Gemeinsamer Bundesausschuss

Justification

to 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
Mirikizumab (new therapeutic indication: Crohn's disease, pretreated)

of 4 September 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all 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 studies the pharmaceutical company have 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 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 mirikizumab (Omvoh) was listed for the first time on 1 September 2023 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 12 February 2025, mirikizumab 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 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, sentence 7).

On 10 March 2025, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company have submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 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 mirikizumab with the new therapeutic indication

"Adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic treatment.".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 16 June 2025 on the G-BA website (www.g-ba.de), 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 mirikizumab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA have 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 mirikizumab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have 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 Mirikizumab (Omvoh) in accordance with the product information

Adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic treatment.

Therapeutic indication of the resolution (resolution of 4 September 2025):

See the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy

Appropriate comparator therapy for mirikizumab:

- Adalimumab or infliximab or risankizumab or ustekinumab or vedolizumab

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

Appropriate comparator therapy for mirikizumab:

- Adalimumab or infliximab or risankizumab or upadacitinib or ustekinumab or vedolizumab

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

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.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1. Taking into account the specifications in the respective product information, medicinal products that are generally approved in the therapeutic indication, in addition to the medicinal product to be assessed here, are corticosteroids (topical, systemic: budenoside, hydrocortisone acetate, methylprednisolone, prednisone, prednisolone), Indian psyllium and psyllium husk, immunosuppressants (azathioprine, methotrexate) as well as 5-aminosalicylates (mesalazine, sulfasalazine), the TNF-α antagonists adalimumab and infliximab, the interleukin inhibitors risankizumab and ustekinumab, the integrin inhibitor vedolizumab and the JAK inhibitor upadacitinib. The therapeutic indications for budesonide, methotrexate, mesalazine and sulphasalazine are only partially consistent with the indication "moderately to severely active Crohn's disease".

On 2. A non-medicinal treatment cannot be considered as an appropriate comparator therapy in this therapeutic indication. Surgical resection is a patient-individual option that requires a case-by-case decision and is not the standard case. Thus, surgical resection is not to be considered for the determination of the appropriate comparator therapy.

On 3. In the therapeutic indication of Crohn's disease, there are resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V for the active ingredient vedolizumab dated 8 January 2015, for the active ingredient risankizumab dated 15 June 2023 and for the active ingredient upadacitinib dated 19 October 2023.

In addition, there is a resolution on the amendment to the Pharmaceuticals Directive (AM-RL): Annex VI (off-label use) - 6-mercaptopurine for immunosuppression in the therapy of chronic inflammatory bowel diseases (resolution of 21 October 2021).

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 therapeutic indication.

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.

On the basis of the established therapy algorithms and approved medicinal products in the present therapeutic indication, the G-BA divided the patient groups as follows:

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy
b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

Extensive published data and guidelines are available for the indication of moderately to severely active Crohn's disease to be assessed.

Conventional treatment for Crohn's disease includes 5-aminosalicylates, corticosteroids and the immunosuppressants azathioprine and methotrexate. These active ingredients or product classes are therefore no longer considered as the appropriate comparator therapy for the present treatment setting. Likewise, Indian psyllium and psyllium husk are not considered as the appropriate comparator therapy as they are only used as supportive therapy in Crohn's disease.

Accordingly, as approved medicinal treatment options, TNF-α antagonists (adalimumab, infliximab), interleukin inhibitors (risankizumab, ustekinumab), the integrin inhibitor vedolizumab and the JAK inhibitor upadacitinib are still considered as the appropriate comparator therapy.

The current German S3 guideline[2] Crohn's disease equally recommends these active ingredients for patients with moderately to severely active Crohn's disease who have had an inadequate response or lost response to conventional therapy or therapy with TNF-α antagonists.

However, in view of the fact that the use of JAK inhibitors is associated with an increased risk of serious side effects[3], the G-BA believes that upadacitinib does not have the same significance in clinical care as the other active ingredients recommended in the guidelines in the earlier treatment setting, i.e. after failure of or intolerance to conventional therapy. The JAK inhibitor upadacitinib is therefore not determined as the appropriate comparator therapy for patient group a).

However, for patients who require further therapy escalation and thus a broader spectrum of therapy options in this difficultly adjustable treatment setting, as they have already responded inadequately to a biologic agent or have not tolerated it (patient group b), the JAK inhibitor upadacitinib is viewed to be another suitable therapy option, taking into account the authorisation status and previous therapy (therapies), and is therefore considered as the appropriate comparator therapy for this patient group.

