab (BE SURE) and secukinumab (BE RADIANT) in adults with moderate to severe plaque psoriasis. Plaque psoriasis severity was defined as body surface area [BSA] ≥ 10% and Psoriasis Area and Severity Index [PASI] ≥ 12 and Investigator's Global Assessment [IGA] ≥ 3 on a five-point scale. The presented severity definition is a sufficient representation of moderate to severe plaque psoriasis.

A total of 478 patients were enrolled in the BE SURE study and randomised in a 1:1:1 ratio to treatment with bimekizumab at 4-week intervals (Q4W) (N = 158), bimekizumab at 4-week intervals followed by 8-week intervals starting at week 16 (Q4W/Q8W) (N = 161) and adalimumab followed by bimekizumab Q4W starting at week 24 (N = 159). The study design included a screening phase (2 to 5 weeks) followed by a 24-week, active-controlled treatment phase, followed by a dose-blinded phase up to and including week 56. The dose-blinded phase (week 24 to week 56) is not relevant for the assessment due to the lack of comparison to adalimumab, and is therefore not considered further. Likewise, the bimekizumab Q4W arm is not included in the assessment due to the 4-week continuous dosage that is not compliant with the marketing authorisation.

A total of 743 patients were enrolled in the BE RADIANT study and randomised in a 1:1 ratio to a treatment with bimekizumab Q4W (N = 373) and secukinumab (N = 370). The study design includes a screening phase (2 to 5 weeks) followed by a 48-week, active-controlled, double-blinded treatment phase. After the first 16 weeks of treatment, patients in the bimekizumab Q4W arm were randomised in a 1:2 ratio to a treatment with bimekizumab at 4-week intervals (Q4W, N = 147) or 8-week intervals (Q4W/Q8W, N = 215). The present assessment is based

on the data of the active-controlled treatment phase. As in the case of the BE SURE study, the bimekizumab Q4W arm is not included in the assessment due to the dosage not being compliant with the marketing authorisation.

Both studies included patients who, in the opinion of the principal investigator, were candidates for systemic therapy and/or phototherapy and for whom therapy with the respective comparator medication (adalimumab or secukinumab) was suitable according to the local product information. The populations of both studies were therefore broader than the populations of patient groups a) and b) addressed here. The pharmaceutical company therefore submits the results of a subpopulation in each case according to the patient group breakdown of the G-BA.

The pharmaceutical company includes in the evaluation for patient group a) those patients of both BE SURE and BE RADIANT studies who had not yet received systemic psoriasis therapy at the time of enrolment in the study and who, according to the pharmaceutical company, were not candidates for a conventional therapy. The subpopulations used for patient group a) correspond to about one third of the patients originally randomised to the study arms of both studies. In total, 45 patients in the bimekizumab arm and 49 patients in the adalimumab arm met the inclusion criteria for patient group a) in the BE SURE study. In the BE RADIANT study, there were 58 patients in the bimekizumab arm and 98 patients in the secukinumab arm.

Patient group b) included those patients who were already receiving systemic psoriasis therapy at the time of enrolment in the study and had discontinued this therapy due to inadequate response and/or intolerance. The subpopulation used for patient population b) in the BE SURE study comprises 87 patients in the bimekizumab arm and 84 patients in the adalimumab arm, which corresponds to approximately half of the patients originally randomised to the study arms. In the BE RADIANT study, this was approximately 60%, with 128 patients in the bimekizumab arm and 228 patients in the secukinumab arm.

The co-primary endpoints of the BE SURE study are PASI 90 and an IGA score of 0 or 1 with a concurrent improvement of at least 2 scale points at week 16 compared to the start of the study. Patient-relevant secondary endpoints are remission (PASI 100) at week 24, endpoints on symptomatology, health-related quality of life, and side effects. The primary endpoint of the BE RADIANT study is remission (PASI 100) at week 16. Patient-relevant secondary endpoints are remission (PASI 100 at week 48), endpoints on symptomatology, health-related quality of life, and side effects.

Due to the different observation periods (48 and 24 weeks), a meta-analytical summary of the BE RADIANT and BE SURE studies is considered not appropriate.

However, both studies are used to derive the additional benefit since they provide significant data compared to a comparator of the equally appropriate comparator therapies adalimumab and secukinumab.

In a chronic disease such as plaque psoriasis, longer study durations are of particular importance due to the longer observation period since the sustainability of the effects can be better assessed.

a) Adults with moderate to severe plaque psoriasis for whom conventional therapy is not an option in the context of first-time systemic therapy

Extent and probability of the additional benefit

Mortality

No deaths occurred in the BE SURE and BE RADIANT studies until weeks 24 and 48, respectively.

