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Secukinumab (non-radiographic axial spondyloarthritis) –

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

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Secukinumab (nicht röntgenologische axiale Spondyloarthritis) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 27 November 2020). 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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[2] Table numbers start with "2" as numbering follows that of the full dossier assessment.

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
nr-axSpA	non-radiographic axial spondyloarthritis
NSAID	nonsteroidal anti-inflammatory drug
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
TNF	tumour necrosis factor

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 secukinumab. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 28 August 2020.

Due to the working conditions during the coronavirus pandemic, the present assessment was conducted without the use of strictly confidential data presented in Module 5 of the company's dossier.

Research question

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

Table 2 shows the research question of the benefit assessment and the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of secukinumab

Therapeutic indication	**ACT[a]**
Adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated CRP and/or MRI evidence who have responded inadequately to NSAIDs[b]	A TNFα inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)
a. Presentation of the ACT specified by the G-BA. b. According to the G-BA, the patient population considered for the research question also includes patients who have not tolerated previous NSAID therapy. ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: nonsteroidal anti-inflammatory drug; TNF: tumour necrosis factor	

The company followed the specification of the G-BA and named a tumour necrosis factor (TNF)α inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol) as ACT.

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 the added benefit.

Results

Concurring with the company, the check of the completeness of the study pool identified no RCTs that would allow a direct comparison of secukinumab versus the ACT.

In the absence of directly comparative data, the company examined the possibility of conducting an adjusted indirect comparison. However, it stated that the studies identified using its inclusion criteria were not suitable for this purpose because either there was no common comparator, the study design was not sufficiently similar or the available data were not suitable, and that an adjusted indirect comparison could therefore not be performed. This assessment of the company is appropriate.

Thus, the company did not present any data in its dossier for the assessment of the added benefit of secukinumab in comparison with the ACT for adult patients with active nr-axSpA with objective signs of inflammation as indicated by elevated CRP and/or MRI evidence who have responded inadequately to NSAIDs. This resulted in no hint of an added benefit of secukinumab 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 the added benefit of secukinumab.

Table 3: Secukinumab – probability and extent of added benefit

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

a. Presentation of the ACT specified by the G-BA.
b. According to the G-BA, the patient population considered for the research question also includes patients who have not tolerated previous NSAID therapy.

ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; 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].

2.2 Research question

The aim of the present report is the assessment of the added benefit of secukinumab in comparison with the ACT in adult patients with active nr-axSpA with objective signs of inflammation as indicated by elevated CRP and/or MRI evidence who have responded inadequately to NSAIDs.

Table 4 shows the research question of the benefit assessment and the ACT specified by the G-BA.

Table 4: Secukinumab – probability and extent of added benefit: Research question of the benefit assessment of secukinumab

Therapeutic indication	**ACT[a]**
Adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated CRP and/or MRI evidence who have responded inadequately to NSAIDs[b]	A TNFα inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)
a. Presentation of the ACT specified by the G-BA. b. According to the G-BA, the patient population considered for the research question also includes patients who have not tolerated previous NSAID therapy. ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: nonsteroidal anti-inflammatory drug; TNF: tumour necrosis factor	

The company followed the specification of the G-BA and named a TNFα inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol) as ACT.

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 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 secukinumab (status: 14 July 2020)
- bibliographical literature search on secukinumab (last search on 12 June 2020)
- search in trial registries for studies on secukinumab (last search on 17 June 2020)
- bibliographical literature search on the ACT (last search on 12 June 2020)
- search in trial registries for studies on the ACT (last search on 17 June 2020)

To check the completeness of the study pool:

- search in trial registries for studies on secukinumab (last search on 7 September 2020)

Concurring with the company, the check of the completeness of the study pool identified no RCTs that would allow a direct comparison of secukinumab versus the ACT.

In the absence of directly comparative data, the company examined the possibility of conducting an adjusted indirect comparison using a common comparator. For this purpose, using its inclusion criteria, it first identified the RCTs PREVENT [3] and ACHILLES [4], each of which compared secukinumab with placebo, on the intervention side. From these studies, placebo emerged as the only possible common comparator for an adjusted indirect comparison. For the comparator therapy, the company identified a total of 10 potentially relevant studies [5-14]. However, it stated that it is not possible to carry out an adjusted indirect comparison on the basis of these studies, as they are not suitable for this for various reasons. This assessment of the company is appropriate. The reasoning of the company for not including the 10 studies on the comparator side is described in more detail below.

