Baricitinib (enthesitis-associated arthritis)

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

EXTRACT

Project: A23-114 Version: 1.0 Status: 6 Feb 2024 DOI: 10.60584/A23-114_en

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Baricitinib (Enthesitis-assoziierte Arthritis) – 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.

Publishing details

Publisher

Institute for Quality and Efficiency in Health Care

Topic

Baricitinib (enthesitis-associated arthritis) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

14 November 2023

Internal Project No.

A23-114

DOI-URL

https://doi.org/10.60584/A23-114_en

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

- Jacqueline Detert, Rheumatological-immunological practice, Germany

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

No feedback of persons concerned was received within the framework of the present dossier assessment.

IQWiG employees involved in the dossier assessment

- Helmut Hörn
- Nadia Abu Rajab
- Ulrich Grouven
- Simone Heß
- Deborah Ingenhag-Reister
- Prateek Mishra
- Daniela Preukschat
- Felix Schwarz

Keywords

Baricitinib, Arthritis – Juvenile, Child – Preschool, Child, Adolescent, Benefit Assessment

Part I: Benefit assessment

I Table of contents

I List of tables[2]

Page

[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
bDMARD	biologic DMARD
csDMARD	conventional synthetic DMARD
DMARD	disease-modifying antirheumatic drug
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MTX	methotrexate
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) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug baricitinib. 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 14 November 2023.

Research question

Aim of the present report is the assessment of the added benefit of baricitinib in comparison with the appropriate comparator therapy (ACT) in children and adolescents aged 2 years and older with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic disease-modifying antirheumatic drugs (DMARDs). Baricitinib may be used as monotherapy or in combination with methotrexate (MTX).

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

Table 2:Research questions of the benefit assessment of baricitinib

Research question	Therapeutic indication	ACT[a]
1	Children aged 2 to 5 years with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept[c]
2	Children and adolescents aged 6 years and older with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept (≥ 12 years)

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, it is assumed that the patients covered by the therapeutic indication are not (no longer) eligible for (symptomatic) treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or glucocorticoids alone. The use of glucocorticoids (systemic and/or intra-articular) should be possible as part of a relapse therapy.
c. There are no approved treatment options available for patients aged 2 to 5 years in the present therapeutic indication. According to the G-BA, the use of etanercept and adalimumab as non-approved treatment options is medically necessary in the definable patient population of children aged 2 to 5 years in the absence of approved alternatives according to §6 (2) No. 3 ANV. According to the G-BA, it is therefore appropriate to determine the off-label use of the drugs adalimumab or etanercept as ACT for this patient population.

ACT: appropriate comparator therapy; ANV: Regulation for Early Benefit Assessment of New Pharmaceuticals; DMARD: disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; NSAID: nonsteroidal anti-inflammatory drug

In deviation from the G-BA, the company defined only one patient population (children and adolescents aged 2 years and older). The company named a treatment of physician's choice as comparator therapy and stated that, according to the G-BA, the drugs adalimumab and etanercept could be regarded as a suitable comparators. The company's deviation from the patient populations specified by the G-BA will not be further commented below, as the company did not present any suitable data for the benefit assessment – neither compared with a comparator therapy designated by the company nor compared with the ACT 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. 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 directly comparative RCT for the comparison of baricitinib versus the ACT.

Results on added benefit

For baricitinib for the treatment of children and adolescents aged 2 years and older with active enthesitis-associated arthritis who have previously had an inadequate response or intolerance to 1 or more conventional synthetic or biologic DMARDs, suitable data for the assessment of the added benefit over the ACT are lacking for both research questions. For both research questions, there was no hint of added benefit of baricitinib 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 presents a summary of the probability and extent of the added benefit of baricitinib.

[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: Baricitinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Children aged 2 to 5 years with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept[c]	Added benefit not proven
2	Children and adolescents aged 6 years and older with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept (≥ 12 years)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, it is assumed that the patients covered by the therapeutic indication are not (no longer) eligible for (symptomatic) treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or glucocorticoids alone. The use of glucocorticoids (systemic and/or intra-articular) should be possible as part of a relapse therapy.
c. There are no approved treatment options available for patients aged 2 to 5 years in the present therapeutic indication. According to the G-BA, the use of etanercept and adalimumab as non-approved treatment options is medically necessary in the definable patient population of children aged 2 to 5 years in the absence of approved alternatives according to §6 (2) No. 3 ANV. According to the G-BA, it is therefore appropriate to determine the off-label use of the drugs adalimumab or etanercept as ACT for this patient population.

ACT: appropriate comparator therapy; ANV: Regulation for Early Benefit Assessment of New Pharmaceuticals; DMARD: disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; NSAID: nonsteroidal anti-inflammatory drug

The G-BA decides on the added benefit.

I 2 Research question

Aim of the present report is the assessment of the added benefit of baricitinib in comparison with the ACT in children and adolescents aged 2 years and older with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs. Baricitinib may be used as monotherapy or in combination with MTX.