Morbidity

Psoriasis Area and Severity Index (PASI)

In the German health care context, the PASI represents a standard instrument for the classification of severity by doctors and is considerably relevant for the diagnosis and monitoring of disease severity in health care. The PASI is used in conjunction with other instruments to determine the severity grade of psoriasis disease. The symptoms redness, thickening and scaling of the skin are assessed by the physician for each of the body regions head, trunk, upper limbs and lower limbs with a score between 0 (absent) and 4 (very severe). The proportion of the body surface area affected is estimated by the principal investigator as a percentage of the total body surface area. Based on the evaluation of the symptoms and the assessment of the affected body surface, an overall score is obtained. The PASI score can range from 0 (no evidence of psoriasis) to 72.

The results on the percentage of patients with an improvement in the PASI score from the start of the study to week 48 (BE RADIANT study) and to week 24 (BE SURE study) by 100% (PASI 100), 90% (PASI 90) and 75% (PASI 75), respectively, are used for the present benefit assessment.

Remission (PASI 100)

For the endpoint remission, determined by the PASI 100, both studies showed a statistically significant effect to the advantage of bimekizumab. However, this is lower in the longer BE RADIANT study than in the BE SURE study.

Response (PASI 90 and PASI 75)

For the response endpoint, determined by the PASI 90, both studies showed a statistically significant effect to the advantage of bimekizumab. However, this is less the case with the longer BE RADIANT study than in the BE SURE study.

In the percentage of patients with a 75% improvement in PASI score compared to the start of the study (PASI 75), the BE SURE study showed a statistically significant effect to the advantage of bimekizumab. However, in the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

Absence of any symptom on the scalp (scalp IGA = 0)

For the endpoint of absence of any symptom on the scalp (scalp IGA = 0), the BE SURE study showed a statistically significant difference to the advantage of bimekizumab compared to adalimumab at week 24. However, for the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

Absence of any symptom on fingernails (mNAPSI 100)

A reduction in mNAPSI of 100% (mNAPSI 100), which describes a complete reduction in nail psoriasis, is considered patient-relevant. There was a statistically significant difference to the advantage of bimekizumab for the mNAPSI 100 in patients with nail infestation at the start of the study in both studies.

Absence of any symptom on palms and soles (pp-IGA = 0)

The presence of plaque psoriasis on the palms and soles was assessed by pp-IGA. This is a standardised, global estimate and assessment of the severity of the symptoms of redness, thickening and scaling of palmar and plantar psoriasis on a numerical scale from 0 (not at all) to 4 (very severe) by the principal investigator. The assessment of the examination in the area of the palms and soles is assessed as patient-relevant, especially the absence of any symptom on the palms and soles (pp-IGA of 0). For the endpoint pp-IGA = 0, there was no statistically significant difference between the treatment arms of both studies.

Patient-reported absence of symptoms

The Patient Symptom Diary (PSD) is an electronic diary designed by pharmaceutical company themselves, which is used as a measuring instrument for recording patient-relevant psoriasis symptomatology. The diary contains 14 domains that are intended to take into account the different aspects of the disease and its impact on the patient's quality of life: These include itching, pain, scaling, redness, burning, cracking, dryness, irritation, sensitivity, lesions, thickening, fatigue, embarrassment and choice of clothing. For the BE SURE study, all 14 domains were assessed daily. In contrast, in the BE RADIANT study, only 3 of the 14 domains (itching, pain, scaling) were initially assessed every 4 weeks and then every 16 weeks and presented in the dossier.

For the assessment of the additional benefit, the individual items mentioned are included as separate endpoints.

PSD itching, PSD pain

For the endpoints of PSD itching and PSD pain, the longer BE RADIANT study at week 48 shows a statistically significant difference to the advantage of bimekizumab over secukinumab. For the BE SURE study, there is no significant difference between the treatment arms for either endpoint.

PSD scaling

For the endpoint of PSD scaling, the BE RADIANT study showed a statistically significant difference between the treatment arms at week 48 to the advantage of bimekizumab over secukinumab. For the BE SURE study, there was no statistically significant difference between the treatment arms.

PSD thickening

For the endpoint of PSD thickening, the BE SURE study showed a statistically significant difference to the advantage of bimekizumab over adalimumab. This endpoint was not assessed in the BE RADIANT study.

Other patient-reported absence of symptoms (other PSD scales)

For other endpoints of patient-reported absence of symptoms (other PSD domains), the BE SURE study showed no statistically significant difference between the treatment arms. This endpoint was not assessed in the BE RADIANT study.

