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 Risankizumab (new therapeutic indication: psoriatic arthritis, monotherapy or in combination with methotrexate)

of 19 May 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 active ingredient risankizumab (Skyrizi) was listed for the first time on 1 June 2019 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 15 November 2021, Skyrizi received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2 number 2 letter a to Regulation (EC) No. 1234/2008 of the European Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7).

On 30 November 2021, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-

BA on the active ingredient Chapter 8 (1) number 2 of the G-BA's Rules of Procedure (VerfO) on the active ingredient risankizumab with the new therapeutic indication (Skyrizi, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 March 2022 on the G-BA website (www.g-ba.de), therefore 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 risankizumab compared to the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG and the statements submitted in the written statement and oral hearing procedure. 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 risankizumab.

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 Risankizumab (Skyrizi) in accordance with the product information

Skyrizi, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).

Therapeutic indication of the resolution (resolution of 19 May 2022):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.

Appropriate comparator therapy for risankizumab:

- a TNF-alpha antagonist (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or an interleukin inhibitor (ixekizumab or secukinumab or ustekinumab), if necessary, in combination with methotrexate

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

b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy.

Appropriate comparator therapy for risankizumab:

- switching to another biological disease-modifying antirheumatic drug (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab or ixekizumab or secukinumab or ustekinumab), if necessary, in combination with methotrexate

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. 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 patient-relevant benefit has already been determined by the G-BA 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. In the therapeutic indication for psoriatic arthritis, the following active ingredients of different product classes are approved:

- steroidal antirheumatic drugs: prednisolone, prednisone, triamcinolone
- non-steroidal anti-inflammatory drugs (NSAIDs): e.g. acemetacin
- conventional synthetic disease-modifying antirheumatic drugs (csDMARDs): methotrexate, leflunomide
- biological disease-modifying antirheumatic drugs (bDMARDs):
  - TNF-alpha inhibitors: adalimumab, certolizumab pegol, etanercept, golimumab, infliximab
  - Interleukin inhibitors: guselkumab, ixekizumab, secukinumab, ustekinumab
  - Inhibitor of T-cell activation: abatacept
- targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs):
  - JAK inhibitors: tofacitinib, upadacitinib
  - phosphodiesterase-4 inhibitor: apremilast

on 2. Non-medical measures as sole appropriate comparator therapy are not considered in the present therapeutic indication.

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 ixekizumab dated 16 August 2018.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient tofacitinib from the 21 February 2019.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient secukinumab dated 18 February 2021.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient guselkumab dated 20 May 2021.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient upadacitinib dated 15 July 2021.

on 4. The general state of medical knowledge, on which the decision of the G-BA is based, was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present therapeutic indication.

Risankizumab is approved for patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug. Mere treatment of these patients with non-steroidal anti-inflammatory drugs or glucocorticoids is no longer adequate. Even if the local injection of glucocorticoids in particular may be used as add-on therapy in some patients, non-steroidal anti-inflammatory drugs and glucocorticoids do not represent an appropriate treatment option in the present therapeutic indication, which is why both product classes are not considered further in the determination of the appropriate comparator therapy.

The inhibitor of T-cell activation abatacept and the phosphodiesterase-4 inhibitor apremilast are not relevant in the treatment of active psoriatic arthritis and are only considered as a secondary treatment option in the current therapy recommendations of the European League Against Rheumatism (EULAR 2020)[2]. Against the background of the diverse treatment options, both active ingredients are therefore not seen as part of the appropriate comparator therapy.

In addition, it is pointed out that the benefit-risk profile of the JAK inhibitors tofacitinib and upadacitinib is currently being reviewed by the EMA within the framework of a PRAC procedure. The significance of the selective IL-23 inhibitor guselkumab cannot be conclusively assessed against the background of the unproven additional benefit and the lack of guideline recommendations. For this reason, tofacitinib, upadacitinib and guselkumab are not considered at this time for determining the appropriate comparator therapy.

[2] Gossec L, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 2020;79:700-712.

On a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

For patients who have had an inadequate response or intolerance to previous conventional disease-modifying antirheumatic (csDMARD) therapy, initial treatment with a bDMARD is indicated. For these patients, therapy with a TNF-alpha inhibitor (adalimumab, certolizumab pegol, etanercept, golimumab and infliximab), an interleukin-17 inhibitor (ixekizumab and secukinumab) or an interleukin-12/23 inhibitor (ustekinumab) is recommended according to the current therapy recommendations of the European League Against Rheumatism (EULAR 2020)[2].

