GBA
Gemeinsamer
Bundesausschuss

Justification

for the Resolution of the Federal Joint Committee (GBA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Retifanlimab (Merkel cell carcinoma, metastatic or relapsed, monotherapy, first-line)

of 1 October 2026

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1. Legal basis

According to Section 35a, paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (GBA) assess the benefit of all reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit of an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V in conjunction with Chapter 5, Sections 5 et seqq. of the Rules of Procedure (VerfO) of the GBA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. In accordance with Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company shall provide evidence - within three months of being requested to do so by the GBA - in accordance with Chapter 5, Section 5, paragraphs 1 to 6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy specified by the GBA in accordance with Chapter 5, Section 6 VerfO, and in this evidence, demonstrate the additional benefit over the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the GBA decide whether to carry out the benefit assessment themselves or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation, the GBA modified the procedure for the benefit assessment of orphan drugs at their session on 15 March 2012 to the effect that, for orphan drugs, the GBA initially no longer independently determine an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the GBA indicating the significance of the evidence.

Accordingly, at their session on 15 March 2012, the GBA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V such that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover limit according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the GBA must be completed within three months of the relevant date for submission of the evidence and published on the internet.

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According to Section 35a, paragraph 3 SGB V, the GBA decide 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 retifanlimab (Zynyz) was listed for the first time on 1 March 2026 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit is assessed on the basis of the approval studies by the GBA.

On 28 November 2025, the pharmaceutical company submitted an application for postponement of the date for the start of the benefit assessment procedure for retifanlimab in the therapeutic indication Merkel cell carcinoma in accordance with Section 35a, paragraph 5b SGB V.

At their session on 22 January 2026, the GBA approved the application pursuant to Section 35a, paragraph 5b SGB V and postponed the relevant date for the start of the benefit assessment and the submission of a dossier for the benefit assessment for the therapeutic indication in question to four weeks after the marketing authorisation of the other therapeutic indication of the therapeutic indication covered by the application, at the latest six months after the first relevant date. The marketing authorisation for the other therapeutic indication covered by the application according to Section 35a, paragraph 5b SGB V was granted within the 6-month period.

On 1 March 2026, retifanlimab was granted an extension of the marketing authorisation for the therapeutic indication "metastatic or unresectable locally recurrent squamous cell carcinoma of the anal canal". The mentioned extension of the marketing authorisation is 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 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 from 12.12.2008, sentence 7).

On 31 March 2026, the pharmaceutical company submitted a dossier in due time in accordance with Section 4, paragraph 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 2 of the Rules of Procedure (VerfO) of the GBA concerning the active ingredient retifanlimab with the therapeutic indication "Zynyz is indicated as monotherapy for the first-line treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy".

The GBA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published along with the IQWiG assessment on 1 July 2026 on the GBA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The GBA have adopted their resolution on the basis of the dossier of the pharmaceutical company, the dossier assessment carried out by the GBA, the assessment of treatment costs

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and patient numbers (IQWiG G26-07) 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 GBA have assessed the studies relevant to the marketing authorisation on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1, numbers 1 to 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of retifanlimab.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Retifanlimab (Zynyz) in accordance with the product information

Zynyz is indicated as monotherapy for the first-line treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy.

Therapeutic indication of the resolution (resolution of 1 October 2026):

See the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

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

Adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy; first-line

Hint of non-quantifiable additional benefit since the scientific data does not allow quantification.

Justification:

The pharmaceutical company submitted the results of the pivotal, single-arm, unblinded phase II POD1UM-201 study for the assessment of the extent of the additional benefit of retifanlimab in the therapeutic indication "first-line treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy".

Adult patients (aged ≥ 18 years) with metastatic or recurrent, locally advanced MCC not amenable to curative surgery or radiation therapy were enrolled. Patients should have an ECOG performance status of 0 to 1 and must not have received any prior systemic therapy for the condition. A total of 140 patients were screened, of whom 107 received treatment. Of these, 101 were chemotherapy-naïve and therefore formed part of the modified safety population (metastatic: n = 91; relapsed, advanced: n = 10).

The study was carried out between 2019 and 2024 at 34 study sites in 11 countries across Europe and North America.

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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The primary endpoint was the objective response rate according to RECIST criteria, as assessed by an independent central review committee. Secondary endpoints were progression-free survival (PFS), overall survival, as well as other endpoints in the categories of morbidity, health-related quality of life and side effects. The final data cut-off from 1 July 2024 is available for the study.