Patient-reported symptomatology (Patient Global Assessment)

For the endpoint of patient-reported symptomatology (PGA), the BE SURE study showed a statistically significant difference between the treatment arms to the advantage of bimekizumab over adalimumab. However, the 95% confidence interval of the standardised mean difference (Hedges' g) is not completely outside the irrelevance range of -0.2 to 0.2. Thus, it cannot be inferred that the observed effect is relevant. For the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

Health status (EQ-5D VAS)

Health status was assessed using the visual analogue scale (VAS) of the EQ-5D questionnaire. In this questionnaire the patient assesses the current health status on a VAS from 0 mm to 100 mm. 0 mm stands for the worst health status and 100 mm for the best health status perceived. The recording of health status by means of a VAS is classified as patient-relevant.

For the endpoint of health status measured by the EQ-5D VAS, the BE SURE study showed a statistically significant difference between the treatment arms to the advantage of bimekizumab over adalimumab. For the longer BE RADIANT study, there is no statistically significant difference between the treatment arms. However, the 95% confidence interval of the standardised mean difference (SMD) (Hedges' g) is not completely outside the irrelevance range of -0.2 to 0.2. Thus, it cannot be inferred that the observed effect is relevant.

Quality of life

Dermatology Life Quality Index (DLQI)-Response

The DLQI is a validated questionnaire for the assessment of disease-specific health-related quality of life in adult patients with dermatological diseases. 10 items for 6 domains are recorded: Symptoms and well-being, daily activities, leisure time, work and school, personal relationships and treatment; the questionnaire is completed by the patient. Each item has 4 response categories ranging from 0 (not at all) to 3 (very strongly). A total score is then formed (values from 0 to 30). The lower the score, the better is the health-related quality of life. A DLQI of 0 or 1 indicates a barely or no longer impaired quality of life. The assessment of the health-related quality of life via the DLQI is classified as patient-relevant.

For the endpoint of health-related quality of life measured by the DLQI, the analysis only shows a statistically significant difference between the treatment arms to the advantage of bimekizumab compared to adalimumab in the BE SURE study. For the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

SF-36

The Health Survey Short Form 36 (SF-36) is a generic instrument for measuring health-related quality of life, consisting of 8 domains and a total of 36 questions. The physical sum scale (PCS) and the mental sum scale (MCS) of the generic quality-of-life questionnaire SF-36 were used in the assessment.

For the endpoint of health-related quality of life measured by the SF-36, there was no statistically significant difference between the treatment arms for either of the two sum

scores (PCS; MCS) in the BE SURE study. This endpoint was not assessed in the BE RADIANT study.

Side effects

Serious adverse events (SAEs)

For the endpoint of SAEs, there is a statistically significant difference to the disadvantage of bimekizumab in the BE RADIANT study at week 48. In the BE SURE study, no SAEs occurred up to and including week 24.

Discontinuation due to AEs

For the endpoint of discontinuation due to AEs, there is no statistically significant difference between the treatment arms of both studies.

Specific AE "in detail":

Infections and infestations (SOC, AE)

For the endpoint of infections and infestations (AE), there was no statistically significant difference between the treatment arms.

Fungal infections (HLGT, AE)

For the endpoint of fungal infections (AE), there is a statistically significant difference between the treatment arms of both studies to the disadvantage of bimekizumab versus adalimumab or secukinumab.

Overall assessment

For adult patients with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy, both BE SURE and BE RADIANT studies were presented. The studies compared bimekizumab with adalimumab (BE SURE) and secukinumab (BE RADIANT).

In the morbidity category, remission and response were recorded using the PASI. Both studies show statistically significant advantages of bimekizumab in the endpoint categories of remission based on the PASI 100 as well as in the improvement of the PASI score by 90%. In addition, the BE SURE study showed a statistically significant advantage of bimekizumab over adalimumab in the form of 75% improvement in the PASI score. The BE RADIANT study continued to show statistically significant advantages of bimekizumab over secukinumab in patient-reported symptomatology in the subscales of itching, pain and scaling. In the BE SURE study, a statistically significant advantage of bimekizumab over adalimumab was demonstrated in other morbidity endpoints (absence of any symptom on the scalp; absence of any symptom on fingernails; health status; PSD thickening). Overall, an advantage of bimekizumab over adalimumab as well as over secukinumab is derived in the endpoint category of morbidity.

For disease-specific health-related quality of life measured by the DLQI, the analysis only shows a statistically significant difference between the treatment arms to the advantage of bimekizumab over adalimumab in the BE SURE study. For the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

In the side effects category, the endpoint SAE shows a statistically significant difference to the disadvantage of bimekizumab in the longer BE RADIANT study. No SAEs occurred in the BE

SURE study. For the endpoint of discontinuation due to AEs, there is no statistically significant difference between the treatment arms of both studies. In detail, for the endpoint of fungal infections (AE), there was a statistically significant difference between the treatment arms of both studies to the disadvantage of bimekizumab compared to adalimumab or secukinumab.