For adults who have had an inadequate response or have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy, the TNF-alpha inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab and infliximab), the interleukin-17 inhibitors ixekizumab and secukinumab and the interleukin-12/23 inhibitor ustekinumab, if necessary, in combination with methotrexate, are therefore determined to be equally appropriate therapeutic options.

On b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy.

For adults who have responded inadequately to, or who are intolerant to a biologic disease-modifying antirheumatic drug treatment (bDMARDs), switching to another bDMARD (TNF-alpha inhibitor, interleukin inhibitor) is recommended.

For adults who have responded inadequately to, or who are intolerant to a biologic disease-modifying antirheumatic drug treatment (bDMARDs), TNF-alpha inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab and infliximab), the interleukin-17 inhibitors ixekizumab and secukinumab and the interleukin-12/23 inhibitor ustekinumab, if necessary, in combination with methotrexate, were determined to be equally appropriate treatment options in case of change of therapy. 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 risankizumab is assessed as follows:

a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.

For adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy, an additional benefit of risankizumab compared with the appropriate comparator therapy has not been proven.

b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy.

For adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD)

therapy, an additional benefit of risankizumab compared with the appropriate comparator therapy has not been proven.

Justification for patient populations a) and b):

The pharmaceutical company submits the UltIMMa-1 and UltIMMa-2 studies for the benefit assessment. Both studies were already subject of the initial assessment of the active ingredient risankizumab in the indication for plaque psoriasis.

The UltIMMa-1 and UltIMMa-2 studies are randomised, double-blind twin studies with an identical study protocol. In both studies, risankizumab was compared to placebo and ustekinumab in adults with plaque psoriasis. Patients with moderate to severe plaque psoriasis (affected body surface area [BSA] ≥ 10%, psoriasis area and severity index [PASI] ≥ 12, and static physician's global assessment [sPGA] ≥ 3) who were eligible for systemic therapy or phototherapy and who were suitable for a therapy with ustekinumab according to local product information were enrolled in the study. The presence of psoriatic arthritis was not a prerequisite for enrolment in the studies. Nevertheless, patients who also had psoriatic arthritis in addition to plaque psoriasis could also be enrolled in the studies. Patients with a positive history of psoriatic arthritis or suspected psoriatic arthritis were evaluated according to CASPAR (*Classification Criteria for the Diagnosis of Psoriatic Arthritis*) in select study sites and further surveys were conducted if psoriatic arthritis was confirmed.

The design of the two studies included a screening phase (1 to 6 weeks) followed by a 52-week blinded treatment phase (last dose of study medication at week 40). The patients could then either discontinue from the study or take part in an open-label extension study (M15-997 study). This benefit assessment is based on data at the end of treatment after 52 weeks.

The primary endpoints of both studies were PASI 90 and an sPGA score of 0 or 1 at week 16. Patient-relevant secondary endpoints were overall mortality, endpoints on symptomatology, health-related quality of life, and side effects.

<u>Sub-population relevant for the benefit assessment</u>

For the present benefit assessment, only those patients are relevant who, in addition to plaque psoriasis, also had psoriatic arthritis. Accordingly, the pharmaceutical company presents evaluations from both studies on the sub-population of patients who had active psoriatic arthritis according to CASPAR. It cannot be ruled out that the sub-population of the pharmaceutical company also includes patients without prior DMARD therapy. This sub-population was not further restricted to patients who had previously received treatment with at least one DMARD. Furthermore, no separate analyses were presented for patient populations a) and b). An adequate operationalisation of both patient populations is not possible due to lack of information on the patients' previous therapy.

<u>Overall assessment of patient population a)</u>

Due to the lack of information on the pretreatment of patients, no conclusions on the additional benefit of risankizumab compared to ustekinumab in adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy can be derived on the basis of the data presented. An additional benefit is not proven.

<u>Overall assessment of patient population b)</u>

Due to the lack of information on the pretreatment of patients, no conclusions on the additional benefit of risankizumab compared to ustekinumab in adults with active psoriatic

arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy can be derived on the basis of the data presented. An additional benefit is not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient risankizumab.

The therapeutic indication assessed here is as follows: Skyrizi, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).

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

a) Adults with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.

b) Adults with active psoriatic arthritis who have had an inadequate response or have been intolerant to a prior biological disease-modifying antirheumatic drug (bDMARD) therapy.

On patient population a)

The G-BA determined a TNF-alpha antagonist (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or an interleukin inhibitor (ixekizumab or secukinumab or ustekinumab), if necessary, in combination with MTX, as an appropriate comparator therapy.

