Risankizumab (ulcerative colitis)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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[1] Translation of Sections I 1 to I 4 of the dossier assessment *Risankizumab (Colitis ulcerosa) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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No advisor on medical and scientific questions was involved in the present dossier assessment.

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No patients or families were involved in the present dossier assessment.

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Part I: Benefit assessment

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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug risankizumab. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 20 August 2024.

Research question

The aim of this report is to assess the added benefit of risankizumab in comparison with the appropriate comparator therapy (ACT) in adults with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to either conventional treatment or a biologic drug.

The research questions presented in Table 2 result from the ACT specified by the G-BA.

Table 2: Research questions of the benefit assessment of risankizumab

Research question	Therapeutic indication	ACT[a]
Adults with moderately to severely active ulcerative colitis[b]		
1	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment	A TNF-α antagonist (adalimumab or golimumab or infliximab[c]) or vedolizumab or ustekinumab or ozanimod
2	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment[d]	Vedolizumab or tofacitinib or ustekinumab or filgotinib or ozanimod or a TNF-α antagonist[c] (adalimumab or golimumab or infliximab[c])[e]

a. Presented is the respective ACT specified by the G-BA. Risankizumab is assumed to be administered as long-term therapy (induction and maintenance). Hence, drugs which are options only for the initial reduction of disease activity according to the guideline are disregarded below. Corticosteroids are generally deemed appropriate for flare treatment. Continuation of an inadequate therapy does not constitute an implementation of the ACT.
b. For patients who continue to be candidates for drug therapy, a decision in favour of surgical resection is presumed to represent an individualized choice for that particular patient if necessary and to not be the rule; surgical resection is therefore to be disregarded when determining the ACT.
c. If infliximab is used, it should be combined with a thiopurine, if necessary.
d. As biologic agents, the G-BA has listed the following: TNF-α antagonist or integrin inhibitor or interleukin inhibitor.
e. Switching within or between drug classes is permitted. Any potential dose adjustment options are assumed to have already been exhausted. In case of primary failure of TNF-α antagonist treatment, switching to another drug class is indicated. In secondary failure of TNF-α antagonist treatment, a switch within the drug class may be contemplated.

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

The company followed the G-BA's specification of the ACT in both research questions. The company stated that it did not present research questions 1 and 2 separately, as it did not identify any evidence for a direct comparison of risankizumab with the ACT. In line with the G-BA's specification, the present benefit assessment is conducted separately for the 2 research questions, each in comparison with the ACT specified by the G-BA.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 24 weeks were used for deriving any added benefit.

Results

Concurring with the company, the check for completeness of the study pool identified no relevant study for the direct comparison of risankizumab with the ACT for any of the research questions. Due to a lack of studies of direct comparisons, the company presented results from individual sub-studies of the approval studies INSPIRE (M16-067) and COMMAND (M16-066) in the dossier to assess the efficacy and tolerability of risankizumab.

Concurring with the company, the studies INSPIRE and COMMAND are not suitable for the benefit assessment of risankizumab versus the ACT. The induction study INSPIRE and the maintenance study COMMAND are studies comparing risankizumab with placebo. Consequently, patients under treatment with placebo did not receive active therapy in the sense of the ACT.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of risankizumab in comparison with the ACT for either research question; an added benefit is therefore not proven for either of the two research questions.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 summarizes the probability and extent of added benefit of risankizumab.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Risankizumab – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
Adults with moderately to severely active ulcerative colitis[b]			
1	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment	A TNF-α antagonist[c] (adalimumab or golimumab or infliximab[c]) or vedolizumab or ustekinumab or ozanimod	Added benefit not proven
2	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment[d]	Vedolizumab or tofacitinib or ustekinumab or filgotinib or ozanimod or a TNF-α antagonist (adalimumab or golimumab or infliximab[c])[e]	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA. Risankizumab is assumed to be administered as long-term therapy (induction and maintenance). Hence, drugs which are options only for the initial reduction of disease activity according to the guideline are disregarded below. Corticosteroids are generally deemed appropriate for flare treatment. Continuation of an inadequate therapy does not constitute an implementation of the ACT.
b. For patients who continue to be candidates for drug therapy, a decision in favour of surgical resection is presumed to represent an individualized choice for that particular patient if necessary and to not be the rule; surgical resection is therefore to be disregarded when determining the ACT.
c. If infliximab is used, it should be combined with a thiopurine, if necessary.
d. As biologic agents, the G-BA has listed the following: TNF-α antagonist or integrin inhibitor or interleukin inhibitor.
e. Switching within or between drug classes is permitted. Any potential dose adjustment options are assumed to have already been exhausted. In case of primary failure of TNF-α antagonist treatment, switching to another drug class is indicated. In secondary failure of TNF-α antagonist treatment, a switch within the drug class may be contemplated.

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

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report is to assess the added benefit of risankizumab in comparison with the ACT in adults with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to either conventional treatment or a biologic drug.