Overall, there are advantages in morbidity in both studies, especially in remission measured by the PASI 100 and response measured by the PASI 90. In the BE RADIANT study versus secukinumab, these results are further supported by advantages in patient-reported symptomatology. In addition, an advantage in health-related quality of life measured by the DLQI is shown exclusively in comparison with adalimumab. Disadvantages are shown for bimekizumab in both studies in the category of side effects.

In the overall analysis of the advantages and disadvantages, the effects of bimekizumab are therefore assessed as moderate and anything but minor improvement of the therapy-relevant benefit according to section 2 paragraph 3 that is currently unattained, compared to the appropriate comparator therapy, and the extent of the additional benefit is classified as low.

Reliability of data (probability of additional benefit)

The cross-endpoint risk of bias is rated as low for both studies.
The assessment of additional benefit is based on two studies in which bimekizumab was compared with a comparator of the equally appropriate comparators adalimumab and secukinumab.
A meta-analytic summary was not possible due to the different study durations. In the present case, due to the wide-ranging nature of the patient population in both studies, an overall indication is derived for the reliability of data.

b) Adults with moderate to severe plaque psoriasis who have responded inadequately to, or have not tolerated systemic therapy

Extent and probability of the additional benefit

Mortality

For the endpoint of overall mortality, there is no statistically significant difference between the treatment arms of the BE RADIANT study. There were no deaths in the BE SURE study.

Morbidity

Remission (PASI 100)

For the endpoint remission, determined by the PASI 100, both studies showed a statistically significant effect to the advantage of bimekizumab. However, this is less the case with the longer BE RADIANT study than in the BE SURE study.

Response (PASI 90 and PASI 75)

For the response endpoint, determined by the PASI 90, there is a statistically significant effect to the advantage of bimekizumab.

In the percentage of patients with a 75% improvement in PASI score compared to the start of the study (PASI 75), the BE SURE study showed a statistically significant effect to the advantage of bimekizumab. In the BE RADIANT study, there was no statistically significant difference between the treatment arms.

Absence of any symptom on the scalp (scalp IGA = 0)

For the endpoint of absence of any symptom on the scalp (scalp IGA = 0), the BE SURE study showed a statistically significant difference to the advantage of bimekizumab compared to adalimumab at week 24. However, for the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

Absence of any symptom on fingernails (mNAPSI 100)

A reduction in mNAPSI of 100% (mNAPSI 100), which describes a complete reduction in nail psoriasis, is considered patient-relevant. In patients with nail infestation at the start of the study, there was no statistically significant difference in mNAPSI 100 between the treatment arms.

Absence of any symptom on palms and soles (pp-IGA = 0)

For the endpoint pp-IGA = 0, there was no statistically significant difference between the treatment arms of both studies.

Patient-reported absence of symptoms

The Patient Symptom Diary (PSD) is an electronic diary designed by pharmaceutical company themselves, which is used as a measuring instrument for recording patient-relevant psoriasis symptomatology. The diary contains 14 domains that are intended to take into account the different aspects of the disease and its impact on the patient's quality of life: These include itching, pain, scaling, redness, burning, cracking, dryness, irritation, sensitivity, lesions, thickening, fatigue, embarrassment and choice of clothing. For the BE SURE study, all 14 domains were assessed daily. In contrast, in the BE RADIANT study, only 3 of the 14 domains (itching, pain, scaling) were initially assessed every 4 weeks and then every 16 weeks and presented in the dossier.

For the assessment of the additional benefit, the individual items mentioned are included as separate endpoints.

PSD itching

For the endpoint of PSD itching, there is a statistically significant difference between the treatment arms in the BE RADIANT study. In the BE SURE study, there was no statistically significant difference between the treatment arms.

PSD pain

For the endpoint of PSD pain, there was no statistically significant difference between the treatment arms of the BE RADIANT study. In the BE SURE study, there is a statistically significant difference between the treatment arms.

PSD scaling

For the endpoint of PSD scaling, there is a statistically significant difference between the treatment arms of both studies to the advantage of bimekizumab versus adalimumab or secukinumab.

PSD redness, PSD lesions, PSD thickening, PSD embarrassment

For the endpoints of PSD redness, PSD lesions, PSD thickening and PSD embarrassment, there is a statistically significant difference between the treatment arms of the BE SURE study to the

advantage of bimekizumab over adalimumab. This endpoint was not assessed in the BE RADIANT study.

