Mirikizumab (Crohn's disease)

Addendum to Project A25-42 (dossier assessment)[1]

ADDENDUM (DOSSIER ASSESSMENT)

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List of abbreviations

Abbreviation	Meaning
AP	abdominal pain
CDAI	Crohn's Disease Activity Index
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
PRO2	patient-reported outcome 2
RCT	randomized controlled trial
SF	stool frequency
SGB	Sozialgesetzbuch (Social Code Book)

1 Background

On 29 July 2025, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Project A25-42 (Mirikizumab – Benefit assessment according to §35a Social Code Book V) [1].

In its comments, the pharmaceutical company (hereinafter referred to as the "company") submitted supplementary information [2], which went beyond the information provided in the dossier, to prove the added benefit. The commission comprised the assessment of the analyses on Crohn's Disease Activity Index on abdominal pain (CDAI-AP) and on stool frequency (CDAI-SF) with predefined response criteria, which were presented by the company in the commenting procedure, taking into account the information in the dossier [3].

The responsibility for this assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

The double-blind, multicentre randomized controlled trial (RCT) VIVID-1 comparing mirikizumab with ustekinumab or placebo was used for both research questions for benefit assessment A25-42 of mirikizumab [1] in adults 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 agent (tumour necrosis factor α antagonist or integrin inhibitor or interleukin inhibitor). A detailed description of the VIVID-1 study can be found in benefit assessment A25-42 [1].

The outcome corticosteroid-free clinical remission, recorded in the study using patient-reported outcome 2 (PRO2), was used for both research questions. The PRO2 has 2 scales: one scale to record stool frequency (CDAI-SF) and one scale to record abdominal pain (CDAI-AP). According to the predefinition in the study design, remission by PRO2 was defined as an unweighted daily average stool frequency (CDAI-SF) ≤ 3 and unweighted daily average abdominal pain (CDAI-AP) ≤ 1 (each averaged over a period of 7 days) at Week 52, with both values no worse than baseline. According to the study design, the recording of CDAI-SF and CDAI-AP was prespecified as components of PRO2, but not as independent outcomes. In Module 4 A [3], the company did not provide any information on the 2 individual components of PRO2 with the respective predefined response criteria. This information was subsequently submitted by the company in the commenting procedure.

As already explained in the dossier assessment [1], the analyses of CDAI-SF and CDAI-AP, together with the prespecified response criteria, were a comprehensive representation of remission and were thus adequately and sufficiently recorded in the outcome of corticosteroid-free clinical remission. Therefore, the analyses of CDAI-SF and CDAI-AP submitted during the commenting procedure were not used as independent outcomes for the benefit assessment. Consequently, corticosteroid-free clinical remission, recorded by PRO2, was still used for the benefit assessment. The results including effect estimations of the CDAI-SF and CDAI-AP are presented in Appendix A.

2.1 Research question 1: patients who are not eligible for conventional therapy

Results

Table 1 shows the results for the outcome corticosteroid-free clinical remission, taking into account the subsequently submitted analyses of CDAI-SF and CDAI-AP with the prespecified response criteria (footnote c).

Table 1: Results (morbidity) – RCT, direct comparison: mirikizumab vs. ustekinumab (research question 1: patients who are not eligible for conventional therapy)

Study Outcome category Outcome	Mirikizumab		Ustekinumab		Mirikizumab vs. ustekinumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value[a]
VIVID-1					
Morbidity (Week 52)					
Corticosteroid-free clinical remission (PRO2)[b; c]	331	151 (45.6)	164	71 (43.3)	1.04 [0.84; 1.29]; 0.691

a. RR stratified by SES-CD total score at baseline (< 12 points vs. ≥ 12 points) and either CDAI-SF ≥ 7 points and/or CDAI-AP ≥ 2.5 points at baseline (yes vs. no/unknown) with associated 95% CI according to the Mantel-Haenszel-Sato method and p-value of the Cochran-Mantel-Haenszel test.
b. Predefined as the proportion of patients with unweighted daily average SF score ≤ 3 and unweighted daily average AP score ≤ 1 at Week 52. At the same time, both values at Week 52 were not allowed to be worse than at baseline. For the corticosteroid-free clinical remission, patients were also not allowed to have been treated with corticosteroids between Weeks 40 and 52.
c. At Week 52, a total of 230 (69.5%) vs. 107 (65.2%) of the patients had an unweighted daily average SF score ≤ 3, and 200 (60.4%) vs. 96 (58.5%) of the patients had an unweighted daily average AP score ≤ 1. No information is available on the proportion of patients who were not treated with corticosteroids between Week 40 and Week 52.