No shared common comparator

Three studies [6-8] were not used by the company because they did not share a common comparator. These studies compared etanercept with sulfasalazine, golimumab with pamidronate, or a reduced dose of a TNFα inhibitor with a stable dose of a TNFα inhibitor.

The procedure of the company is appropriate because, as described above, placebo is the only possible common comparator.

Study design not sufficiently similar

Five studies [5,9-12] were excluded by the company because their study design was not comparable with the design of the studies with the intervention, and thus the similarity assumption for an adjusted indirect comparison was violated. These 5 studies, which compared different possible ACTs with placebo, examined the discontinuation of the investigational product in comparison with continued treatment. For this purpose, all patients in these studies first received unblinded treatment with the investigational product for a defined period of time and were then randomized depending on the achievement of certain target parameters to double-blind treatment either with placebo (to investigate the discontinuation of the investigational product) or with the investigational product.

There was no comparable pretreatment in the 2 secukinumab studies PREVENT and ACHILLES, and there are no studies with secukinumab with a comparable design yet. According to the company, this difference in study design does not allow a comparison of the efficacy with placebo as a common comparator in an adjusted indirect comparison. According to the company, the placebo arms in the studies in which patients were pretreated with the investigational product differed systematically from the placebo arms in the studies with the intervention in which patients were not pretreated with the investigational product. This argument of the company is also considered appropriate.

Available data not suitable

Two studies (RAPID-axSpA [14] and C-AXSPAND [13]), each comparing certolizumab pegol with placebo, were not used by the company because no suitable data were available for an adjusted indirect comparison without the company conducting a systematic examination of the similarity of the studies.

For the RAPID-axSpA study, the company justified the non-inclusion with the fact that data on adverse events in particular were missing for the population of nr-axSpA patients relevant to the assessment, so that no risk of harm could be assessed in an adjusted indirect comparison. This assessment of the company is appropriate; a balancing of positive and negative effects would not be possible in an adjusted indirect comparison.

For the C-AXSPAND study, the company stated that an adjusted indirect comparison could not be adequately performed due to incomplete information on adverse events and on individual components of patient-relevant outcomes. This argument of the company is not fully comprehensible, as data are available from the C-AXSPAND study at least for individual outcomes on benefit and harm, so that in principle a balancing of positive and negative effects in an adjusted indirect comparison would be conceivable. Nevertheless, due to the design of the C-AXSPAND study, it is very unlikely that this study would be suitable for the derivation of an added benefit in an adjusted indirect comparison, as a treatment switch from placebo to the intervention was permitted at any time point in the study. Such treatment switches occurred to a large extent; at week 52, 60.8% of the patients had switched from placebo to the intervention, with the majority of treatment switches already occurring between week 12 and week 24. Also according to the company, the data carried at least a high risk of bias due to the high proportion of patients who switched treatment from placebo to the intervention. This means that the requirements for the certainty of results for carrying out an adjusted indirect comparison would not be met.

2.4 Results on added benefit

In its dossier, the company presented no data for the assessment of the added benefit of secukinumab in comparison with the ACT. This resulted in no hint of an added benefit of secukinumab in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

The company presented no data for the assessment of the added benefit of secukinumab. An added benefit of secukinumab in comparison with the ACT is therefore not proven for adult patients with active nr-axSpA with objective signs of inflammation as indicated by elevated CRP and/or MRI evidence who have responded inadequately to NSAIDs.

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

Table 5: Secukinumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation as indicated by elevated CRP and/or MRI evidence who have responded inadequately to NSAIDs[b]	A TNFα inhibitor (etanercept or adalimumab or golimumab or certolizumab pegol)	Added benefit not proven
a. Presentation of the ACT specified by the G-BA. b. According to the G-BA, the patient population considered for the research question also includes patients who have not tolerated previous NSAID therapy. ACT: appropriate comparator therapy; CRP: C-reactive protein; G-BA: Federal Joint Committee; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: nonsteroidal anti-inflammatory drug; TNF: tumour necrosis factor		

The assessment described above corresponds to that of the company, which stated that it did not claim an added benefit because no studies with secukinumab and one of the specified ACTs had been identified.

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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