Other patient-reported absence of symptoms (other PSD scales)

For other endpoints of patient-reported absence of symptoms (other PSD domains), the BE SURE study showed no statistically significant difference between the treatment arms. This endpoint was not assessed in the BE RADIANT study.

Patient-reported symptomatology (Patient Global Assessment)

For the endpoint of patient-reported symptomatology (PGA), both BE SURE and BE RADIANT studies showed a statistically significant difference between the treatment arms to the advantage of bimekizumab over adalimumab or secukinumab. For the BE SURE study, the 95% confidence interval of the SMD (Hedges' g) is completely outside the irrelevance range of -0.2 to 0.2. The observed effect is therefore classified as relevant.

However, for the BE RADIANT study, the 95% confidence interval of the SMD (Hedges' g) is not completely outside the irrelevance range of -0.2 to 0.2. Thus, it cannot be deduced that the observed effect is relevant for the PGA endpoint in the BE RADIANT study.

Health status (EQ-5D VAS)

The health status was assessed using the VAS of the EQ-5D. In this questionnaire the patient assesses the current health status on a VAS from 0 mm to 100 mm. 0 mm stands for the worst health status and 100 mm for the best health status perceived. The recording of health status by means of a VAS is classified as patient-relevant.

For the endpoint of health status (EQ-5D VAS), there is no statistically significant difference between the treatment arms of both studies.

Quality of life

Dermatology Life Quality Index (DLQI)-Response

The DLQI is a validated questionnaire for the assessment of disease-specific health-related quality of life in adult patients with dermatological diseases. 10 items for 6 domains are recorded: Symptoms and well-being, daily activities, leisure time, work and school, personal relationships and treatment; the questionnaire is completed by the patient. Each item has 4 response categories ranging from 0 (not at all) to 3 (very strongly). A total score is then formed (values from 0 to 30). The lower the score, the better is the health-related quality of life. A DLQI of 0 or 1 indicates a barely or no longer impaired quality of life. The assessment of the health-related quality of life via the DLQI is classified as patient-relevant.

For the endpoint of health-related quality of life measured by the DLQI, the analysis only shows a statistically significant difference between the treatment arms to the advantage of bimekizumab compared to adalimumab in the BE SURE study. For the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

SF-36

The Health Survey Short Form 36 (SF-36) is a generic instrument for measuring health-related quality of life, consisting of 8 domains and a total of 36 questions. The physical sum scale (PCS) and the mental sum scale (MCS) of the generic quality-of-life questionnaire SF-36 were used in the assessment.

SF-36 PCS

For the endpoint of health-related quality of life measured by the SF-36, the PCS for the BE SURE study shows no statistically significant difference between the treatment arms. This endpoint was not assessed in the BE RADIANT study.

SF-36 MCS

For the endpoint of health-related quality of life measured by the SF-36, the MCS for the BE SURE study shows no statistically significant difference between the treatment arms. However, the confidence interval for the Hedges' g is not completely outside the irrelevance range [-0.2; 0.2]. Thus, it cannot be inferred that the effect is relevant. This endpoint was not assessed in the BE RADIANT study.

Side effects

Serious adverse events (SAEs), discontinuation due to SAEs and infections and infestations (UE)

For the endpoints SAEs, discontinuation due to AEs and infections and infestations (AE), there was no statistically significant difference between the treatment arms of both studies.

Fungal infections (AE)

For the endpoint of fungal infections (AE), there is a statistically significant difference between the treatment arms of both studies to the disadvantage of bimekizumab versus adalimumab or secukinumab.

Overall assessment / conclusion

For adult patients with moderate to severe plaque psoriasis who inadequately responded to, or have not tolerated systemic therapy, both BE SURE and BE RADIANT studies were presented. The studies compared bimekizumab with adalimumab (BE SURE) and secukinumab (BE RADIANT).

In the morbidity category, remission and response were recorded using the PASI. Both studies show statistically significant advantages of bimekizumab in the endpoint categories of remission based on the PASI 100 as well as in the improvement of the PASI score by 90%. In the BE SURE study, there is also a statistically significant advantage of bimekizumab over adalimumab in the form of 75% improvement in PASI score and in patient-reported symptomatology as measured by PGA. In the BE RADIANT study, there are still statistically significant advantages of bimekizumab over secukinumab in patient-reported absence of symptoms in the itching and scaling subscales. In the BE SURE study, a statistically significant advantage of bimekizumab over adalimumab was demonstrated in other morbidity endpoints (absence of any symptom on the scalp; PSD pain; PSD scaling; PSD redness, PSD lesions, PSD thickening and PSD embarrassment). Overall, in the endpoint category of morbidity, an advantage of bimekizumab over the appropriate comparator therapies adalimumab or secukinumab is derived.