Following failure of a prior therapy with a biologic agent, the overall body of evidence is low. With regard to therapeutic efficacy as well as to the question of the side-effect profile or the safety risk, no evidence-based information was found that one of the active ingredients mentioned is generally preferable in patients who have a failed response to a biologic agent. No prioritisation can be made within the TNF-α antagonists either. In addition to a change of product class, a change within the product class can also be considered overall in this line of therapy.

It is also assumed that a patient-individual, case-by-case decision on surgical resection may be made as needed for patients who are still eligible for medicinal therapy; however, this does not represent the standard case. Thus, surgical resection is not considered for the determination of the appropriate comparator therapy.

In the overall assessment, the active ingredients adalimumab, infliximab, risankizumab, ustekinumab or vedolizumab are determined to be equally appropriate therapy options for patient group a) adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to conventional therapy.

For patient group b) adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor), a change of

[2] Sturm A et al. Updated S3 guideline Crohn's disease (version 4.2). Z Gastroenterol 2024; 62: 1229 – 1318
[3] see product information for Rinvoq (upadacitinib) last revised July 2024

therapy to adalimumab, infliximab, risankizumab, upadacitinib, ustekinumab or vedolizumab is determined as the appropriate comparator therapy. For all options, both the previous therapy given in each case and the marketing authorisation of the respective active ingredients must be taken into account.

Each of the appropriate comparator therapies determined here includes several therapeutic alternatives. These therapeutic alternatives are equally appropriate for the comparator therapy. The additional benefit can be demonstrated in each case compared to one of the therapeutic alternatives mentioned.

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 mirikizumab is assessed as follows:

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy

An additional benefit is not proven.

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

An additional benefit is not proven.

Justification:

The pharmaceutical company presented the VIVID-1 study for the assessment of the additional benefit of mirikizumab in adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to either conventional therapy or a biologic treatment.

The VIVID-1 study is a double-blind RCT comparing mirikizumab with ustekinumab or placebo in adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy (with corticosteroids, azathioprine, 6-mercaptopurine or methotrexate), a TNF-α antagonist or an integrin inhibitor.

A total of 1,152 patients were enrolled in the study and randomly assigned in a ratio of 6:3:2 to treatment with mirikizumab (N = 631), ustekinumab (N = 309) or placebo (N = 212), whereby the placebo arm is not relevant for the present assessment. The study includes relevant sub-populations for both patient group a (331 vs 164 patients) and patient group b (300 vs 145 patients). The patient characteristics of the relevant sub-populations at the start of the study are sufficiently comparable between the two treatment arms. However, significantly fewer patients in the sub-population of patient group b came from the European region (38% vs 34%) than in patient group a (68% vs 74%).

The study is divided into a screening phase of up to 5 weeks, a 52-week treatment phase (52 weeks or until worsening of the disease requiring specific medicines not permitted in the study, or surgery, until unacceptable toxicity or until therapy discontinuation by investigator decision or at patient request) and a maximum 16-week follow-up phase.

Co-primary endpoints of the study were clinical response at week 12 using PRO2 followed by endoscopic response at week 25 and clinical response at week 12 using PRO2 followed by clinical remission at week 52 using CDAI. In addition, patient-relevant endpoints on morbidity, health-related quality of life and side effects were assessed.

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy

Extent and probability of the additional benefit

Mortality

For the "overall mortality" endpoint, there was no statistically significant difference between the treatment arms.

Morbidity

Patient-reported outcome 2 (PRO2)
The PRO2 comprises the 2 scales of the CDAI on stool frequency (CDAI-SF) and on abdominal pain (CDAI-AP; on a scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe pain), each of which is collected using a patient diary.

Clinical remission (PRO2)
The endpoint of clinical remission was operationalised using PRO2. According to the predefinition at study planning, remission using PRO2 was defined as an unweighted daily average stool frequency (CDAI-SF) ≤ 3 and simultaneous unweighted daily average abdominal pain (CDAI-AP) ≤ 1 (each averaged over a period of 7 days) at week 52. Both values may not be worse than at the start of the study. This operationalisation corresponds to the absence of symptoms in patients to a large extent.
For the endpoint of clinical remission, assessed using PRO2, there was no statistically significant difference between the treatment arms.