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

Table 4: Research questions of the benefit assessment of baricitinib

Research question	Therapeutic indication	ACT[a]
1	Children aged 2 to 5 years with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept[c]
2	Children and adolescents aged 6 years and older with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept (≥ 12 years)

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, it is assumed that the patients covered by the therapeutic indication are not (no longer) eligible for (symptomatic) treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or glucocorticoids alone. The use of glucocorticoids (systemic and/or intra-articular) should be possible as part of a relapse therapy.
c. There are no approved treatment options available for patients aged 2 to 5 years in the present therapeutic indication. According to the G-BA, the use of etanercept and adalimumab as non-approved treatment options is medically necessary in the definable patient population of children aged 2 to 5 years in the absence of approved alternatives according to §6 (2) No. 3 ANV. According to the G-BA, it is therefore appropriate to determine the off-label use of the drugs adalimumab or etanercept as ACT for this patient population.

ACT: appropriate comparator therapy; ANV: Regulation for Early Benefit Assessment of New Pharmaceuticals; DMARD: disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; NSAID: nonsteroidal anti-inflammatory drug

In deviation from the G-BA, the company defined only one patient population (children and adolescents aged 2 years and older). The company named a treatment of physician's choice as comparator therapy and stated that, according to the G-BA, the drugs adalimumab and etanercept could be regarded as a suitable comparators. The company's deviation from the patient populations specified by the G-BA will not be further commented below, as the company did not present any suitable data for the benefit assessment – neither compared with a comparator therapy designated by the company nor compared with the ACT 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 24 weeks were used for deriving any 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 baricitinib (status: 7 September 2023)
- bibliographical literature search on baricitinib (last search on 7 September 2023)
- search in trial registries/trial results databases for studies on baricitinib (last search on 07 September 2023)
- search on the G-BA website for baricitinib (last search on 07 September 2023)

To check the completeness of the study pool:

- search in trial registries for studies on baricitinib (last search on 27 November 2023); 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 RCT for the comparison of baricitinib versus the ACT.

In Module 3 A, the company presents the results of the label-enabling study I4V-MC-JAHV (JUVE-BASIS) [3]. The JUVE-BASIS study included patients aged 2 to 17 years inclusively with active juvenile idiopathic arthritis of the subtypes polyarticular juvenile idiopathic arthritis, extended oligoarticular juvenile idiopathic arthritis, juvenile psoriatic arthritis and enthesitis-associated arthritis who had previously responded inadequately to or were intolerant of 1 or more conventional synthetic DMARDs (csDMARDs) or biologic DMARDs (bDMARDs). Initially, all patients received baricitinib for 12 weeks, followed by a double-blind treatment phase lasting up to 32 weeks, during which patients with a response were randomly assigned to further treatment with baricitinib or placebo. Under certain conditions, MTX, other csDMARDS, oral corticosteroids, non-steroidal anti-inflammatory drugs and analgesics were permitted as concomitant therapy. The use of bDMARDs was not allowed. Patients with relapse could discontinue the randomized phase and switch to an open-label extension study with treatment with baricitinib. Primary outcome was the time to relapse.

As can be seen from the design, the JUVE-BASIS study does not allow a comparison of treatment with baricitinib versus treatment with the ACT and is therefore not included in the benefit assessment. This concurs with the company’s approach.

I 4 Results on added benefit

For baricitinib for the treatment of children and adolescents aged 2 years and older with active enthesitis-associated arthritis who have previously had an inadequate response or intolerance to 1 or more conventional synthetic or biologic DMARDs, suitable data for the assessment of the added benefit over the ACT are lacking for both research questions. For both research questions, there was no hint of added benefit of baricitinib in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of baricitinib in comparison with the ACT is summarized in Table 5.

Table 5: Baricitinib – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Children aged 2 to 5 years with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept[c]	Added benefit not proven
2	Children and adolescents aged 6 years and older with active enthesitis-associated arthritis who have had an inadequate response or intolerance to one or more conventional synthetic or biologic DMARDs[b]	Adalimumab or etanercept (≥ 12 years)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. According to the G-BA, it is assumed that the patients covered by the therapeutic indication are not (no longer) eligible for (symptomatic) treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or glucocorticoids alone. The use of glucocorticoids (systemic and/or intra-articular) should be possible as part of a relapse therapy.
c. There are no approved treatment options available for patients aged 2 to 5 years in the present therapeutic indication. According to the G-BA, the use of etanercept and adalimumab as non-approved treatment options is medically necessary in the definable patient population of children aged 2 to 5 years in the absence of approved alternatives according to §6 (2) No. 3 ANV. According to the G-BA, it is therefore appropriate to determine the off-label use of the drugs adalimumab or etanercept as ACT for this patient population.

ACT: appropriate comparator therapy; ANV: Regulation for Early Benefit Assessment of New Pharmaceuticals; DMARD: disease-modifying antirheumatic drug; G-BA: Federal Joint Committee; NSAID: nonsteroidal anti-inflammatory drug

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.

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.

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://doi.org/10.1002/bimj.201300274.

3. Ramanan AV, Quartier P, Okamoto N et al. Baricitinib in juvenile idiopathic arthritis: an international, phase 3, randomised, double-blind, placebo-controlled, withdrawal, efficacy, and safety trial. Lancet 2023; 402(10401): 555-570. https://doi.org/10.1016/s0140-6736(23)00921-2.

The full report (German version) is published under https://www.iqwig.de/en/projects/a23-114.html.