For this patient group, the pharmaceutical company presents the RCTs UltIMMa-1 and UltIMMa-2, which studied risankizumab in comparison to ustekinumab in adults with plaque psoriasis. Patients who also had psoriatic arthritis were analysed. However, it is unclear whether they received a prior DMARD therapy. Furthermore, no subdivision was made according to previous therapy with a bDMARD, so that it is not possible to assign the patients to the patient populations defined by the G-BA.

Due to the lack of information on pretreatment, no statements on the additional benefit of risankizumab can be derived. An additional benefit is not proven.

On patient population b)

The G-BA determined the change to another bDMARD (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab or ixekizumab or secukinumab or ustekinumab), possibly in combination with MTX, as an appropriate comparator therapy.

For this patient group, the pharmaceutical company presents the RCTs UltIMMa-1 and UltIMMa-2, which studied risankizumab in comparison to ustekinumab in adults with plaque psoriasis. Patients who also had psoriatic arthritis were analysed. However, it is unclear whether they received a prior DMARD therapy. Furthermore, no subdivision was made according to previous therapy with a bDMARD, so that it is not possible to assign the patients to the patient populations defined by the G-BA.

Due to the lack of information on pretreatment, no statements on the additional benefit of risankizumab can be derived. An additional benefit is not proven.

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 data from the G-BA resolution on ixekizumab of 2018[3] and the resolutions on secukinumab, guselkumab and upadacitinib of 2021[4,5,6] are used as a basis.

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 Skyrizi (active ingredient: risankizumab) at the following publicly accessible link (last access: 4 March 2022):

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

Treatment with risankizumab should only be initiated and monitored by doctors experienced in treating adults with psoriatic arthritis.

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: 1 May 2022).

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.

For the cost representation only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

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.

Risankizumab is approved alone or in combination with methotrexate for the treatment of adult patients with active psoriatic arthritis. The active ingredients of the appropriate comparator therapy for both patient groups can also be used both as part of monotherapy and in combination with methotrexate. Thus, if applicable, the corresponding costs for methotrexate are incurred both for the medicinal product under assessment and for the appropriate comparator therapy and are therefore not listed separately.

[3] Benefit assessment resolution of the G-BA on ixekizumab dated 16 August 2018.

[4] Benefit assessment resolution of the G-BA on secukinumab dated 18 February 2021.

[5] Benefit assessment resolution of the G-BA on guselkumab dated 20 May 2021.

[6] Benefit assessment resolution of the G-BA on upadacitinib dated 15 July 2021.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Risankizumab	Continuously, 1 x every 84 days	4.3	1	4.3
Appropriate comparator therapy				
Patient populations a) and b)				
Adalimumab	Continuously, 1 x every 14 days	26.1	1	26.1
Certolizumab pegol	Continuously, 1 x every 14 days	26.1	1	26.1
Etanercept	Continuously, 1 x every 7 days	52.1	1	52.1
Golimumab	Continuously, 1 x monthly (always on the same day)	12	1	12
Infliximab	Continuously, 1 x every 56 days	6.5	1	6.5
Ixekizumab	Continuously, 1 x every 28 days	13	1	13
Secukinumab	Continuously, 1 x monthly	12	1	12
Ustekinumab	Continuously, 1 x every 84 days	4.3	1	4.3

Consumption:

For dosages depending on body weight, the average body measurements from the official representative statistics “Microcensus 2017 – body measurements of the population” were applied (average body weight: 77.0 kg)[7].

[7] 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					
Risankizumab	150 mg	150 mg	1 x 150 mg	4.3	4.3 x 150 mg
Appropriate comparator therapy					
Patient populations a) and b)					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Certolizumab pegol	200 mg	200 mg	1 x 200 mg	26.1	26.1 x 200 mg
Etanercept	50 mg	50 mg	1 x 50 mg	52.1	52.1 x 50 mg
Golimumab	50 mg	50 mg	1 x 50 mg	12	12 x 50 mg
Infliximab	5 mg/kg = 385 mg	385 mg	4 x 100 mg	6.5	26 x 100 mg
Ixekizumab	80 mg	80 mg	1 x 80 mg	13	13 x 80 mg
Secukinumab	150 mg - 300 mg	150 mg - 300 mg	1 x 150 mg – 1 x 300 mg	12	12 x 150 mg - 12 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.