The on-label sub-population within the therapeutic indication comprising 101 chemotherapy-naïve patients was used for the benefit assessment.

Mortality

In the POD1UM-201 study, overall survival was operationalised as the time from the first dose of the study medication to death from any cause. At the time of the final data cut-off, a total of 39 patients (38.6%) had died. The median overall survival had not been reached at the time of the data cut-off, with a median duration of observation of just under 3 years from enrolment (35.7 months). The estimated probability of survival was 79.0% after one year, 67.0% after two years and 63.0% after three years.

Due to the single-arm study design, a comparative assessment of overall survival is not possible.

Morbidity

Progression-free survival (PFS)

PFS was assessed as a secondary endpoint in the POD1UM-201 study. It was operationalised as the time from the first dose of the study treatment to the first documented disease progression according to RECIST criteria v1.1 or death from any cause, based on the assessment by an independent central review (ICR) committee.

The present PFS endpoint is a composite endpoint consisting of endpoints from the "mortality" and "morbidity" categories. The endpoint component "mortality" is already assessed via the endpoint "overall survival" as an independent endpoint. The morbidity component of disease progression was assessed according to RECIST criteria and thus predominantly by means of imaging procedures.

Taking into account the aspects mentioned above, there are different opinions within the GBA regarding the patient relevance of the PFS endpoint. The overall statement on the extent of the additional benefit remains unaffected. Nevertheless, a comparative assessment is not possible due to the single-arm study design.

Objective response rate (ORR)

In the POD1UM-201 study, ORR was operationalised as all patients with a confirmed overall response of "complete response" or "partial response" from baseline until disease progression or the start of a new cancer treatment, as assessed in accordance with RECIST criteria v1.1 by an independent central review (ICR) committee.

55 of the patients (54.5%) showed an objective response.

The assessment of ORR was carried out by means of an independent radiological review and was therefore not based on symptoms, but primarily on imaging procedures. For this reason, this endpoint is classified as not patient-relevant. As this is the primary endpoint of the POD1UM-201 study, the results are presented additionally.

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Nevertheless, the results of the POD1UM-201 study regarding the ORR endpoint do not allow a statement to be made on the extent of the additional benefit, as a comparative assessment is not possible due to the single-arm study design.

Health status

In the POD1UM-201 study, patients' health status was assessed using the VAS of the EQ-5D questionnaire.

Due to low return rates (< 70% from the first post-baseline survey), no suitable results on health status are available. Nevertheless, a comparative assessment is not possible due to the single-arm study design.

Quality of life

Health-related quality of life was assessed in the POD1UM-201 study using the FACT-M.

Due to low return rates (< 70% from the first post-baseline survey), no suitable results on quality of life are available. Nevertheless, a comparative assessment is not possible due to the single-arm study design.

Side effects

Total adverse events (AEs)

Almost all patients experienced an adverse event (91.1%). These are only presented additionally.

Serious adverse events (SAEs)

26 out of 101 patients (25.7%) had experienced at least one serious adverse event.

Severe adverse events (CTCAE grade ≥ 3)

At least one severe AE with CTCAE grade ≥ 3 occurred in 32 out of 101 patients (31.7%).

Therapy discontinuation due to adverse events

In 21 out of 101 patients (20.8%), an adverse event occurred that led to the discontinuation of the study medication.

Due to the single-arm study design, a comparative assessment of side effects is not possible.

Overall assessment

Results on mortality, morbidity, quality of life and side effects from the pivotal, single-arm, unblinded phase II POD1UM-201 study are available for the benefit assessment of retifanlimab for first-line treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy.

No statement on the extent of the additional benefit can be made on the basis of the study results due to the single-arm design of the POD1UM-201 study. In the overall assessment, the GBA classify the extent of the additional benefit of retifanlimab in metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy as non-quantifiable since the scientific data does not allow quantification.

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Significance of the evidence

The benefit assessment is based on data from the pivotal, single-arm, unblinded phase II POD1UM-201 study. Due to the single-arm study design, a comparative assessment is not possible and no statement on the extent of the additional benefit can be made on the basis of the study results.

In the overall assessment, this results in the classification of the significance of the evidence in the "hint" category.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Zynyz with the active ingredient retifanlimab.

Retifanlimab was approved as an orphan drug in the following therapeutic indication:

"Zynyz is indicated as monotherapy for the first-line treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy".