The research questions presented in Table 4 result from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of risankizumab

Research question	Therapeutic indication	ACT[a]
Adults with moderately to severely active ulcerative colitis[b]		
1	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment	A TNF-α antagonist[c] (adalimumab or golimumab or infliximab[c]) or vedolizumab or ustekinumab or ozanimod
2	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment[d]	Vedolizumab or tofacitinib or ustekinumab or filgotinib or ozanimod or a TNF-α antagonist[c] (adalimumab or golimumab or infliximab[c])[e]

a. Presented is the respective ACT specified by the G-BA. Risankizumab is assumed to be administered as long-term therapy (induction and maintenance). Hence, drugs which are options only for the initial reduction of disease activity according to the guideline are disregarded below. Corticosteroids are generally deemed appropriate for flare treatment. Continuation of an inadequate therapy does not constitute an implementation of the ACT.
b. For patients who continue to be candidates for drug therapy, a decision in favour of surgical resection is presumed to represent an individualized choice for that particular patient if necessary and to not be the rule; surgical resection is therefore to be disregarded when determining the ACT.
c. If infliximab is used, it should be combined with a thiopurine, if necessary.
d. As biologic agents, the G-BA has listed the following: TNF-α antagonist or integrin inhibitor or interleukin inhibitor.
e. Switching within or between drug classes is permitted. Any potential dose adjustment options are assumed to have already been exhausted. In case of primary failure of TNF-α antagonist treatment, switching to another drug class is indicated. In secondary failure of TNF-α antagonist treatment, a switch within the drug class may be contemplated.

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

The company followed the G-BA's specification of the ACT in both research questions. The company stated that it did not present research questions 1 and 2 separately, as it did not identify any evidence for a direct comparison of risankizumab with the ACT. In line with the G-BA’s specification, the present benefit assessment is conducted separately for the 2 research questions, each in comparison with the ACT specified by the G-BA. Since no suitable data are available for either of the 2 research questions designated by the G-BA, the assessment below is performed in a joint section of the report.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs with a minimum duration of 24 weeks were used for deriving any added benefit. This deviates from inclusion criteria of the company, which specified a minimum study duration of 52 weeks.

I 3 Information retrieval and study pool

The study pool of the assessment was compiled on the basis of the following information:

Sources of the company in the dossier:

- study list on risankizumab (status: 03 June 2024)
- bibliographical literature search on risankizumab (last search on 03 June 2024)
- search in trial registries/trial results databases for studies on risankizumab (last search on 03 June 2024)

To check the completeness of the study pool:

- search in trial registries for studies on risankizumab (last search on 05 September 2024); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check for completeness of the study pool identified no relevant study for the direct comparison of risankizumab with the ACT for any of the research questions.

Due to a lack of studies of direct comparisons, the company presented results from individual sub-studies of the approval studies INSPIRE (M16-067) [3] and COMMAND (M16-066) [3] in the dossier to assess the efficacy and tolerability of risankizumab. The company does not claim an added benefit.

The induction study INSPIRE and the maintenance study COMMAND are studies comparing risankizumab with placebo. In Module 4 A, the company presents the results of substudy 2 at Week 12 (so-called induction period 1) for the INSPIRE study and the results of substudy 1 at Week 52 for the COMMAND study. According to the study protocol, the use of almost all drugs/drug classes listed in the G-BA's ACT was prohibited. Only ozanimod was not explicitly listed as a prohibited concomitant medication in the respective study protocols. However, no patients were treated with ozanimod during the studies INSPIRE and COMMAND. Consequently, patients under treatment with placebo did not receive active therapy in the sense of the ACT (see Table 4). Concurring with the company’s assessment, both studies are thus unsuitable to derive conclusions on the added benefit of risankizumab versus the ACT.

I 4 Results on added benefit

No suitable data are available to assess the added benefit of risankizumab in comparison with the ACT in adults with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional treatment or a biologic agent. There is no hint of added benefit of risankizumab in comparison with the ACT for either research question; an added benefit is therefore not proven for either of them.

I 5 Probability and extent of added benefit

Table 5 summarizes the result of the assessment of the added benefit of risankizumab in comparison with the ACT.

Table 5: Risankizumab – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
Adults with moderately to severely active ulcerative colitis[b]			
1	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment	A TNF-α antagonist (adalimumab or golimumab or infliximab[c]) or vedolizumab or ustekinumab or ozanimod	Added benefit not proven
2	Patients who have had an inadequate response to, lost response to, or are intolerant to biologic treatment[d]	Vedolizumab or tofacitinib or ustekinumab or filgotinib or ozanimod or a TNF-α antagonist (adalimumab or golimumab or infliximab[c])[e]	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA. Risankizumab is assumed to be administered as long-term therapy (induction and maintenance). Hence, drugs which are options only for the initial reduction of disease activity according to the guideline are disregarded below. Corticosteroids are generally deemed appropriate for flare treatment. Continuation of an inadequate therapy does not constitute an implementation of the ACT.
b. For patients who continue to be candidates for drug therapy, a decision in favour of surgical resection is presumed to represent an individualized choice for that particular patient if necessary and to not be the rule; surgical resection is therefore to be disregarded when determining the ACT.
c. If infliximab is used, it should be combined with a thiopurine, if necessary.
d. As biologic agents, the G-BA has listed the following: TNF-α antagonist or integrin inhibitor or interleukin inhibitor.
e. Switching within or between drug classes is permitted. Any potential dose adjustment options are assumed to have already been exhausted. In case of primary failure of TNF-α antagonist treatment, switching to another drug class is indicated. In secondary failure of TNF-α antagonist treatment, a switch within the drug class may be contemplated.

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

The assessment described above concurs with that by the company.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 06.10.2023]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a24-84.html