Corticosteroid-free clinical remission (PRO2)
The endpoint of corticosteroid-free clinical remission was operationalised as clinical remission using PRO2 at week 52 with simultaneous corticosteroid-free status between week 40 and week 52. Corticosteroid-free clinical remission is an important therapeutic goal and is considered patient-relevant. It is also considered to be a more established definition of remission, as the endpoint of clinical remission (PRO2) also includes patients as responders who achieve remission with corticosteroids, or at least received them between week 40 and week 52.
For the endpoint of corticosteroid-free clinical remission, assessed using PRO2, there was no statistically significant difference between the treatment arms.

Inflammatory Bowel Disease Questionnaire (IBDQ)
In addition to the total score (see comments on quality of life), the 2 sub-scores bowel symptoms and systemic symptoms of the IBDQ were used for assessment of symptomatology.

Bowel symptoms (IBDQ)
For the endpoint of bowel symptoms, assessed with the corresponding sub-score of the IBDQ, there was no statistically significant difference between the treatment arms.

Systemic symptoms (IBDQ)
For the endpoint of systemic symptoms, assessed with the corresponding sub-score of the IBDQ, there was no statistically significant difference between the treatment arms.

Remission of the imperative urge to defecate (Urgency NRS)
The Urgency Numerical Rating Scale is a patient-reported 1-item scale that measures the severity grade of urgency (sudden and/or immediate urge) to defecate within the last 24 hours using an 11-point scale ranging from 0 (no urgency) to 10 (highest possible urgency).
For the endpoint of remission of the imperative urge to defecate, assessed by Urgency NRS, there was no statistically significant difference between the treatment arms.

Extraintestinal manifestations
The endpoint of extraintestinal manifestations is generally assessed as patient-relevant. The endpoint is operationalised as the percentage of patients with extraintestinal manifestations (arthralgia, arthritis, iritis, uveitis, erythema nodosum, pyoderma gangraenosum and aphthous stomatitis) at the start of the study in whom these had subsided by week 52. The evaluations therefore do not include patients in whom extraintestinal manifestations only occurred during the course of the study. This is considered inappropriate as not all patients enrolled in the study are included in the evaluation.
No suitable data are therefore available for the endpoint of extraintestinal manifestations.

Fistulas
The endpoint of fistulas is assessed as patient-relevant. The endpoint is operationalised as the percentage of patients with draining skin fistulas at the start of the study and closure of all draining skin fistulas at week 52. The evaluations therefore do not include patients in whom draining skin fistulas only occurred during the course of the study. As previously stated for the endpoint of extraintestinal manifestations, this is considered inappropriate.
No suitable data are therefore available for the endpoint of fistulas.

Fatigue (FACIT-Fatigue)
The endpoint of fatigue was assessed in the present study using the "Functional Assessment of Chronic Illness Therapy-Fatigue" (FACIT-Fatigue) questionnaire.
There was no statistically significant difference between the treatment arms for the percentage of patients with clinically relevant improvement in the FACIT-Fatigue by ≥ 8 points.

Health status (EQ-5D VAS)
For the endpoint of health status, assessed using the VAS of the "European Quality of Life Questionnaire 5 Dimensions" (EQ-5D), there was no statistically significant difference between the treatment arms for the percentage of patients with clinically relevant improvement by ≥ 15 points.

Activity impairment (WPAI-CD item 6)
The "Work Productivity and Activity Impairment Questionnaire – Crohn's Disease" (WPAI-CD) is a questionnaire to measure the impairment of work productivity and activities outside of work due to Crohn's disease. Evaluations were presented on the individual question 6 of the WPAI-CD on the assessment of the limitations of daily activity due to Crohn's disease. This question measures the impairment of daily activities in the last 7 days on a scale from 0 to 10.

Only patients who were employed at the start of the study were included in the evaluations. This means that a relevant percentage of patients are not included in the evaluations.
No suitable data are therefore available for the endpoint of activity impairment, assessed using the WPAI-CD item 6.

Quality of life

Inflammatory Bowel Disease Questionnaire (IBDQ)
The IBDQ is a widely used and validated disease-specific instrument in the present indication of Crohn's disease.
The IBDQ includes a total of 32 questions on aspects of inflammatory bowel disease. The questionnaire includes 4 domains, with 10 questions on bowel symptoms, 5 questions on systemic symptoms, 12 questions on emotional functioning and 5 questions on social functioning. Each question can be rated on a scale of 1 to 7, with higher scores indicating better condition. The total score (IBDQ total score) ranges from 32 to 224 points. Separate sub-scores can be calculated for the 4 domains.
The IBDQ total score is assigned to the endpoint category of health-related quality of life.

