IQWiG Reports – Commission No. A22-33_

Vedolizumab (antibiotic-refractory chronic pouchitis) –

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

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Vedolizumab (Antibiotika-refraktäre, chronische Pouchitis) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 25 May 2022). 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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Address of publisher
Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Medical and scientific advice

- C. F. Dietrich, Germany

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 she experienced the disease and its treatment and about the treatment goals. The respondent was not involved in the actual preparation of the dossier assessment.

IQWiG employees involved in the dossier assessment

- Anne Hüning
- Katharina Frangen
- Charlotte Guddat
- Claudia Kapp
- Florina Kerekes
- Ulrike Seay
- Carolin Weigel

Keywords: Vedolizumab, Pouchitis, Benefit 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)
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 vedolizumab. 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 28 February 2022.

Research question

The aim of the present report is to assess the added benefit of vedolizumab in comparison with treatment of physician's choice as the appropriate comparator therapy (ACT) in adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis.

The research question presented in Table 2 was derived from the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of vedolizumab

Therapeutic indication	**ACT**[a]
Adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis[b]	Treatment of physician's choice[c]
a. Presented is the ACT specified by the G-BA. b. It is assumed that antibiotic therapy is no longer an option for patients with antibiotic-refractory (chronic) pouchitis. c. No drug therapies are approved for the treatment of patients with antibiotic-refractory (chronic) pouchitis. The drugs mentioned in the treatment recommendations are also not specifically approved for the treatment of (chronic) antibiotic-refractory pouchitis. According to the G-BA, the following therapies are considered suitable comparators for the treatment of physician's choice within the framework of a clinical study: oral or topical budesonide, infliximab, adalimumab, ustekinumab and tacrolimus. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification of the ACT.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Results

Concurring with the company, the check of the completeness of the study pool identified no randomized controlled trial (RCT) that would allow a direct comparison of vedolizumab versus treatment of physician's choice.

In addition, the company searched for RCTs for an indirect comparison of vedolizumab with a treatment of physician's choice. For the intervention side, the company identified the EARNEST study, which compared vedolizumab with placebo. The company was unable to identify any studies for the comparator side (treatment of physician's choice). In summary, the company consequently stated that due to the lack of studies for a direct or indirect comparison, an added benefit of vedolizumab versus the ACT was not proven.

There are no suitable data available for the assessment of vedolizumab in comparison to treatment of physician's choice in adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis. This resulted in no hint of an added benefit of vedolizumab versus treatment of physician's choice; an added benefit is therefore not proven.

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

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

Table 3: Vedolizumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis[b]	Treatment of physician's choice[c]	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. It is assumed that antibiotic therapy is no longer an option for patients with antibiotic-refractory (chronic) pouchitis.
c. No drug therapies are approved for the treatment of patients with antibiotic-refractory (chronic) pouchitis. The drugs mentioned in the treatment recommendations are also not specifically approved for the treatment of (chronic) antibiotic-refractory pouchitis. According to the G-BA, the following therapies are considered suitable comparators for the treatment of physician's choice within the framework of a clinical study: oral or topical budesonide, infliximab, adalimumab, ustekinumab and tacrolimus.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

[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].

2.2 Research question

The aim of the present report is to assess the added benefit of vedolizumab in comparison with treatment of physician's choice as the ACT in adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis.

The research question presented in Table 4 was derived from the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of vedolizumab

Therapeutic indication	**ACT[a]**
Adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis[b]	Treatment of physician's choice[c]
a. Presented is the ACT specified by the G-BA. b. It is assumed that antibiotic therapy is no longer an option for patients with antibiotic-refractory (chronic) pouchitis. c. No drug therapies are approved for the treatment of patients with antibiotic-refractory (chronic) pouchitis. The drugs mentioned in the treatment recommendations are also not specifically approved for the treatment of (chronic) antibiotic-refractory pouchitis. According to the G-BA, the following therapies are considered suitable comparators for the treatment of physician's choice within the framework of a clinical study: oral or topical budesonide, infliximab, adalimumab, ustekinumab and tacrolimus. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification on the ACT.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

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 lists on vedolizumab (status: 28 January 2022)
- bibliographical literature search on vedolizumab (last search on 19 January 2022)
- search in trial registries / trial results databases for studies on vedolizumab (last search on 19 January 2022)
- search on the G-BA website for vedolizumab (last search on 19 January 2022)
- bibliographical literature search on the ACT (last search on 19 January 2022)
- search in trial registries/trial results databases for studies on the ACT (last search on 19 January 2022)

- search on the G-BA website for the ACT (last search on 19 January 2022)

To check the completeness of the study pool:

- search in trial registries for studies on vedolizumab (last search on 09 March 2022); 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 vedolizumab versus treatment of physician's choice.

In addition, the company searched for RCTs for an indirect comparison of vedolizumab with a treatment of physician's choice. For the intervention side, the company identified the EARNEST study, which compared vedolizumab with placebo [3]. The company was unable to identify any studies for the comparator side (treatment of physician's choice). In summary, the company consequently stated that due to the lack of studies for a direct or indirect comparison, an added benefit of vedolizumab versus the ACT was not proven. The company explicitly did not include the EARNEST study in the assessment of the added benefit of vedolizumab. However, it presented the design of the EARNEST study and results from this study in Module 4 C [4].

2.4 Results on added benefit

There are no suitable data available for the assessment of vedolizumab in comparison to treatment of physician's choice in adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis. This resulted in no hint of an added benefit of vedolizumab versus treatment of physician's choice; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

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

Table 5: Vedolizumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adults with moderate to severe active chronic pouchitis, who have had an inadequate response with or lost response to antibiotic therapy or have had intolerance to this treatment, and who had undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis[b]	Treatment of physician's choice[c]	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. It is assumed that antibiotic therapy is no longer an option for patients with antibiotic-refractory (chronic) pouchitis.
c. No drug therapies are approved for the treatment of patients with antibiotic-refractory (chronic) pouchitis. The drugs mentioned in the treatment recommendations are also not specifically approved for the treatment of (chronic) antibiotic-refractory pouchitis. According to the G-BA, the following therapies are considered suitable comparators for the treatment of physician's choice within the framework of a clinical study: oral or topical budesonide, infliximab, adalimumab, ustekinumab and tacrolimus.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The assessment described above concurs with that of the company.

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.

1. Institute for Quality and Efficiency in Health Care. General Methods; Version 6.1 [online]. 2022 [Accessed: 17.08.2022]. URL: https://www.iqwig.de/methoden/general-methods_version-6-1.pdf.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a22-33.html.