For the benefit assessment, the pharmaceutical company presented the results from the pivotal, single-arm, unblinded phase II POD1UM-201 study for the endpoints in the categories of mortality, morbidity, quality of life and side effects.

No statement on the extent of the additional benefit can be made on the basis of the study results due to the single-arm design of the POD1UM-201 study.

Consequently, the GBA classify the extent of the additional benefit as non-quantifiable since the scientific data does not allow quantification.

No statement on the extent of the additional benefit can be made on the basis of the study results due to the single-arm study design. The significance of the evidence is classified in the "hint" category.

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

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

The resolution is based on the information provided by the pharmaceutical company in the benefit assessment dossier. The pharmaceutical company's approach is mathematically plausible. Overall, it is however reasonable to assume that the figures for the number of patients in the SHI target population have been underestimated. This underestimation is primarily due to the very low applied incidence of MCC.

The use of age-standardised rates based on the (old) European population per 100,000 subjects leads to uncertainties in the estimation of incidence, as the old, standard European population differs from the current population, and it can be assumed that these differences are also reflected in the overall incidence rates.

Furthermore, the lower limit of the incidence estimate is likely to be an underestimate, as it is based on data from 2008 to 2010, whilst an increase in new cases was observed in Germany in subsequent years.

In addition, the following uncertainties exist:

The upper limit for patients with an initial diagnosis at stage IV is subject to uncertainty due to ambiguities regarding the source used and its applicability to the German healthcare context.

Furthermore, the pharmaceutical company's simplified assumption that the patient population is evenly distributed between stage I and stage II at the time of initial diagnosis, as well as the limited timeliness of the data sources and the questionable applicability to current patient cohorts in Germany, lead to uncertainty in the derivation of the number of patients with recurrence from stages I and II and the classification of patients with recurrence into stage III from stages I to III.

In addition, it is likely that the number of patients with recurrence from stages I and II has been underestimated, as the percentage of patients who relapse from stage III to stage IV is not included. The percentage of patients with a recurrence in stage III from stage III is subject to uncertainty, as it is based on a small patient cohort.

With regard to the number of patients with recurrent, locally advanced MCC (stage III) that is unresectable, it is unclear to what extent the curative intent aspects of surgery and radiotherapy were taken into account. Furthermore, on the one hand, the underlying source for the percentage is unclear and, on the other, the pharmaceutical company extrapolates the percentage to all patients with a recurrence in stage III, even though the percentage only relates to patients who were initially diagnosed at stage I or II and subsequently suffered a recurrence in stage III.

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 Zynyz (active ingredient: retifanlimab) at the following publicly accessible link (last access: 30 June 2026):

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

Treatment with retifanlimab should only be initiated and monitored by specialists in internal medicine, haematology, and oncology who are experienced in the treatment of patients with Merkel cell carcinoma, as well as specialists in skin and sexually transmitted diseases and other doctors from other specialist groups participating in the Oncology Agreement.

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 July 2026).

The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

According to the PI, treatment should be continued for up to 2 years.

The annual treatment costs shown refer to the first year of treatment.

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				
Retifanlimab	1 x every 28 days	13	1	13

Consumption:

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.

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					
Retifanlimab	500 mg	500 mg	1 x 500 mg	13	13 x 500 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

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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. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) not amenable to curative surgery or radiation therapy; first-line

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					
Retifanlimab	1 CIS	€ 13,541.13	€ 1.77	€ 770.00	€ 12,769.36
Abbreviations: CIS = concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 15 July 2026

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.

No additional SHI services required are taken into account for the cost representation.

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 agents 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-apply 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

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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.

4. Process sequence

On 31 March 2026, the pharmaceutical company submitted a dossier for the benefit assessment of retifanlimab to the GBA in due time in accordance with Chapter 5, Section 8, paragraph 2 VerfO.

The benefit assessment of the GBA was published on 1 July 2026 together with the IQWiG assessment of treatment costs and patient numbers on the GBA website (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 22 July 2026.

The oral hearing was held on 10 August 2026.

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 were discussed at the Subcommittee's session on 22 September 2026, and deliberation of the draft resolution was concluded.

At their session on 1 October 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

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Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	23 June 2026	Information of the benefit assessment of the GBA
Working group Section 35a	4 August 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	10 August 2026	Conduct of the oral hearing
Working group Section 35a	18 August 2026 15 September 2026	Consultation on the dossier assessment by the GBA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee on Medicinal Products	22 September 2026	Concluding discussion of the draft resolution
Plenum	1 October 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 1 October 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Dr Optendrenk

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