IBDQ total score
For the health-related quality of life, assessed using the IBDQ total score, there was no statistically significant difference between the treatment arms.

Short Form (36) Health Survey (SF-36)
The SF-36 is a non-disease-specific measurement instrument for assessing health-related quality of life.

SF-36 Physical Component Summary (PCS) score
For the health-related quality of life, assessed using the SF-36 Physical Component Summary (PCS) score, there was no statistically significant difference between the treatment arms.

SF-36 Mental Component Summary (MCS) score
For the health-related quality of life, assessed using the SF-36 Mental Component Summary (MCS) score, there was no statistically significant difference between the treatment arms.

Side effects

Serious adverse events (SAE)
For the endpoint of SAEs, there was no statistically significant difference between the treatment arms.

Therapy discontinuation due to adverse events (AEs)
For the endpoint of discontinuation due to AEs, there was no statistically significant difference between the treatment arms.

Specific AEs
In detail, there was no statistically significant difference between the treatment arms for the specific AE "Infections", operationalised as infections and infestations (SOC, AEs).

Overall assessment

The double-blind RCT VIVID-1 comparing mirikizumab with ustekinumab or placebo, which includes adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy, a TNF-α antagonist or an integrin inhibitor, is available for the benefit assessment.

For the endpoint of overall mortality in the mortality category, there was no statistically significant difference between the treatment arms.

In the morbidity category, there were no statistically significant differences between the treatment arms for the endpoints of clinical remission (PRO2), corticosteroid-free clinical remission (PRO2), bowel symptoms (IBDQ), systemic symptoms (IBDQ), remission of imperative urge to defecate (Urgency NRS), fatigue (FACIT Fatigue) and health status (EQ-5D VAS). No suitable data are available for the endpoints of extraintestinal manifestations, fistulas and activity impairment (WPAI-CD item 6).

In the health-related quality of life category, there were no statistically significant differences for the endpoints of IBDQ total score, SF-36 Physical Component Summary (PCS) score and SF-36 Mental Component Summary (MCS) score respectively.

In the side effects category, there were no statistically significant differences between the treatment arms in the overall rates of SAEs and discontinuation due to AEs or in detail for the specific AE "Infections".

The overall assessment of the results therefore did not show any statistically significant differences between the treatment arms across categories. Consequently, no additional benefit of mirikizumab over ustekinumab can be identified in adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy.

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

Extent and probability of the additional benefit

Mortality

For the "overall mortality" endpoint, there was no statistically significant difference between the treatment arms.

Morbidity

Patient-reported outcome 2 (PRO2)
The PRO2 comprises the 2 scales of the CDAI on stool frequency (CDAI-SF) and on abdominal pain (CDAI-AP; on a scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe pain), each of which is collected using a patient diary.

Clinical remission (PRO2)
The endpoint of clinical remission was operationalised using PRO2. According to the predefinition at study planning, remission using PRO2 was defined as an unweighted daily average stool frequency (CDAI-SF) ≤ 3 and simultaneous unweighted daily average abdominal pain (CDAI-AP) ≤ 1 (each averaged over a period of 7 days) at week 52. Both values may not

be worse than at the start of the study. This operationalisation corresponds to the absence of symptoms in patients to a large extent.
For the endpoint of clinical remission, assessed using PRO2, there was no statistically significant difference between the treatment arms.

Corticosteroid-free clinical remission (PRO2)
The endpoint of corticosteroid-free clinical remission was operationalised as clinical remission using PRO2 at week 52 with simultaneous corticosteroid-free status between week 40 and week 52. Corticosteroid-free clinical remission is an important therapeutic goal and is considered patient-relevant. It is also considered to be a more established definition of remission, as the endpoint of clinical remission (PRO2) also includes patients as responders who achieve remission with corticosteroids, or at least received them between week 40 and week 52.
For the endpoint of corticosteroid-free clinical remission, assessed using PRO2, there was no statistically significant difference between the treatment arms.

Inflammatory Bowel Disease Questionnaire (IBDQ)
In addition to the total score (see comments on quality of life), the 2 sub-scores bowel symptoms and systemic symptoms of the IBDQ were used for assessment of symptomatology.

Bowel symptoms (IBDQ)
For the endpoint of bowel symptoms, assessed with the corresponding sub-score of the IBDQ, there was no statistically significant difference between the treatment arms.