AP: abdominal pain; CDAI: Crohn's Disease Activity Index; CI: confidence interval; n: number of patients with (at least one) event; N: number of patients analysed; PRO2: patient-reported outcome 2 (abdominal pain and stool frequency); RCT: randomized controlled trial; RR: relative risk; SES-CD: Simple Endoscopic Score for Crohn's Disease; SF: stool frequency

As already shown in the dossier assessment, there was no statistically significant difference between the treatment groups for the outcome corticosteroid-free clinical remission (recorded using PRO2). There was no hint of an added benefit of mirikizumab in comparison with ustekinumab; an added benefit is therefore not proven.

2.2 Research question 2: patients who are not eligible for a biologic agent

Results

Table 2 shows the results for the outcome corticosteroid-free clinical remission, taking into account the subsequently submitted analyses of CDAI-SF and CDAI-AP with the prespecified response criteria (footnote c).

Table 2: Results (morbidity) – RCT, direct comparison: mirikizumab vs. ustekinumab (research question 2: patients who are not eligible for a biologic agent)

Study Outcome category Outcome	Mirikizumab		Ustekinumab		Mirikizumab vs. ustekinumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value[a]
VIVID-1					
Morbidity (Week 52)					
Corticosteroid-free clinical remission (PRO2)[b; c]	300	118 (39.3)	145	51 (35.2)	1.12 [0.87; 1.46]; 0.367

a. RR stratified by SES-CD total score at baseline (< 12 points vs. ≥ 12 points) and either CDAI-SF ≥ 7 points and/or CDAI-AP ≥ 2.5 points at baseline (yes vs. no/unknown) with associated 95% CI according to the Mantel-Haenszel-Sato method and p-value of the Cochran-Mantel-Haenszel test.
b. Predefined as the proportion of patients with unweighted daily average SF score ≤ 3 and unweighted daily average AP score ≤ 1 at Week 52. At the same time, both values at Week 52 were not allowed to be worse than at baseline. For the corticosteroid-free clinical remission, patients were also not allowed to have been treated with corticosteroids between Weeks 40 and 52.
c. At Week 52, a total of 189 (63%) vs. 79 (54.5%) of the patients had an unweighted daily average SF score ≤ 3, and 183 (61%) vs. 84 (57.9%) of the patients had an unweighted daily average AP score ≤ 1. No information is available on the proportion of patients who were not treated with corticosteroids between Week 40 and Week 52.

AP: abdominal pain; CDAI: Crohn's Disease Activity Index; CI: confidence interval; n: number of patients with (at least one) event; N: number of patients analysed; PRO2: patient-reported outcome 2 (abdominal pain and stool frequency); RCT: randomized controlled trial; RR: relative risk; SES-CD: Simple Endoscopic Score for Crohn's Disease; SF: stool frequency

As already shown in the dossier assessment, there was no statistically significant difference between the treatment groups for the outcome corticosteroid-free clinical remission (recorded using PRO2). There was no hint of an added benefit of mirikizumab in comparison with ustekinumab; an added benefit is therefore not proven.

2.3 Summary

The data subsequently submitted by the company in the commenting procedure do not change the conclusion on the added benefit of mirikizumab drawn in dossier assessment A25-42 [1].

The following Table 3 shows the result of the benefit assessment of mirikizumab under consideration of dossier assessment A25-42 and this addendum.

