IQWiG Reports – Commission No. A21-165

Tofacitinib (ankylosing spondylitis) –

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

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Tofacitinib (ankylosierende Spondylitis) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 8 March 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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No advisor on medical and scientific questions was available for the present dossier assessment.

Patient and family involvement

No feedback was received in the framework of the present 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)
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 tofacitinib. 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 13 December 2021.

Research question

The aim of this report is to assess the added benefit of tofacitinib in comparison with the appropriate comparator therapy (ACT) in adult patients with active ankylosing spondylitis who have had an inadequate response to conventional therapy.

The ACT specified by the G-BA differs depending on the patients' pretreatment. The resulting research questions are shown in Table 2.

Table 2: Research questions on the benefit assessment of tofacitinib

Research question	Therapeutic indication	ACT[a]
Adults with active ankylosing spondylitis[b]		
1	Patients who have responded inadequately to conventional therapy	TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL17 inhibitor (secukinumab)
2	Patients who have had an inadequate response or shown intolerance to prior therapy with bDMARDs	Switch to another bDMARD: TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL-17 inhibitor (secukinumab)

a. Presented is the respective ACT specified by the G-BA.
b. Also known as active radiographic axial spondyloarthritis.

ACT: appropriate comparator therapy; bDMARD: biologic disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; IL: interleukin; TNF: tumour necrosis factor

The company used the specified ACT for both research questions.

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 24 weeks were used for the derivation of added benefit.

Results

Concurring with the company's assessment, the check for completeness of the study pool did not identify any relevant RCT allowing a comparison of tofacitinib with the ACT for either of the 2 research questions.

Overall, no data are therefore available to assess the added benefit of tofacitinib in comparison with the ACT in adult patients with ankylosing spondylitis who have responded inadequately to conventional therapy. Consequently, there is no hint of added benefit of tofacitinib in comparison with the ACT for either research question; 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 the probability and extent of added benefit of tofacitinib.

Table 3: Tofacitinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
Adults with active ankylosing spondylitis[b]			
1	Patients who have responded inadequately to conventional therapy	TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL17 inhibitor (secukinumab)	Added benefit not proven
2	Patients who have had an inadequate response or shown intolerance to prior therapy with bDMARDs	Switch to another bDMARD: TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL-17 inhibitor (secukinumab)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. Also known as active radiographic axial spondyloarthritis.

ACT: appropriate comparator therapy; bDMARD: biologic disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; IL: interleukin; TNF: tumour necrosis factor

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 this report is to assess the added benefit of tofacitinib in comparison with the ACT in adult patients with active ankylosing spondylitis who have had an inadequate response to conventional therapy.

The ACT specified by the G-BA differs depending on the pretreatment of the patients. The resulting research questions are shown in Table 4.

Table 4: Research questions on the benefit assessment of tofacitinib

Research question	Therapeutic indication	ACT[a]
Adults with active ankylosing spondylitis[b]		
1	Patients who have responded inadequately to conventional therapy	TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL17 inhibitor (secukinumab)
2	Patients who have had an inadequate response or shown intolerance to prior therapy with bDMARDs	Switch to another bDMARD: TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL-17 inhibitor (secukinumab)

a. Presented is the respective ACT specified by the G-BA.
b. Also known as active radiographic axial spondyloarthritis.

ACT: appropriate comparator therapy; bDMARD: biologic disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; IL: interleukin; TNF: tumour necrosis factor

The company used the specified ACT for both research questions.

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 24 weeks were used for the derivation of 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 tofacitinib (status: 8 November 2021)
- bibliographical literature search on tofacitinib (last search on 1 November 2021)
- search in trial registries / study results databases on tofacitinib (last search on 1 November 2021)
- search on the G-BA website on tofacitinib (last search on 1 November 2021)

To check the completeness of the study pool:

- search in trial registries for studies on tofacitinib (last search on 13 January 2022); for search strategies, see Appendix A of the full dossier assessment

The check of completeness did not find any relevant RCT for assessing the added benefit of tofacitinib in comparison with the ACT. This applies to both research questions and corresponds to the company's assessment.

The company reports that 2 RCTs have been conducted on tofacitinib in the indication of ankylosing spondylitis: A3921119 [3] and A3921120 [4]. Given their respective study durations of 12 and 16 weeks, however, the company argues that both studies are too short for inclusion in the benefit assessment, which would require a minimum duration of 24 weeks. This reasoning is plausible. Hence, the company's dossier failed to present any evidence for assessing the added benefit of tofacitinib in comparison with the ACT.

2.4 Results on added benefit

No data are available for assessing the added benefit of tofacitinib in comparison the ACT in adults with active ankylosing spondylitis. This applies both to patients who have had an inadequate response to conventional therapy (research question 1) and to patients who have had an inadequate response or shown intolerance to prior bDMARD therapy (research question 2). Consequently, there is no hint of added benefit of tofacitinib in comparison with the ACT for either research question; 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 tofacitinib in comparison with the ACT.

Table 5: Tofacitinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
Adults with active ankylosing spondylitis[b]			
1	Patients who have responded inadequately to conventional therapy	TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL17 inhibitor (secukinumab)	Added benefit not proven
2	Patients who have had an inadequate response or shown intolerance to prior therapy with bDMARDs	Switch to another bDMARD: TNF-α inhibitor (adalimumab or certolizumab pegol or etanercept or golimumab or infliximab) or IL-17 inhibitor (secukinumab)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. Also known as active radiographic axial spondyloarthritis.

ACT: appropriate comparator therapy; bDMARD: biologic disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; IL: interleukin; TNF: tumour necrosis factor

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 6.0 [online]. 2020 [Accessed: 22.03.2021]. URL: https://www.iqwig.de/methoden/general-methods_version-6-0.pdf.

2. Skipka G, Wieseler B, Kaiser T et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2016; 58(1): 43-58. https://dx.doi.org/10.1002/bimj.201300274.

3. van der Heijde D, Deodhar A, Wei JC et al. Tofacitinib in patients with ankylosing spondylitis: a phase II, 16-week, randomised, placebo-controlled, dose-ranging study. Ann Rheum Dis 2017; 76(8): 1340-1347. https://dx.doi.org/10.1136/annrheumdis-2016-210322.

4. Deodhar A, Sliwinska-Stanczyk P, Xu H et al. Tofacitinib for the treatment of ankylosing spondylitis: a phase III, randomised, double-blind, placebo-controlled study. Ann Rheum Dis 2021; 80(8): 1004-1013. https://dx.doi.org/10.1136/annrheumdis-2020-219601.

The full report (German version) is published under https://www.iqwig.de/en/projects/a21-165.html.