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					
Risankizumab 150 mg	1 SFI	€ 4,956.49	€ 1.77	€ 0.00	€ 4,954.72
Appropriate comparator therapy					
Adalimumab 40 mg[8]	6 SFI	€ 2,859.17	€ 1.77	€ 228.57	€ 2,628.83
Certolizumab pegol 200 mg[8]	6 SFI	€ 2,859.17	€ 1.77	€ 228.57	€ 2,628.83
Etanercept 50 mg[8]	12 SFI	€ 2,859.17	€ 1.77	€ 228.57	€ 2,628.83
Golimumab 50 mg[8]	3 IFE	€ 2,605.92	€ 1.77	€ 0.00	€ 2,604.15
Infliximab 100 mg[8]	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
Secukinumab 150 mg	6 SFI	€ 4,653.99	€ 1.77	€ 0.00	€ 4,652.22
Secukinumab 300 mg	3 SFI	€ 4,653.99	€ 1.77	€ 0.00	€ 4,652.22
Ustekinumab 45 mg	1 SFI	€ 5,284.67	€ 1.77	€ 298.52	€ 4,984.38
Abbreviations: IFE = solution for injection in a pre-filled syringe; SFI = solution for injection; PIC = powder for the preparation of an infusion solution concentrate					

LAUER-TAXE® last revised: 1 May 2022

Costs for additionally required SHI services:

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 some active ingredients of the appropriate comparator therapy (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, 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-

[8] Fixed reimbursement rate

complex (except BCG)) and a chest radiograph. The tuberculin skin test is not presented due to lack of sensitivity and specificity as well as the possibility of "sensitisation". These examinations are also required for the use of risankizumab as the medicinal product to be assessed, but not for the use of ixekizumab and secukinumab as the appropriate comparator therapy.

Diagnosis of chronic hepatitis B

Patients must be tested for the presence of HBV infection before initiating treatment with adalimumab, certolizumab pegol, etanercept, golimumab and infliximab. However, these examinations are not required for the use of ixekizumab, secukinumab and ustekinumab as the appropriate comparator therapy and for the medicinal product to be assessed, risankizumab.

For the diagnosis of suspected chronic hepatitis B, sensibly coordinated steps are required[9]. 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.

In deviation from this, additional necessary SHI services are required for the examination of suspected chronic hepatitis B, which usually differ between the drug to be evaluated and the appropriate comparator therapy and are consequently considered as additionally required SHI services in the resolution.

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Medicinal product to be assessed				
Risankizumab	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
	Chest radiograph (GOP 34241)	1	€ 16.45	€ 16.45
Appropriate comparator therapy				
Adalimumab Certolizumab pegol	Quantitative determination of an in vitro interferon-	1	€ 58.00	€ 58.00

[9] "Update of the S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/11" https://www.awmf.org/uploads/tx_szleitlinien/021-011l_S3_Prophylaxe-Diagnostik-Therapie-der-Hepatitis-B-Virusinfektion_2021-07.pdf

Designation of the therapy	Designation of the service	Number	Unit cost	Costs per patient per year
Etanercept Golimumab Infliximab Ustekinumab	gamma release after ex vivo stimulation with antigens (at least ESAT-6 and CFP-10) specific for Mycobacterium tuberculosis-complex (except BCG) (GOP 32670)			
	Chest radiograph (GOP 34241)	1	€ 16.45	€ 16.45
Adalimumab Certolizumab pegol Etanercept Golimumab Infliximab	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50
	Anti-HBs antibody (GOP 32617)[10]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV DNA (GOP 32823)[11]	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.

[10] Only if HBs antigen negative and anti-HBc antibody positive.

[11] Invoicing for GOP 32823 possible before or during antiviral therapy with interferon and/or nucleic acid analogues.

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.

4. Process sequence

At its session on 7 December 2021, the Subcommittee on Medicinal Products recently confirmed the appropriate comparator therapy.

On 30 November 2021, the pharmaceutical company submitted a dossier for the benefit assessment of risankizumab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

By letter dated 30 November 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 risankizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 21 February 2022, and the written statement procedure was initiated with publication on the website of the G-BA on 1 March 2022. The deadline for submitting written statements was 22 March 2022.

The oral hearing was held on 11 April 2022.

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 10 May 2022, and the proposed resolution was approved.

At its session on 19 May 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	7 December 2021	Confirmation of the appropriate comparator therapy
Working group Section 35a	5 April 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	11 April 2022	Conduct of the oral hearing

Working group Section 35a	20 April 2022 3 May 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal products	10 May 2022	Concluding discussion of the draft resolution
Plenum	19 May 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 19 May 2022

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

Prof. Hecken