IQWiG Reports – Commission No. A22-92

Upadacitinib (non-radiographic axial spondyloarthritis) –

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

Extract

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Upadacitinib (nicht röntgenologische axiale Spondyloarthritis) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 29 November 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 her 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 Eberhard Bärthel.

IQWiG thanks the respondent for participating in the written exchange about how he 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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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
CRP	C-reactive protein
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MRI	magnetic resonance imaging
NSAID	nonsteroidal anti-inflammatory drug
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 upadacitinib. 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 29 August 2022.

Research question

The aim of the present report is to assess the added benefit of upadacitinib in comparison with the appropriate comparator therapy (ACT) for the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs).

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

Table 2: Research question of the benefit assessment of upadacitinib

Therapeutic indication	**ACT**[a]
Active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated CRP and/or MRI who have responded inadequately to NSAIDs.	A TNF-α inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)[b]
a. Presented is the ACT specified by the G-BA. b. If a TNF-α inhibitor failed, then a change within the drug class is indicated. ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; NSAID: nonsteroidal anti-inflammatory drug; TNF: tumour necrosis factor	

The company follows 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. Randomized controlled trials (RCTs) with a minimum duration of 24 weeks were used for the derivation of added benefit.

Results

Concurring with the company, no relevant study was identified for assessing the added benefit of upadacitinib in comparison with the ACT.

Since no relevant study is available for the benefit assessment, there is no hint of an added benefit of upadacitinib in comparison with the ACT; 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 probability and extent of added benefit of upadacitinib.

Table 3: Upadacitinib – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated CRP and/or MRI who have responded inadequately to NSAIDs.	A TNF-α inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)[b]	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. If a TNF-α inhibitor failed, then a change within the drug class is indicated.

ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; NSAID: nonsteroidal anti-inflammatory drug; 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].

I 2 Research question

The aim of the present report is to assess the added benefit of upadacitinib in comparison with the ACT for the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated CRP and/or MRI who have responded inadequately to NSAIDs.

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

Table 4: Research question of the benefit assessment of upadacitinib

Therapeutic indication	**ACT**[a]
Active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated CRP and/or MRI who have responded inadequately to NSAIDs.	A TNF-α inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)[b]
a. Presented is the respective ACT specified by the G-BA. b. If a TNF-α inhibitor failed, then a change within the drug class is indicated. ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; NSAID: nonsteroidal anti-inflammatory drug; TNF: tumour necrosis factor	

The company follows 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. RCTs with a minimum duration of 24 weeks are used for the derivation of added benefit. This concurs with the company’s inclusion criteria.

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 upadacitinib (status: 4 July 2022)
- bibliographical literature search on upadacitinib (last search on 5 July 2022)
- search in trial registries / trial results databases for studies on upadacitinib (last search on 5 July 2022)
- search on the G-BA website for upadacitinib (last search on 5 July 2022)

To check the completeness of the study pool:

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

No relevant study was identified from the check.

The company concurred by reporting not to have identified any relevant studies for the present research question. Nevertheless, the company presented results of the placebo-controlled SELECT-AXIS 2 study [3]. However, instead of using the study to derive any added benefit, it presented its results only as supplementary information. The company's approach is appropriate.

The SELECT-AXIS 2 study is a placebo-controlled RCT. It included adult patients who had active non-radiographic axial spondyloarthritis with objective signs of inflammation who exhibited an inadequate response to NSAID therapy or for whom NSAID therapy was unsuitable or not indicated. Patients were randomized in a 1:1 ratio to treatment with upadacitinib 15 mg once daily or placebo.

The study offers no comparison with the ACT and is therefore irrelevant for the assessment of added benefit.

I 4 Results on added benefit

Since no relevant study is available for the benefit assessment, there is no hint of an added benefit of upadacitinib in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

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

Table 5: Upadacitinib – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated CRP and/or MRI who have responded inadequately to NSAIDs.	A TNF-α inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)[b]	Added benefit not proven
a. Presented is the respective ACT specified by the G-BA. b. If a TNF-α inhibitor failed, then a change within the drug class is indicated. ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; NSAID: nonsteroidal anti-inflammatory drug; TNF: tumour necrosis factor		

The assessment described above concurs with that of 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.

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.

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. Deodhar A, Van den Bosch F, Poddubnyy D et al. Upadacitinib for the treatment of active non-radiographic axial spondyloarthritis (SELECT-AXIS 2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2022; 400(10349): 369-379. https://dx.doi.org/10.1016/S0140-6736(22)01212-0.

The full report (German version) is published under https://www.iqwig.de/en/projects/a22-92.html.