IQWiG Reports – Commission No. A21-155

Filgotinib (ulcerative colitis) –

Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Filgotinib (Colitis ulcerosa) – Nutzenbewertung gemäß § 35a SGB V* (Version 2.0; Status: 16 May 2022). Please note: This document was translated by an external translator and 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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IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Birgit Kaltz.

IQWiG thanks the respondent for participating in the written exchange about how they experienced the disease and its treatment and about the treatment goals. The respondent was not involved in the actual preparation of the dossier assessment.

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

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)
JAK	Janus kinase
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

2 Benefit assessment

2.1 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 filgotinib. 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 1 December 2021.

Research question

This aim of this report is to assess the added benefit of filgotinib in comparison with the appropriate comparator therapy (ACT) in adult patients with moderately to severely active ulcerative colitis and an inadequate response, loss of response, or intolerance to conventional therapy or a biologic agent.

The research questions shown in Table 2 resulted from the ACT specified by the G-BA.

Table 2: Research questions of the benefit assessment of filgotinib

Research question	Therapeutic indication	ACT[a]
1	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or have intolerance or contraindications to conventional treatment[b]	A TNF-α antagonist (adalimumab or infliximab or golimumab) or vedolizumab or tofacitinib or ustekinumab
2	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to treatment with a biologic drug (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)[b]	Vedolizumab or tofacitinib or a TNF-α antagonist (adalimumab or infliximab or golimumab) or ustekinumab, each in consideration of approval and prior treatment(s)[c]

a. Presented is the respective ACT specified by the G-BA. Filgotinib is assumed to be used as long-term therapy (induction and maintenance). Hence, drugs whose use is weighed only for the initial reduction of disease activity in accordance with the guideline are disregarded below. Corticosteroids are generally deemed adequate flare therapy. Continuation of an inadequate therapy does not represent an implementation of the ACT.
b. Patients who are still candidates for pharmacological therapy (such as biologics and JAK inhibitors) are assumed to not yet be candidates for proctocolectomy.
c. Switching between or within drug classes is allowed. Any potential dose modification 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 considered.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; JAK: Janus kinase; TNF-α: tumour necrosis factor alpha

For both research questions, the company followed the specification of the ACT without choosing one of the ACT options specified by the G-BA in each case.

The assessment was 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 12 months were used for the derivation of the added benefit.

Results

Concurring with the company, the check of the completeness of the study pool identified no RCT that would allow a direct comparison of filgotinib versus the ACT for either of the two research questions.

In the absence of directly comparative data, the company examined the possibility of conducting an adjusted indirect comparison using the common comparator of placebo. However, the company reports that the studies identified based on its inclusion criteria are, on the comparator side, unsuitable for an indirect comparison and foregoes such a comparison.

No suitable data are available for assessing the added benefit of filgotinib in comparison with the ACT in adult patients with moderate to severe active ulcerative colitis who did not adequately respond to, no longer respond to, or do not tolerate conventional therapy or a biologic agent. This results in no hint of added benefit of filgotinib in comparison with the ACT for either of the 2 research questions; an added benefit is therefore not proven for either of them.

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

Table 3 shows a summary of probability and extent of the added benefit of filgotinib.

[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: Filgotinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or have intolerance or contraindications to conventional treatment[b]	A TNF-α antagonist (adalimumab or infliximab or golimumab) or vedolizumab or tofacitinib or ustekinumab	Added benefit not proven
2	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to treatment with a biologic drug (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)[b]	Vedolizumab or tofacitinib or a TNF-α antagonist (adalimumab or infliximab or golimumab) or ustekinumab, each in consideration of approval and prior treatment(s)[c]	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA. Filgotinib is assumed to be used as long-term therapy (induction and maintenance). Hence, drugs whose use is weighed only for the initial reduction of disease activity in accordance with the guideline are disregarded below. Corticosteroids are generally deemed adequate flare therapy. Continuation of an inadequate therapy does not represent an implementation of the ACT.
b. Patients who are still candidates for pharmacological therapy (such as biologics and JAK inhibitors) are assumed to not yet be candidates for proctocolectomy.
c. Switching between or within drug classes is allowed. Any potential dose modification 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 considered.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; JAK: Janus kinase; TNF-α: tumour necrosis factor alpha

The G-BA decides on the added benefit.

2.2 Research question

This aim of this report is to assess the added benefit of filgotinib in comparison with the ACT in adult patients with moderately to severely active ulcerative colitis who did not adequately respond to, no longer respond to, or do not tolerate conventional therapy or a biologic agent.

The research questions shown in Table 4 resulted from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of filgotinib

Research question	Therapeutic indication	ACT[a]
1	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or have intolerance or contraindications to conventional treatment[b]	A TNF-α antagonist (adalimumab or infliximab or golimumab) or vedolizumab or tofacitinib or ustekinumab
2	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to treatment with a biologic drug (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)[b]	Vedolizumab or tofacitinib or a TNF-α antagonist (adalimumab or infliximab or golimumab) or ustekinumab, each in consideration of approval and prior treatment(s)[c]

a. Presented is the respective ACT specified by the G-BA. Filgotinib is assumed to be used as long-term therapy (induction and maintenance). Hence, drugs whose use is weighed only for the initial reduction of disease activity in accordance with the guideline are disregarded below. Corticosteroids are generally deemed adequate flare therapy. Continuation of an inadequate therapy does not represent an implementation of the ACT.
b. Patients who are still candidates for pharmacological therapy (such as biologics and JAK inhibitors) are assumed to not yet be candidates for proctocolectomy.
c. Switching between or within drug classes is allowed. Any potential dose modification 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 considered.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; JAK: Janus kinase; TNF-α: tumour necrosis factor alpha

On receipt of the dossier, the G-BA adjusted the ACT on 14 December 2021 in accordance with the presentation in Table 4 [3]. This results in no changes for research question 1. For research question 2, the modification excludes patients who have had an inadequate response to, lost response to, or are intolerant to treatment with a Janus kinase (JAK) inhibitor from the relevant patient population. The drugs / drug classes specified as ACTs are unaffected by the modification. The present benefit assessment was conducted in accordance with the adjusted ACT.