For disease-specific health-related quality of life measured by the DLQI, the analysis shows a statistically significant difference between the treatment arms to the advantage of bimekizumab over adalimumab in the BE SURE study. For the longer BE RADIANT study, there is no statistically significant difference between the treatment arms.

In the category of side effects, there was no statistically significant difference between the treatment arms of both studies for the endpoints SAEs, discontinuation due to AEs and, in detail, infections and infestations (AE). In detail, for the endpoint of fungal infections (AE),

there was a statistically significant difference between the treatment arms of both studies to the disadvantage of bimekizumab compared to adalimumab or secukinumab.

Overall, there are advantages in morbidity in both studies, especially in remission measured by the PASI 100 and response measured by the PASI 90. These results are partially supported by advantages in patient-reported symptomatology or absence of symptoms. In addition, an advantage in health-related quality of life measured by the DLQI is shown exclusively in comparison with adalimumab. Disadvantages are shown for bimekizumab in both studies in the category of side effects.

In the overall analysis of the advantages and disadvantages, the effects of bimekizumab are therefore assessed as moderate and anything but minor improvement of the therapy-relevant benefit according to section 2 paragraph 3 that is currently unattained, compared to the appropriate comparator therapy, and the extent of the additional benefit is classified as low.

Reliability of data (probability of additional benefit)

The cross-endpoint risk of bias is rated as low for both studies.
The assessment of additional benefit is based on two studies in which bimekizumab was compared with a comparator of the equally appropriate comparators adalimumab and secukinumab.
A meta-analytic summary was not possible due to the different study durations. In the present case, due to the wide-ranging nature of the patient population in both studies, an overall indication is derived for the reliability of data.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Bimzelx with the active ingredient bimekizumab.

Bimekizumab is approved for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy.

In the therapeutic indication to be considered, two patient groups were distinguished:

a) Adults with moderate to severe plaque psoriasis for whom conventional therapy is not an option in the context of first-time systemic therapy

b) Adults with moderate to severe plaque psoriasis who have responded inadequately to, or have not tolerated systemic therapy

About patient group a)

The G-BA determined the biologics adalimumab, guselkumab, ixekizumab and secukinumab as appropriate comparator therapies.

For this patient group, both BE SURE and BE RADIANT studies were presented. The studies compared bimekizumab with adalimumab (BE SURE) and secukinumab (BE RADIANT).

Both studies show statistically significant advantages of bimekizumab in the endpoint categories of remission based on the PASI 100 as well as in the improvement of the PASI score by 90%. In addition, the BE RADIANT study showed statistically significant advantages of bimekizumab over secukinumab in patient-reported symptomatology in the subscales of itching, pain and scaling. Compared to adalimumab, there are still advantages in health-related quality of life, measured by the DLQI. Disadvantages are shown for bimekizumab in both studies in the category of side effects.

In the weighing of the advantages and disadvantages, the effects of bimekizumab are therefore assessed as moderate and anything but minor improvement of the therapy-relevant benefit that is currently unattained, compared to the appropriate comparator therapy, and the extent of the additional benefit is classified as low.

Uncertainties remain due to the wide-ranging nature of the patient population in both studies.

In the overall assessment, an indication of a minor additional benefit of bimekizumab compared to the appropriate comparator therapy is determined.

About patient group b)

The G-BA determined the biologics adalimumab, brodalumab, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab and ustekinumab as appropriate comparator therapies.

For this patient group, both BE SURE and BE RADIANT studies were presented. The studies compared bimekizumab with adalimumab (BE SURE) and secukinumab (BE RADIANT).

Both studies show statistically significant advantages of bimekizumab in the endpoint categories of remission based on the PASI 100 as well as in the improvement of the PASI score by 90%. In addition, the BE RADIANT study showed statistically significant advantages of bimekizumab over secukinumab in patient-reported symptomatology in the subscales of itching and scaling. Compared to adalimumab, there are still advantages in health-related quality of life, measured by the DLQI. Disadvantages are shown for bimekizumab in both studies in the category of side effects.

In the weighing of the advantages and disadvantages, the effects of bimekizumab are therefore assessed as moderate and anything but minor improvement of the therapy-relevant benefit that is currently unattained, compared to the appropriate comparator therapy, and the extent of the additional benefit is classified as low.

Uncertainties remain due to the wide-ranging nature of the patient population in both studies.

In the overall assessment, an indication of a minor additional benefit of bimekizumab compared to the appropriate comparator therapy is determined.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The number of patients is based on the target population in statutory health insurance (SHI).

The number of patients stated by the pharmaceutical company for patient group a) are subject to uncertainties. For patient group b), the stated number of patients is rather a lower limit due to the methodological imponderables and in view of the fact that the entirety of patients with psoriatic arthritis were excluded from the routine data analyses. The information provided by the pharmaceutical company in IQWiG's dossier assessment (mandate A21-110) is therefore not used.