Systemic symptoms (IBDQ)
For the endpoint of systemic symptoms, assessed with the corresponding sub-score of the IBDQ, there was no statistically significant difference between the treatment arms.
However, there was an effect modification by the characteristic CDAI total score (< 300/ ≥ 300) at the start of the study. For patients with CDAI total score < 300 at the start of the study, there was a statistically significant difference to the advantage of mirikizumab over ustekinumab. For patients with CDAI total score ≥ 300 at the start of the study, there was no statistically significant difference between the treatment arms.

Remission of the imperative urge to defecate (Urgency NRS)
The Urgency Numerical Rating Scale is a patient-reported 1-item scale that measures the severity grade of urgency (sudden and/or immediate urge) to defecate within the last 24 hours using an 11-point scale ranging from 0 (no urgency) to 10 (highest possible urgency).
For the endpoint of remission of the imperative urge to defecate, assessed by Urgency NRS, there was a statistically significant advantage of mirikizumab over ustekinumab.

Extraintestinal manifestations
The endpoint of extraintestinal manifestations is generally assessed as patient-relevant. The endpoint is operationalised as the percentage of patients with extraintestinal manifestations (arthralgia, arthritis, iritis, uveitis, erythema nodosum, pyoderma gangraenosum and aphthous stomatitis) at the start of the study in whom these had subsided by week 52. The evaluations therefore do not include patients in whom extraintestinal manifestations only occurred during the course of the study. This is considered inappropriate as not all patients enrolled in the study are included in the evaluation.
No suitable data are therefore available for the endpoint of extraintestinal manifestations.

Fistulas

The endpoint of fistulas is assessed as patient-relevant. The endpoint is operationalised as the percentage of patients with draining skin fistulas at the start of the study and closure of all draining skin fistulas at week 52. The evaluations therefore do not include patients in whom draining skin fistulas only occurred during the course of the study. As previously stated for the endpoint of extraintestinal manifestations, this is considered inappropriate.
No suitable data are therefore available for the endpoint of fistulas.

Fatigue (FACIT-Fatigue)
The endpoint of fatigue was assessed in the present study using the "Functional Assessment of Chronic Illness Therapy-Fatigue" (FACIT-Fatigue) questionnaire.
There was no statistically significant difference between the treatment arms for the percentage of patients with clinically relevant improvement in the FACIT-Fatigue by ≥ 8 points.

Health status (EQ-5D VAS)
For the endpoint of health status, assessed using the VAS of the "European Quality of Life Questionnaire 5 Dimensions" (EQ-5D), there was no statistically significant difference between the treatment arms for the percentage of patients with clinically relevant improvement by ≥ 15 points.

Activity impairment (WPAI-CD item 6)
The "Work Productivity and Activity Impairment Questionnaire – Crohn's Disease" (WPAI-CD) is a questionnaire to measure the impairment of work productivity and activities outside of work due to Crohn's disease. Evaluations were presented on the individual question 6 of the WPAI-CD on the assessment of the limitations of daily activity due to Crohn's disease. This question measures the impairment of daily activities in the last 7 days on a scale from 0 to 10. Only patients who were employed at the start of the study were included in the evaluations. This means that a relevant percentage of patients are not included in the evaluations.
No suitable data are therefore available for the endpoint of activity impairment, assessed using the WPAI-CD item 6.

Quality of life

Inflammatory Bowel Disease Questionnaire (IBDQ)
The IBDQ is a widely used and validated disease-specific instrument in the present indication of Crohn's disease.
The IBDQ includes a total of 32 questions on aspects of inflammatory bowel disease. The questionnaire includes 4 domains, with 10 questions on bowel symptoms, 5 questions on systemic symptoms, 12 questions on emotional functioning and 5 questions on social functioning. Each question can be rated on a scale of 1 to 7, with higher scores indicating better condition. The total score (IBDQ total score) ranges from 32 to 224 points. Separate sub-scores can be calculated for the 4 domains.
The IBDQ total score is assigned to the endpoint category of health-related quality of life.

IBDQ total score
For the health-related quality of life, assessed using the IBDQ total score, there was no statistically significant difference between the treatment arms.

Short Form (36) Health Survey (SF-36)
The SF-36 is a non-disease-specific measurement instrument for assessing health-related quality of life.

