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)
Deucravacitinib (plaque psoriasis)

of 5 October 2023

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 start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient deucravacitinib on 15 April 2023 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. 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 13 April 2023.

The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on the G-BA website (www.g-ba.de) on 17 July 2023, 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 deucravacitinib 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 deucravacitinib.

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 Deucravacitinib (Sotyktu) in accordance with the product information

Sotyktu 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 05.10.2023):

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 who are not candidates for a conventional therapy in the context of a first-time systemic therapy

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

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.
   - Resolutions 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 (adults), 17 August 2017 (adults) and 18 February 2021 (children and adolescents 6 years and older).
   - Resolutions 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 (adults) and 21 January 2021 (children and adolescents 6 years and older).
   - 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.
- Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient bimekizumab dated 3 March 2022.

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 deucravacitinib 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.

<u>Patient population a)</u>

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. esters of fumaric acid, methotrexate, ciclosporin) are not expected to be successful. The European *EuroGuiderm Guideline for the systemic treatment of Psoriasis vulgaris* from 2022, on which the German guideline is based, also recommends the active

[2] Nast A et al. German S3 guideline on the therapy of Psoriasis vulgaris; update 2021 [online]. AWMF register number 013-001. Berlin (GER): Association of the Scientific-Medical Societies; 2021. [Accessed: 28.08.2023]. URL: https://register.awmf.org/assets/guidelines/013-001l_S3_Therapie-Psoriasis-vulgaris_2021-07-verlaengert_01.pdf

ingredient bimekizumab[3] for the treatment of the above-mentioned patient population.

The interleukin inhibitors bimekizumab, 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 esters of fumaric acid. The active ingredient bimekizumab showed a minor additional benefit compared to the appropriate comparator therapy. 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.

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 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 comparator data are available for the active ingredient compared with the appropriate comparator therapy. Certolizumab is therefore not part of the appropriate comparator therapy.

Therefore, based on the available evidence, the biologics adalimumab, bimekizumab, guselkumab, ixekizumab and secukinumab are 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 European *EuroGuiderm Guideline for the systemic treatment of Psoriasis vulgaris* from 2022, on which the German guideline is based, also recommends the active ingredient bimekizumab for the treatment of the above-mentioned patient population[3].

The interleukin antagonists bimekizumab, 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 therefore part of the appropriate comparator therapy. For the interleukin antagonist tildrakizumab,

[3] Nast A et al. EuroGuiderm Guideline for the systemic treatment of Psoriasis vulgaris [online]. European Dermatology Forum, 2022 [Accessed: 28.08.2023].
URL: https://www.guidelines.edf.one//uploads/attachments/cl27nt7yb001q90jnmykcah83-euroguiderm-pso-gl-feb-2022.pdf

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 comparator 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 comparative study was submitted. Within the framework of the written statement procedure, it was also confirmed by clinical experts that apremilast is a therapy option, especially for patients with less severe manifestation of the disease, but compared to the listed biologics, a weaker effect can be assumed. Therefore, apremilast is not seen as an equally appropriate therapy option compared to the listed biologics and is not included in the appropriate comparator therapy.

Therefore, based on the available evidence, the biologics adalimumab, bimekizumab, 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.

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

a) <u>Adults with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy</u>

For the treatment of adults with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy, the additional benefit is not proven.

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

For the treatment of adults with moderate to severe plaque psoriasis who have responded inadequately to, or have not tolerated systemic therapy, the additional benefit is not proven.

Justification:

The pharmaceutical company submits the IM011046 and IM011047 studies for the benefit assessment dossier. Each was a double-blind, randomised, multicentre study that enrolled adult patients with plaque psoriasis who were eligible for phototherapy or systemic therapy. Furthermore, at least 10% of the body surface area had to be affected at start of study and a Psoriasis Area and Severity Index (PASI) score ≥ 12 and a Static Physician's Global Assessment (sPGA) score ≥ 3 had to be present. A total of 666 patients were enrolled in the IM011046 study and a total of 1,020 patients were enrolled in the IM011047 study. These were randomised in a 2:1:1 ratio to the treatment arms deucravacitinib, apremilast or placebo respectively.

The pharmaceutical company uses the two studies IM011046 and IM011047 for its assessment of the additional benefit of deucravacitinib for adult patients with moderate to severe plaque psoriasis - both for patients for whom conventional therapy is not an option in the context of initial systemic therapy (patient group a) and for those who have responded inadequately to, or have not tolerated systemic therapy (patient group b). For this purpose, the pharmaceutical company submits results for the comparison of deucravacitinib vs apremilast in each case.

The approach of the pharmaceutical company is inappropriate. Apremilast is not part of the defined comparator therapies for both patient group a) and patient group b). The studies are therefore unsuitable for making statements on the additional benefit of deucravacitinib compared to the respective appropriate comparator therapy - neither for adult patients with moderate to severe plaque psoriasis for whom conventional therapy is not an option in the context of initial systemic therapy (patient group a), nor for those who have responded inadequately to, or have not tolerated systemic therapy (patient group b).