In contrast, the information in the resolution on bimekizumab is based on the data from the resolution of the G-BA on risankizumab[3] in the therapeutic indication of moderate to severe plaque psoriasis with an indication for a systemic therapy.

[3] Resolution of the G-BA on the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a SGB V of 22 November 2019

2.3 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 Bimzelx (active ingredient: bimekizumab) at the following publicly accessible link (last access: 21 January 2022):

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

Consider discontinuing treatment in patients who do not show a response after 16 weeks of treatment.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 February 2022).

For the presentation of the costs, one year is assumed for all medicinal products. This does not take into account the fact that treatment may be discontinued prematurely due to non-response or intolerance. The discontinuation criteria according to the product information of the individual active ingredients must be taken into account when using the medicinal products.

Treatment period:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

Designation of the therapy	Treatment mode	Number of treatments/ patient /year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Bimekizumab	Continuously, every 56 days	6.5	1	6.5
Appropriate comparator therapy				
Patient population a)				
Adalimumab	Continuously, every 14 days	26.1	1	26.1
Guselkumab	Continuously, every 56 days	6.5	1	6.5

Designation of the therapy	Treatment mode	Number of treatments/ patient /year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Ixekizumab	Continuously, every 28 days	13.0	1	13.0
Secukinumab	Continuously, 1 x monthly	12.0	1	12.0
Patient population b)				
Adalimumab	Continuously, every 14 days	26.1	1	26.1
Brodalumab	Continuously, every 14 days	26.1	1	26.1
Guselkumab	Continuously, every 56 days	6.5	1	6.5
Infliximab	Continuously, every 56 days	6.5	1	6.5
Ixekizumab	Continuously, every 28 days	13.0	1	13.0
Risankizumab	Continuously, every 84 days	4.3	1	4.3
Secukinumab	Continuously, 1 x monthly	12.0	1	12.0
Ustekinumab	Continuously, every 84 days	4.3	1	4.3

Consumption:

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

For the calculation of the consumption of medicinal products to be dosed according to weight, the G-BA generally uses non-indication-specific average weights as a basis. Therefore, an average body weight of 77 kg is assumed for the German population aged 18 years and older, according to the official representative statistics "Microcensus 2017"[4]. Consequently, patient-individual weight differences between women and men, which may be above or below the average value of 77 kg, are not taken into account for the cost calculation.

[4] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Bimekizumab	320 mg	320 mg	2 x 160 mg	6.5	13.0 x 160 mg
Appropriate comparator therapy					
Patient population a)					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Guselkumab	100 mg	100 mg	1 x 100 mg	6.5	6.5 x 100 mg
Ixekizumab	80 mg	80 mg	1 x 80 mg	13.0	13.0 x 80 mg
Secukinumab	300 mg	300 mg	1 x 300 mg	12.0	12.0 x 300 mg
Patient population b)					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Brodalumab	210 mg	210 mg	1 x 210 mg	26.1	26.1 x 210 mg
Guselkumab	100 mg	100 mg	1 x 100 mg	6.5	6.5 x 100 mg
Infliximab	5 mg / kg BW	385 mg	4 x 100 mg	6.5	26 x 100 mg
Ixekizumab	80 mg	80 mg	1 x 80 mg	13.0	13.0 x 80 mg
Risankizumab	150 mg	150 mg	1 x 150 mg	4.3	4.3 x 150 mg
Secukinumab	300 mg	300 mg	1 x 300 mg	12.0	12.0 x 300 mg
Ustekinumab	45 mg	45 mg	1 x 45 mg	4.3	4.3 x 45 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. If a fixed reimbursement rate is available, this will be used as the basis for calculating the costs.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Bimekizumab 160 mg	4 SFI	€ 6,826.13	€ 1.77	€ 386.55	€ 6,437.81
Appropriate comparator therapy					
Patient population a)					
Adalimumab 40 mg	6 SFI	€ 2,859.17	€ 1.77	€ 228.57	€ 2,628.83
Guselkumab 100 mg	2 SFI	€ 5,563.83	€ 1.77	€ 0.00	€ 5,562.06
Ixekizumab 80 mg	3 IFE	€ 3,989.28	€ 1.77	€ 0.00	€ 3,987.51
Secukinumab 300 mg	3 SFI	€ 4,653.99	€ 1.77	€ 0.00	€ 4,652.22
Patient population b)					
Adalimumab 40 mg	6 SFI	€ 2,859.17	€ 1.77	€ 228.57	€ 2,628.83
Brodalumab 210 mg	6 SFI	€ 4,153.91	€ 1.77	€ 0.00	€ 4,152.14
Guselkumab 100 mg	2 SFI	€ 5,563.83	€ 1.77	€ 0.00	€ 5,562.06
Infliximab 100 mg	5 PIC	€ 3,490.53	€ 1.77	€ 280.08	€ 3,208.68
Ixekizumab 80 mg	3 IFE	€ 3,989.28	€ 1.77	€ 0.00	€ 3,987.51
Risankizumab 150 mg	1 SFI	€ 4,956.49	€ 1.77	€ 0.00	€ 4,954.72
Secukinumab 300 mg	3 SFI	€ 4,653.99	€ 1.77	€ 0.00	€ 4,652.22
Ustekinumab 45 mg	1 IFE	€ 5,284.67	€ 1.77	€ 298.52	€ 4,984.38
Abbreviations: SFI = solution for injection; IFE = solution for injection in a pre-filled syringe; PIC = powder for the preparation of an infusion solution concentrate					