SF-36 Physical Component Summary (PCS) score
For the health-related quality of life, assessed using the SF-36 Physical Component Summary (PCS) score, there was no statistically significant difference between the treatment arms.

SF-36 Mental Component Summary (MCS) score
For the health-related quality of life, assessed using the SF-36 Mental Component Summary (MCS) score, there was no statistically significant difference between the treatment arms.

Side effects

Serious adverse events (SAE)
For the endpoint of SAEs, there was no statistically significant difference between the treatment arms.

Therapy discontinuation due to adverse events (AEs)
For the endpoint of discontinuation due to AEs, there was no statistically significant difference between the treatment arms.

Specific AEs
In detail, there was a statistically significant advantage of mirikizumab over ustekinumab for the specific AE "Infections", operationalised as infections and infestations (SOC, AEs).

Effect modification across endpoints

There was an effect modification due to the geographic region characteristic. A statistically significant advantage can only be seen in the "Other" region. This concerns the endpoints of clinical remission (PRO2), corticosteroid-free clinical remission (PRO2), bowel symptoms (IBDQ – improvement), remission of the imperative urge to defecate (Urgency NRS) and IBDQ total score (improvement). The descent/ ethnicity characteristic is very similar to the geographical region characteristic.

Overall assessment

The double-blind RCT VIVID-1 comparing mirikizumab with ustekinumab or placebo, which includes adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy, a TNF-α antagonist or an integrin inhibitor, is available for the benefit assessment.

For the endpoint of overall mortality in the mortality category, there was no statistically significant difference between the treatment arms.

In the morbidity category, there was a statistically significant advantage of mirikizumab over ustekinumab for the endpoint of remission of the imperative urge to defecate (Urgency NRS). There were no statistically significant differences between the treatment arms for the endpoints of clinical remission (PRO2), corticosteroid-free clinical remission (PRO2), bowel symptoms (IBDQ), fatigue (FACIT Fatigue) and health status (EQ-5D VAS). For the endpoint of systemic symptoms (IBDQ), there was no statistically significant difference between the treatment arms overall. There is however an effect modification here due to the CDAI total score (< 300/ ≥ 300) at the start of the study. For patients with CDAI total score < 300, there was a statistically significant advantage of mirikizumab over ustekinumab. No suitable data are available for the endpoints of extraintestinal manifestations, fistulas and activity impairment (WPAI-CD item 6).

In the health-related quality of life category, there were no statistically significant differences for the endpoints of IBDQ total score, SF-36 Physical Component Summary (PCS) score and SF-36 Mental Component Summary (MCS) score.

In the category of side effects, there were no statistically significant differences between the treatment arms in the overall rates of SAEs and discontinuation due to AEs respectively. In detail, for the specific AE "Infections", there was a statistically significant advantage of mirikizumab. In the overall assessment of the results in the side effects category, no additional benefit of mirikizumab compared to ustekinumab was derived.

Subgroup analyses on the geographical region characteristic show numerous significant effect modifications that affect almost all key endpoints. There were statistically significant advantages only in the "Other" region, which comprises around 80% of patients in Asia. In contrast, the effects are not statistically significant for the Europe and North America regions. The descent/ ethnicity characteristic is very similar to the geographical region characteristic.

The overall assessment of the results thus show a statistically significant advantage of mirikizumab over ustekinumab in one morbidity endpoint (remission of the imperative urge to defecate). However, it is questionable whether the results can be transferred to the German healthcare context due to the effect modification for the geographical region characteristic observed across endpoints. Therefore, in the overall weighting, no additional benefit of mirikizumab over ustekinumab was identified in adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient mirikizumab. The therapeutic indication assessed here is "Adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic treatment".

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

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy.
b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor).

For both patient groups, the pharmaceutical company presented the RCT VIVID-1 comparing mirikizumab with ustekinumab or placebo, which includes adults with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy, a TNF-α antagonist or an integrin inhibitor.

<u>Patient group a)</u>

The G-BA determined "adalimumab or infliximab or risankizumab or ustekinumab or vedolizumab" as the appropriate comparator therapy.

There were no statistically significant differences between the treatment arms across categories.

In the overall assessment, no additional benefit of mirikizumab over ustekinumab can be identified.

Patient group b)

The G-BA determined "adalimumab or infliximab or risankizumab or upadacitinib or ustekinumab or vedolizumab" as the appropriate comparator therapy.