The G-BA's modification of the patient population for research question 2 remains without consequence for the benefit assessment part of the present dossier assessment because the company follows the specified modified ACT for both research questions without selecting, in each case, one of the ACT options specified by the G-BA.

The assessment was 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 12 months were used for the derivation of the added benefit. This concurs with the company's inclusion criteria.

2.3 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 filgotinib (status: 10 September 2021)
- bibliographical literature search on filgotinib (last search on 9 September 2021)
- search in trial registries / trial results databases for studies on filgotinib (last search on 21 September 2021)
- search on the G-BA website for filgotinib (last search on 21 September 2021)
- bibliographical literature search on ACTs (last search on 10 September 2021)
- search in trial registries for studies on ACTs (last search on 13 September 2021)

To check the completeness of the study pool:

- search in trial registries for studies on filgotinib (last search on 21 December 2021); for search strategies, see Appendix A of the full dossier assessment

Concurring with the company, the check of the completeness of the study pool identified no RCT that would allow a direct comparison of filgotinib versus the ACT for either of the two research questions.

In Module 4 A, the company nevertheless submitted, for all research questions, results on its SELECTION RCT [4] which compares filgotinib with placebo. However, reasoning consistently, the company did not derive any added benefit from it (see the below section on the SELECTION study).

In the absence of directly comparative data, the company examined the possibility of conducting an adjusted indirect comparison using the common comparator of placebo. For this purpose, the company used its inclusion criteria to identify, on the intervention side, its SELECTION RCT. For the comparator therapy, the company identified a total of 13 potentially relevant studies [5-13]. However, it stated that it is not possible to carry out an adjusted indirect comparison on the basis of these studies, as they are unsuitable for various reasons. In this regard, the company cited differences in the duration of the induction phases as well as deviations in the included patient populations and rerandomization schemes between the identified studies for the comparator therapy and the SELECTION RCT on the intervention side. Overall, the company therefore did not carry out an adjusted indirect comparison. All

things considered, the company sees no proof of added benefit of filgotinib in comparison with the ACT.

Evidence on filgotinib presented by the company

SELECTION study

The SELECTION study is a randomized double-blind, study comparing filgotinib with placebo. It included adult patients (aged 18–75 years) with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to treatment with at least 1 corticosteroid or immunomodulator or at least 1 biologic agent. In the induction phase, patients were randomized in a 2:2:1 ratio to treatment with 200 mg filgotinib or 100 mg filgotinib or placebo. Patients who exhibited a clinical response at Week 10 were rerandomized as follows for the subsequent 48-week maintenance phase: patients who had received 200 mg (or 100 mg) filgotinib in the induction phase were randomized in a 2:1 ratio to continuation of 200 mg (or 100 mg) filgotinib or placebo. Patients who had received placebo in the induction phase continued on placebo during the maintenance phase.

The study did not implement the ACT for either of the 2 research questions. Concurring with the company, the SELECTION study is therefore deemed unsuitable for assessing added benefit of filgotinib in comparison with the ACT.

2.4 Results on added benefit

No suitable data are available for assessing the added benefit of filgotinib in comparison with the ACT in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to conventional therapy or a biologic agent. This results in no hint of added benefit of filgotinib in comparison with the ACT for either of the 2 research questions; an added benefit is therefore not proven for either of them.

2.5 Probability and extent of added benefit

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

Table 5: Filgotinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or have intolerance or contraindications to conventional treatment[b]	A TNF-α antagonist (adalimumab or infliximab or golimumab) or vedolizumab or tofacitinib or ustekinumab	Added benefit not proven
2	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or are intolerant to treatment with a biologic drug (TNF-α antagonist or integrin inhibitor or interleukin inhibitor)[b]	Vedolizumab or tofacitinib or a TNF-α antagonist (adalimumab or infliximab or golimumab) or ustekinumab, each in consideration of approval and prior treatment(s)[c]	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA. Filgotinib is assumed to be used as long-term therapy (induction and maintenance). Hence, drugs whose use is weighed only for the initial reduction of disease activity in accordance with the guideline are disregarded below. Corticosteroids are generally deemed adequate flare therapy. Continuation of an inadequate therapy does not represent an implementation of the ACT.
b. Patients who are still candidates for pharmacological therapy (such as biologics and JAK inhibitors) are assumed to not yet be candidates for proctocolectomy.
c. Switching between or within drug classes is allowed. Any potential dose modification 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 considered.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; JAK: Janus kinase; TNF-α: tumour necrosis factor alpha

The assessment described above concurs with that of the company in each case.

The G-BA decides on the added benefit.

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.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a21-155.html.