IQWiG Reports – Commission No. A21-96

Teriflunomide (multiple sclerosis in children and adolescents aged 10 years and older) –

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

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Teriflunomid (multiple Sklerose bei Kindern und Jugendlichen ab 10 Jahren) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 28 October 2021). 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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Medical and scientific advice

No advisor on medical and scientific questions was involved in the present dossier assessment.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Jutta Scheiderbauer and one other person.

IQWiG thanks the respondents for participating in the written exchange about how they experienced the disease and its treatment as well as their treatment goals. The respondents were not involved in the actual preparation of the dossier assessment.

IQWiG employees involved in the dossier assessment

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Keywords: Teriflunomide, Multiple Sclerosis – Relapsing-Remitting, Child, Adolescent, 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
RRMS	relapsing-remitting multiple sclerosis
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 teriflunomide. 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 20 July 2021.

Research question

The aim of this report was to assess the added benefit of teriflunomide in comparison with the appropriate comparator therapy (ACT) in children and adolescents ≥ 10 to < 18 years of age with relapsing-remitting multiple sclerosis (RRMS).

The G-BA's specification of the ACT results in the research questions presented in Table 2.

Table 2: Research questions of the benefit assessment of teriflunomide

Research question	Therapeutic indication	ACT[a]
1	Children and adolescents ≥ 10 to < 18 years of age with RRMS without prior disease-modifying therapy or children and adolescents with prior disease-modifying therapy whose disease is not highly active	Interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status
2	Children and adolescents ≥ 10 to < 18 years of age with highly active RRMS despite treatment with disease-modifying therapy	Fingolimod or, if indicated, switch within the basic therapeutic agents (interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status)

a. Presented is the ACT specified by the G-BA.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; RRMS: relapsing-remitting multiple sclerosis

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

The assessment was conducted by means of patient-relevant outcomes on the basis of the data submitted by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 12 months were used for deriving any added benefit.

Since the company did not submit any data for any of the subpopulations identified by the G-BA, the research questions were analysed together.

Results

For children and adolescents ≥ 10 to <18 years of age with RRMS, the company did not submit any data for assessing the added benefit of teriflunomide in comparison with the ACT. Consequently, there is no added benefit of teriflunomide 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 added benefit of teriflunomide.

Table 3: Teriflunomide – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Children and adolescents ≥ 10 to < 18 years of age with RRMS without prior disease-modifying therapy or children and adolescents with prior disease-modifying therapy whose disease is not highly active	Interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status	Added benefit not proven
2	Children and adolescents ≥ 10 to <18 years of age with highly active RRMS despite treatment with disease-modifying therapy	Fingolimod or, if indicated, switch within the basic therapeutic agents (interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status)	Added benefit not proven

a. Presented is the ACT specified by the G-BA.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; RRMS: relapsing-remitting multiple sclerosis

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 was to assess the added benefit of teriflunomide in comparison with the ACT in children and adolescents ≥ 10 to < 18 years of age with RRMS.

The G-BA's specification of the ACT results in the research questions presented in Table 4.

Table 4: Research questions of the benefit assessment of teriflunomide

Research question	Therapeutic indication	ACT[a]
1	Children and adolescents ≥ 10 to < 18 years of age with RRMS without prior disease-modifying therapy or children and adolescents with prior disease-modifying therapy whose disease is not highly active	Interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status
2	Children and adolescents ≥ 10 to <18 years of age with highly active RRMS despite treatment with disease-modifying therapy	Fingolimod or, if indicated, switch within the basic therapeutic agents (interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status)

a. Presented is the ACT specified by the G-BA.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; RRMS: relapsing-remitting multiple sclerosis

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

The assessment was conducted by means of patient-relevant outcomes on the basis of the data submitted by the company in the dossier. RCTs with a minimum duration of 12 months were used for deriving any added benefit. This deviates from the company's inclusion criterion of a minimum duration of 24 weeks.

Since the company did not submit any data for any of the research questions identified by the G-BA, the research questions were analysed together (see Sections 2.3, 2.4, and 2.5). This concurs with the company's approach.

2.3 Information retrieval and study pool

The study pool of the assessment was compiled on the basis of the following information:

Sources cited by the company in the dossier:

- Study list on teriflunomide (as of 3 May 2021)
- Bibliographic literature search on teriflunomide (most recent search on 3 May 2021)
- Search in trial registries / study results databases on teriflunomide (most recent search on 3 May 2021)
- Search on the G-BA website on teriflunomide (most recent search on 3 May 2021)

To check the completeness of the study pool:

- Search in trial registries for studies on teriflunomide (most recent search on 5 August 2021); see Appendix A of the full dossier assessment for search strategies.

The company's dossier did not identify any suitable studies. Likewise, no relevant study was identified from the check.

2.4 Results on added benefit

For children and adolescents ≥ 10 to <18 years of age with RRMS, the company did not submit any data for assessing the added benefit of teriflunomide in comparison with the ACT. Consequently, there is no added benefit of teriflunomide in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

Table 5 presents a summary of the results of the benefit assessment of teriflunomide in comparison with the ACT.

Table 5: Teriflunomide – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Children and adolescents ≥ 10 to < 18 years of age with RRMS without prior disease-modifying therapy or children and adolescents with prior disease-modifying therapy whose disease is not highly active	Interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status	Added benefit not proven
2	Children and adolescents ≥ 10 to < 18 years of age with highly active RRMS despite treatment with disease-modifying therapy	Fingolimod or, if indicated, switch within the basic therapeutic agents (interferon-β 1a or interferon-β 1b or glatiramer acetate, taking into account approval status)	Added benefit not proven

a. Presented is the ACT specified by the G-BA.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; RRMS: relapsing-remitting multiple sclerosis

The above assessment 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.

The full report (German version) is published under https://www.iqwig.de/en/projects/a21-95.html.