There was an advantage in the endpoint of remission of the imperative urge to defecate (Urgency NRS). However, it is questionable whether the advantage can be transferred to the German healthcare context due to an effect modification observed across endpoints for the geographical region characteristic, in which the statistically significant advantage remains exclusively in the "Other" region (at approx. 80% Asia).

In the overall assessment, no additional benefit of mirikizumab over ustekinumab can be identified.

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 data are based on the patient numbers from the statement received from the pharmaceutical company (Lilly Deutschland GmbH) as part of the written statement procedure for mirikizumab, and on the patient numbers from the dossier for guselkumab for the same therapeutic indication (Johnson & Johnson). The patient numbers differ significantly between the data provided by Lilly Deutschland GmbH and Johnson & Johnson respectively. The discrepancy between the determined patient numbers lies in particular in the operationalisation of moderately to severely active Crohn's disease and inadequate response or intolerance.

For this purpose, as part of an update of the patient numbers in the statement based on a routine data analysis, Lilly Deutschland GmbH identified cases that had at least one prescription of a biologic agent in the year of analysis 2023 or in the 3-year prior observation period with a diagnosis of Crohn's disease in the same quarter. The calculated patient number was then divided into the respective research questions and forecast for the year 2025 based on the prevalence trend of Crohn's disease.

In contrast, Johnson & Johnson only assessed patients who either received a biologic agent for the first time in the year of analysis (patient group a) or who changed the biologic agent in the year of analysis (patient group b), resulting in a lower percentage range. The derivation by Johnson & Johnson is therefore limited to patients with a change of therapy in the year under review.

The number of patients determined in each case is subject to uncertainty, particularly due to the operationalisation of moderately to severely active Crohn's disease as well as inadequate response and/or intolerance. The existing uncertainties can be taken into account to a greater extent by using total ranges formed using both derivations.

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 Omvoh (active ingredient: mirikizumab) at the following publicly accessible link (last access: 2 July 2025):

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

Treatment with mirikizumab should only be initiated and monitored by specialists experienced in treating ulcerative colitis or Crohn's disease.

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 August 2025).

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.

Treatment period:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient 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.

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional 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				
Mirikizumab	Continuously, 1 x every 28 days	13.0	1	13.0
Appropriate comparator therapy				
Adalimumab	Continuously, 1 x every 14 days	26.1	1	26.1
Infliximab	Continuously, 1 x every 56 days	6.5	1	6.5

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Risankizumab	Continuously, 1 x every 56 days	6.5	1	6.5
Ustekinumab	Continuously, 1 x every 84 days	4.3	1	4.3
Vedolizumab	Continuously, 1 x every 14 days	26.1	1	26.1

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Mirikizumab	Continuously, 1 x every 28 days	13.0	1	13.0
Appropriate comparator therapy				
Adalimumab	Continuously, 1 x every 14 days	26.1	1	26.1
Infliximab	Continuously, 1 x every 56 days	6.5	1	6.5
Risankizumab	Continuously, 1 x every 56 days	6.5	1	6.5
Ustekinumab	Continuously, 1 x every 84 days	4.3	1	4.3
Upadacitinib	Continuously, 1 x daily	365.0	1	365.0
Vedolizumab	Continuously, 1 x every 14 days	26.1	1	26.1

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: 77.7 kg).[4]

As it is not always possible to achieve the exact calculated dose per day with the commercially available dosage strengths, in these cases rounding up or down to the next higher or lower available dose that can be achieved with the commercially available dose potencies as well as the scalability of the respective dosage form.

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy

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					
Mirikizumab	300 mg	300 mg	1 x 200 mg + 100 mg	13.0	13 x 200 mg + 100 mg
Appropriate comparator therapy					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Infliximab	5 mg/kg BW = 388.5 mg	388.5 mg	4 x 100 mg	6.5	26 x 100 mg
Risankizumab	360 mg	360 mg	1 x 360 mg	6.5	6.5 x 360 mg
Ustekinumab	90 mg	90 mg	1 x 90 mg	4.3	4.3 x 90 mg
Vedolizumab	108 mg	108 mg	1 x 108 mg	26.1	26.1 x 108 mg