LAUER-TAXE® last revised: 15.02.2022

<u>Costs for additionally required SHI services:</u>

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Diagnosis of tuberculosis

For the active ingredients bimekizumab, adalimumab, infliximab, risankizumab and ustekinumab, costs are regularly incurred for testing for both active and inactive ("latent") tuberculosis infections. The costs presented are a blood test (quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens specific for Mycobacterium tuberculosis-complex (except BCG)). In addition, a chest radiograph is usually required to detect pulmonary tuberculosis. The tuberculin skin test is not presented due to lack of sensitivity and specificity as well as the possibility of "sensitisation".

Diagnosis of chronic hepatitis B

In addition, patients receiving therapy with adalimumab and infliximab should be tested for the presence of HBV infection before initiating the respective treatment.
For the diagnosis of suspected chronic hepatitis B, sensibly coordinated steps are required[5]. A step-by-step serological diagnosis initially consists of the examination of HBs antigen and anti-HBc antibodies. If both are negative, a past HBV infection can be excluded. If HBs antigen is positive, an active HBV infection is detected.

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Medicinal product to be assessed				
Bimekizumab	Quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens (at least ESAT-6 and CFP-10) specific for Mycobacterium tuberculosis-complex (except BCG) (GOP 32670)	1	€ 58.00	€ 58.00
Bimekizumab	Chest radiograph (GOP 34241)	1	€ 16.45	€ 16.45
Appropriate comparator therapy				
Adalimumab Infliximab Risankizumab Ustekinumab	Quantitative determination of an in vitro interferon-gamma release after ex vivo stimulation with antigens (at least ESAT-6 and CFP-10) specific for Mycobacterium tuberculosis-complex (except BCG) (GOP 32670)	1	€ 58.00	€ 58.00

[5] "Update of the S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011" http://www.dgvs.de/fileadmin/user_upload/Leitlinien/Hepatitis_B/Leitlinie_Hepatitis_B.pdf

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Adalimumab infliximab risankizumab ustekinumab	Chest radiograph (GOP 34241)	1	€ 16.45	€ 16.45
Adalimumab infliximab	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50
	Anti-HBs antibody (GOP 32617)[6]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV-DNA (GOP 32823)[7]	1	€ 89.50	€ 89.50

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic drugs a maximum amount of € 81 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 71 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

[6] Only if HBs antigen negative and anti-HBc antibody positive.
[7] Invoicing for GOP 32823 possible before or during antiviral therapy with interferon and/or nucleic acid analogues.

4. Process sequence

At its session on 22 September 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 25 August 2021, the pharmaceutical company submitted a dossier for the benefit assessment of bimekizumab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 6 September 2021 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient bimekizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 December 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 15 December 2021. The deadline for submitting written statements was 5 January 2022.

The oral hearing was held on 24 January 2022.

By letter dated 25 January 2022, the IQWiG was commissioned with a supplementary assessment. The addendum prepared by IQWiG was submitted to the G-BA on 11 February 2022.

On 11 February 2022, the IQWiG submitted a new version of IQWiG's dossier assessment to the G-BA. This version 1.1 dated 11 February 2022 replaces version 1.0 of the dossier assessment dated 13 December 2021. The assessment result was not affected by the changes in version 1.1 compared to version 1.0.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 22 February 2022, and the proposed resolution was approved.

At its session on 3 March 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	22 September 2020	Determination of the appropriate comparator therapy
Working group Section 35a	18 January 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	24 January 2022	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents

Working group Section 35a	1 February 2022 15 February 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	22 February 2022	Concluding discussion of the draft resolution
Plenum	3 March 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 3 March 2022

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

Prof. Hecken