Table 3: Mirikizumab – probability and extent of the added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	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	Adalimumab or infliximab or risankizumab or ustekinumab or vedolizumab[b, c]	Added benefit not proven
2	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 (TNFα antagonist or integrin inhibitor or interleukin inhibitor)	Adalimumab or infliximab or risankizumab or upadacitinib or ustekinumab or vedolizumab[b, c]	Added benefit not proven[d]

a. Presented are the respective ACTs specified by the G-BA.
b. According to the G-BA, a change of drug class can be considered as well as a change within the drug class. It is assumed that any possible dose adjustments have already been exhausted.
c. According to the G-BA, continuation of an inadequate therapy does not concur with the specified ACT.
d. The VIVID-1 study did not include any patients who had received risankizumab as prior therapy or who had an inadequate response with, lost response to, or were intolerant to ustekinumab as prior therapy. It remains unclear whether the observed effects can be transferred to the corresponding patients.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; TNF: tumour necrosis factor

The G-BA decides on the added benefit.

3 References

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Mirikizumab (Morbus Crohn); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2025 [Accessed: 26.06.2025]. URL: https://doi.org/10.60584/A25-42.

2. Lilly Deutschland. Stellungnahme zum IQWiG-Bericht Nr. 2030: Mirikizumab (Morbus Crohn); Nutzenbewertung gemäß § 35a SGB V. [Soon available at: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1194/#beschluesse in the document "Zusammenfassende Dokumentation"].

3. Lilly Deutschland. Mirikizumab (Omvoh); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2025 [Accessed: 01.07.2025]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1194/#dossier.

Appendix A Supplementary presentation of the outcomes CDAI-AP and CDAI-SF with predefined response criteria

Table 4: Results presented as supplementary information (morbidity) – RCT, direct comparison: mirikizumab vs. ustekinumab (research question 1: patients who are not eligible for conventional therapy)

Study Outcome category Outcome	Mirikizumab		Ustekinumab		Mirikizumab vs. ustekinumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value[a]
VIVID-1					
Morbidity (Week 52)					
Stool frequency (CDAI-SF)[b]	331	230 (69.5)	164	107 (65.2)	1.05 [0.92; 1.2]; 0.427
Abdominal pain (CDAI-AP)[c]	331	200 (60.4)	164	96 (58.5)	1.02 [0.88; 1.19]; 0.776

a. RR stratified by SES-CD total score at baseline (< 12 points vs. ≥ 12 points) and either CDAI-SF ≥ 7 points and/or CDAI-AP ≥ 2.5 points at baseline (yes vs. no/unknown) with associated 95% CI according to the Mantel-Haenszel-Sato method and p-value of the Cochran-Mantel-Haenszel test.
b. Predefined as the proportion of patients with an unweighted daily average SF score ≤ 3 at Week 52.
c. Predefined as the proportion of patients with an unweighted daily average AP score ≤ 1 at Week 52.

AP: abdominal pain; CDAI: Crohn's Disease Activity Index; CI: confidence interval; n: number of patients with (at least one) event; N: number of patients analysed; RCT: randomized controlled trial; RR: relative risk; SES-CD: Simple Endoscopic Score for Crohn's Disease; SF: stool frequency

Table 5: Results presented as supplementary information (morbidity) – RCT, direct comparison: mirikizumab vs. ustekinumab (research question 2: patients who are not eligible for a biologic agent)

Study Outcome category Outcome	Mirikizumab		Ustekinumab		Mirikizumab vs. ustekinumab
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value[a]
VIVID-1					
Morbidity (Week 52)					
Stool frequency (CDAI-SF)[b]	300	189 (63)	145	79 (54.5)	1.16 [0.97; 1.38]; 0.084
Abdominal pain (CDAI-AP)[c]	300	183 (61)	145	84 (57.9)	1.06 [0.9; 1.25]; 0.487

a. RR stratified by SES-CD total score at baseline (< 12 points vs. ≥ 12 points) and either CDAI-SF ≥ 7 points and/or CDAI-AP ≥ 2.5 points at baseline (yes vs. no/unknown) with associated 95% CI according to the Mantel-Haenszel-Sato method and p-value of the Cochran-Mantel-Haenszel test.
b. Predefined as the proportion of patients with an unweighted daily average SF score ≤ 3 at Week 52.
c. Predefined as the proportion of patients with an unweighted daily average AP score ≤ 1 at Week 52.

AP: abdominal pain; CDAI: Crohn's Disease Activity Index; CI: confidence interval; n: number of patients with (at least one) event; N: number of patients analysed; RCT: randomized controlled trial; RR: relative risk; SES-CD: Simple Endoscopic Score for Crohn's Disease; SF: stool frequency