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

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					

[4] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), 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
Mirikizumab	300 mg	300 mg	1 x 200 mg + 100 mg	13.0	13 x 200 mg + 100 mg
Appropriate comparator therapy					
Adalimumab	40 mg	40 mg	1 x 40 mg	26.1	26.1 x 40 mg
Infliximab	5 mg/kg BW = 388.5 mg	388.5 mg	4 x 100 mg	6.5	26 x 100 mg
Risankizumab	360 mg	360 mg	1 x 360 mg	6.5	6.5 x 360 mg
Ustekinumab	90 mg	90 mg	1 x 90 mg	4.3	4.3 x 90 mg
Upadacitinib	15 mg – 30 mg	15 mg – 30 mg	1 x 15 mg – 1 x 30 mg	365.0	365 x 15 mg – 30 mg
Vedolizumab	108 mg	108 mg	1 x 108 mg	26.1	26.1 x 108 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. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

a) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional therapy

and

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

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					
Mirikizumab 100 mg | 200 mg	6 PEN	€ 2,866.96	€ 1.77	€ 160.44	€ 2,704.75

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
Appropriate comparator therapy					
Adalimumab 40 mg[5]	6 SFI	€ 2,804.97	€ 1.77	€ 0.00	€ 2,803.20
Infliximab 100 mg[5]	5 PCI	€ 3,490.57	€ 1.77	€ 0.00	€ 3,488.80
Risankizumab 360 mg	1 SFI	€ 2,925.46	€ 1.77	€ 0.00	€ 2,923.69
Ustekinumab 90 mg	1 SFI	€ 5,818.60	€ 1.77	€ 329.01	€ 5,487.82
Upadacitinib 15 mg	90 SRT	€ 3,494.84	€ 1.77	€ 0.00	€ 3,493.07
Upadacitinib 30 mg	90 SRT	€ 4,459.81	€ 1.77	€ 0.00	€ 4,458.04
Vedolizumab 108 mg	6 SFI	€ 3,602.65	€ 1.77	€ 202.46	€ 3,398.42
Abbreviations: SFI = solution for injection; PEN = solution for injection in a pre-filled pen; PCI = powder for a concentrate for the preparation of an infusion solution					

LAUER-TAXE® last revised: 15 August 2025

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.

The additionally required SHI services for screening for tuberculosis infection are incurred equally for the medicinal product to be assessed and the appropriate comparator therapy, so that they are not presented.

Test for the presence of hepatitis B viral infection prior to the administration of active ingredients of the appropriate comparator therapy (adalimumab, infliximab and upadacitinib). Diagnostics to rule out chronic hepatitis B requires sensibly coordinated steps. 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. In certain case constellations, further steps may be necessary in accordance with current guideline recommendations[6].

[5] Fixed reimbursement rate

[6] S3 guideline on prevention, diagnosis and therapy of hepatitis B virus infection AWMF registry no.: 021/011 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	Costs per unit	Costs per patient per year
Adalimumab Infliximab Upadacitinib	HBV screening			
	HBV test Hepatitis B surface antigen status (GOP 32781)	1	€ 5.06	€ 5.06
	Anti-HBc antibody (GOP 32614)	1	€ 5.43	€ 5.43

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 1 October 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-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.

2.5 Designation of 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 designate 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 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 approved 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 have 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 have 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.

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 requirements 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 have 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 SGB V.

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 moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to conventional 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.

References:
Product information for mirikizumab (Omvoh); Omvoh® 300 mg concentrate for the preparation of an infusion solution; last revised: February 2025

b) Adults with moderately to severely active Crohn's disease who have had an inadequate response, lost response or were intolerant to a biologic agent (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)

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.

References:
Product information for mirikizumab (Omvoh); Omvoh® 300 mg concentrate for the preparation of an infusion solution; last revised: February 2025

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 their session on 6 August 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. At their session on 25 February 2025, the Subcommittee on Medicinal Products adjusted the appropriate comparator therapy.

On 10 March 2025, the pharmaceutical company submitted a dossier for the benefit assessment of mirikizumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 15 March 2025 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 mirikizumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 12 June 2025, and the written statement procedure was initiated with publication on the G-BA website on 16 June 2025. The deadline for submitting statements was 7 July 2025.

The oral hearing was held on 28 July 2025.

By letter dated 29 July 2025, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 15 August 2025.

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 August 2025, and the proposed draft resolution was approved.

At their session on 4 September 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	6 August 2022	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	25 February 2025	Adjustment of the appropriate comparator therapy after positive opinion
Working group Section 35a	15 July 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	28 July 2025	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents

Working group Section 35a	5 August 2025 19 August 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	26 August 2025	Concluding discussion of the draft resolution
Plenum	4 September 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 4 September 2025

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

Prof. Hecken