No suitable data are available for the assessment of the additional benefit of deucravacitinib compared with the appropriate comparator therapy in adult patients with moderate to severe plaque psoriasis for whom conventional therapy is not an option in the context of initial systemic therapy (patient group a) and for those patients who have responded inadequately to or have not tolerated systemic therapy (patient group b). Thus, none of the two questions results in a hint for an additional benefit of deucravacitinib compared to the appropriate comparator therapy; an additional benefit is therefore not proven in either case.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Sotyktu with the active ingredient deucravacitinib. Deucravacitinib 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 who are not candidates for a conventional therapy in the context of a first-time systemic therapy

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

The G-BA determined the biologics adalimumab or bimekizumab or guselkumab or ixekizumab or secukinumab as the appropriate comparator therapy for patient group a). For patient group b), the biologics adalimumab or bimekizumab or brodalumab or guselkumab or infliximab or ixekizumab or risankizumab or secukinumab or ustekinumab were determined as the appropriate comparator therapy.

The pharmaceutical company submits the IM011046 and IM011047 studies for the benefit assessment dossier and uses them for its assessment of the additional benefit of deucravacitinib for adult patients with moderate to severe plaque psoriasis. For this purpose, the pharmaceutical company submits results for the comparison of deucravacitinib vs apremilast in each case. The approach of the pharmaceutical company is inappropriate. Apremilast is not part of the defined comparator therapies for both patient group a) and patient group b). The studies are therefore unsuitable for making statements on the additional benefit of deucravacitinib compared to the respective appropriate comparator therapy.

Therefore, no suitable data are available for the assessment of the additional benefit of deucravacitinib compared with the appropriate comparator therapy, neither for patient group a) nor for patient group b). Thus, none of the two questions results in a hint for an additional benefit of deucravacitinib compared to the appropriate comparator therapy; an additional benefit is therefore not proven in either case.

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

The number of patients is the target population in statutory health insurance (SHI). The information is based on data provided by the pharmaceutical company in the dossier. The patient numbers presented are subject to uncertainties, but are considered to be better estimates for both questions from a methodological point of view than the patient numbers given in previous procedures.

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 Sotyktu (active ingredient: deucravacitinib) at the following publicly accessible link (last access: 14 September 2023):

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

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE (last revised: 15 September 2023).

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:

a) Adults with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Deucravacitinib	Continuously, 1 x daily	365	1	365.0
Appropriate comparator therapy				
Adalimumab or bimekizumab or guselkumab or ixekizumab or secukinumab				
Adalimumab	Continuously, every 14 days	26.1	1	26.1
Bimekizumab	Continuously, every 56 days	6.5	1	6.5
Guselkumab	Continuously, every 56 days	6.5	1	6.5
Ixekizumab	Continuously, every 28 days	13.0	1	13.0
Secukinumab	Continuously, 1 x monthly	12.0	1	12.0

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

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Deucravacitinib	Continuously, 1 x daily	365	1	365.0
Appropriate comparator therapy				
Adalimumab or bimekizumab or brodalumab or guselkumab or infliximab or ixekizumab or risankizumab or secukinumab or ustekinumab				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Adalimumab	Continuously, every 14 days	26.1	1	26.1
Bimekizumab	Continuously, every 56 days	6.5	1	6.5
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/

a) Adults with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy

Designation of the therapy	Dosage / application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Deucravacitinib	6 mg	6 mg	1 x 6 mg	365.0	365 x 6 mg
Appropriate comparator therapy					
Adalimumab or bimekizumab or guselkumab or ixekizumab or secukinumab					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Bimekizumab	320 mg	320 mg	2 x 160 mg	6.5	13.0 x 160 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

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

Designation of the therapy	Dosage / application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Deucravacitinib	6 mg	6 mg	1 x 6 mg	365.0	365 x 6 mg
Appropriate comparator therapy					
Adalimumab or bimekizumab or guselkumab or ixekizumab or secukinumab					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Bimekizumab	320 mg	320 mg	2 x 160 mg	6.5	13.0 x 160 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 = 385 mg	5 mg/kg = 385 mg	4 x 100 mg	6.5	26 x 100 mg

Designation of the therapy	Dosage / application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
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:

a) Adults with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy

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					
Deucravacitinib 6 mg	84 FCT	€ 3,351.64	€ 2.00	€ 322.49	€ 3,027.15
Appropriate comparator therapy					
Adalimumab 40 mg[5]	6 SFI	€ 2,859.20	€ 2.00	€ 228.57	€ 2,628.63
Bimekizumab 160 mg	4 SFI	€ 5,998.30	€ 2.00	€ 242.34	€ 5,753.96
Guselkumab 100 mg	2 SFI	€ 5,488.45	€ 2.00	€ 221.54	€ 5,264.91
Ixekizumab 80 mg	3 PEN	€ 3,989.32	€ 2.00	€ 160.38	€ 3,826.94
Secukinumab 300 mg	3 SFI	€ 4,654.03	€ 2.00	€ 187.50	€ 4,464.53
Abbreviations: FCT = film-coated tablets; SFI = solution for injection; PEN = solution for injection in a pre-filled pen					

[5] Fixed reimbursement rate

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

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					
Deucravacitinib 6 mg	84 FCT	€ 3,351.64	€ 2.00	€ 322.49	€ 3,027.15
Appropriate comparator therapy					
Adalimumab 40 mg[5]	6 SFI	€ 2,859.20	€ 2.00	€ 228.57	€ 2,628.63
Bimekizumab 160 mg	4 SFI	€ 5,998.30	€ 2.00	€ 228.57	€ 5,753.96
Brodalumab 210 mg	6 SFI	€ 4,153.94	€ 2.00	€ 167.10	€ 3,984.84
Guselkumab 100 mg	2 SFI	€ 5,488.45	€ 2.00	€ 221.54	€ 5,264.91
Infliximab 100 mg[5]	5 PIC	€ 3,490.57	€ 2.00	€ 280.08	€ 3,208.49
Ixekizumab 80 mg	3 PEN	€ 3,989.32	€ 2.00	€ 160.38	€ 3,826.94
Risankizumab 150 mg	1 SFI	€ 4,385.33	€ 2.00	€ 176.54	€ 4,206.79
Secukinumab 300 mg	3 SFI	€ 4,654.03	€ 2.00	€ 187.50	€ 4,464.53
Ustekinumab 45 mg	1 IFE	€ 5,818.60	€ 2.00	€ 564.02	€ 5,252.58
Abbreviations: FCT = film-coated tablets; IFE = solution for injection in a pre-filled syringe; SFI = solution for injection; PEN = solution for injection in a pre-filled pen; PIC = powder for the preparation of an infusion solution concentrate					

LAUER-TAXE® last revised: 15 August 2023

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 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[6]. 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				
Deucravacitinib	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
Deucravacitinib	Chest radiograph (GOP 34241)	1	€ 16.78	€ 16.78
Appropriate comparator therapy				
Adalimumab bimekizumab 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
Adalimumab Bimekizumab infliximab risankizumab ustekinumab	Chest radiograph (GOP 34241)	1	€ 16.78	€ 16.78
Adalimumab infliximab	HBs antigen (GOP 32781)	1	€ 5.50	€ 5.50

6 Cornberg M et al. S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011 [Accessed: 14.09.2023] https://register.awmf.org/assets/guidelines/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
	Anti-HBs antibody (GOP 32617)[7]	1	€ 5.50	€ 5.50
	Anti-HBc antibody (GOP 32614)	1	€ 5.90	€ 5.90
	HBV-DNA (GOP 32823)[8]	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 € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs do not add to the pharmacy sales price but follow the rules for calculation in the special agreement on contractual unit costs of retail pharmacist services (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 special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe).

2.5 Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed

7 Only if HBs antigen negative and anti-HBc antibody positive.

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

therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is authorised exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

In the case of information on "determined" or "undetermined" combinations, the assessed medicinal product can be used in a combination therapy according to this information on the basis of the marketing authorisation under Medicinal Products Act. For the designation, the G-BA, within the scope of its legislative discretion, uses the constellation of a "determined" or an "undetermined" combination as a justifiable interpretation variant.

If a designation as a so-called determined or as a so-called indetermined combination is omitted due to the lack of information on a combination therapy in the product information of the assessed medicinal product, the non-designation in the resolution according to Section 35a, paragraph 3, sentence 1 SGB V does not affect the possibility that the assessed medicinal product can be used in an open-label combination under marketing authorisation regulations.

Concomitant active ingredient:

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding information in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGBV.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

a) Adults with moderate to severe plaque psoriasis who are not candidates for a conventional therapy in the context of a first-time systemic therapy

   No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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

   No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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 3 May 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 13 April 2023, the pharmaceutical company submitted a dossier for the benefit assessment of deucravacitinib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 17 April 2023 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit 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 deucravacitinib.

The dossier assessment by the IQWiG was submitted to the G-BA on 11 July 2023, and the written statement procedure was initiated with publication on the G-BA website on 17 July 2023. The deadline for submitting statements was 7 August 2023.

The oral hearing was held on 28 August 2023.

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 26 September 2023, and the proposed resolution was approved.

At its session on 5 October 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	3 May 2023	Determination of the appropriate comparator therapy
Working group Section 35a	1 August 2023	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	28 August 2023	Conduct of the oral hearing

Working group Section 35a	5 September 2023 19 September 2023	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal products	10 October 2023	Concluding discussion of the draft resolution
Plenum	5 October 2023	Adoption of the resolution on the amendment of the AM-RL

Berlin, 5 October 2023

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

Prof. Hecken