IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A17-49

Dimethyl fumarate (plaque psoriasis) –

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

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Dimethylfumarat (Psoriasis vulgaris) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 22 December 2017). 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:

Dimethyl fumarate (plaque psoriasis) – Benefit assessment according to §35a Social Code Book V

Commissioning agency:

Federal Joint Committee

Commission awarded on:

28 September 2017

Internal Commission No.:

A17-49

Medical and scientific advice:

No advisor on medical and scientific questions was available for the present dossier

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

assessment.

IQWiG employees involved in the dossier assessment:

- Natalia Wolfram
- Judith Gibbert
- Charlotte Guddat
- Tatjana Hermanns
- Miriam Luhnen
- Volker Vervölgyi

Keywords: dimethyl fumarate, psoriasis, benefit assessment

Table of contents

Page

List of tables ..... **iv**
List of abbreviations ..... **v**
2 Benefit assessment **1**
2.1 Executive summary of the benefit assessment **1**
2.2 Research question **3**
2.3 Information retrieval and study pool **4**
2.4 Results on added benefit **4**
2.5 Probability and extent of added benefit **5**
2.6 List of included studies **5**
References for English extract **6**

List of tables[2]

Page

Table 2: Research questions of the benefit assessment of dimethyl fumarate 1
Table 3: Dimethyl fumarate – probability and extent of added benefit 2
Table 4: Research questions of the benefit assessment of dimethyl fumarate 3
Table 5: Dimethyl fumarate – probability and extent of added benefit 5

[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)
PUVA	psoralen and ultraviolet-A light
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 dimethyl fumarate. 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 September 2017.

Research question

The aim of the present report was to assess the added benefit of dimethyl fumarate in comparison with the appropriate comparator therapy (ACT) in the treatment of moderate to severe plaque psoriasis in adults in need of systemic medicinal therapy.

The assessment was conducted in comparison with the G-BA's ACT. This ACT is shown in Table 2.

Table 2: Research questions of the benefit assessment of dimethyl fumarate

Research question	Subindication	ACT[a]
1	Adult patients in need of systemic medicinal therapy[b]	**Fumaric acid esters** or **ciclosporin** or **methotrexate** or **oral PUVA** or **secukinumab**[c]
2	Adult patients with inadequate response to other systemic treatments (including ciclosporin, methotrexate or oral PUVA) or with contraindication or intolerance to such treatments[d]	**Adalimumab** or **infliximab** or **ustekinumab** or **secukinumab**[c, e]

a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.
b: This population includes all patients in the approved therapeutic indication except for the patients mentioned in research question 2.
c: The respective approval of the drugs is to be considered.
d: Hereinafter, the text uses the following designation for this research question: adult patients with inadequate response to other systemic treatments or with contraindication or intolerance to such treatments.
e: The company cited etanercept as additional ACT. This expansion was not followed.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; PUVA: psoralen and ultraviolet-A light

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. This concurs with the company's inclusion criteria.

Results

No relevant RCTs were available for the assessment of the added benefit of dimethyl fumarate in comparison with the respective ACT for research question 1 (adult patients in need of systemic medicinal therapy) or for research question 2 (adult patients with inadequate response to other systemic treatments [including ciclosporin, methotrexate or oral psoralen and ultraviolet-A light [PUVA]]) or with contraindication or intolerance to such treatments). This concurs with the company's assessment. Hence there was no hint of an added benefit of dimethyl fumarate in comparison with the respective ACT specified by the G-BA; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

The result of the assessment of the added benefit of dimethyl fumarate in comparison with the ACT is shown in Table 3.

Table 3: Dimethyl fumarate – probability and extent of added benefit

Subindication	ACT[a]	Probability and extent of added benefit
Adult patients in need of systemic medicinal therapy[b]	**Fumaric acid esters** or **ciclosporin** or **methotrexate** or **oral PUVA** or **secukinumab**[c]	Added benefit not proven
Adult patients with inadequate response to other systemic treatments (including ciclosporin, methotrexate or oral PUVA) or with contraindication or intolerance to such treatments	**Adalimumab** or **infliximab** or **ustekinumab** or **secukinumab**[c, d]	Added benefit not proven

a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.
b: This population includes all patients in the approved therapeutic indication except for the patients mentioned in research question 2.
c: The respective approval of the drugs is to be considered.
d: The company cited etanercept as additional ACT. This expansion was not followed.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; PUVA: psoralen and ultraviolet-A light.

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 was to assess the added benefit of dimethyl fumarate in comparison with the ACT in the treatment of moderate to severe plaque psoriasis in adults in need of systemic medicinal therapy.

This resulted in 2 research questions, for which the G-BA specified the ACTs presented in Table 4.

Table 4: Research questions of the benefit assessment of dimethyl fumarate

Research question	Subindication	ACT[a]
1	Adult patients in need of systemic medicinal therapy[b]	**Fumaric acid esters** or **ciclosporin** or **methotrexate** or **oral PUVA** or **secukinumab**[c]
2	Adult patients with inadequate response to other systemic treatments (including ciclosporin, methotrexate or oral PUVA) or with contraindication or intolerance to such treatments[d]	**Adalimumab** or **infliximab** or **ustekinumab** or **secukinumab**[c, e]

a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.
b: This population includes all patients in the approved therapeutic indication except for the patients mentioned in research question 2.
c: The respective approval of the drugs is to be considered.
d: Hereinafter, the text uses the following designation for this research question: adult patients with inadequate response to other systemic treatments or with contraindication or intolerance to such treatments.
e: The company cited etanercept as additional ACT. This expansion was not followed.
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; PUVA: psoralen and ultraviolet-A light

The company largely followed the G-BA's specification of the ACT. Deviations by the company are commented on in Section 2.7.1 of the full dossier assessment.

The present assessment was conducted in comparison with the G-BA's 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 dimethyl fumarate (status: 17 August 2017)
- bibliographical literature search on dimethyl fumarate (last search on 15 August 2017)
- search in trial registries for studies on dimethyl fumarate (last search on 17 August 2017)

To check the completeness of the study pool:

- search in trial registries for studies on dimethyl fumarate (last search on 16 October 2017)

The check identified no relevant studies for research question 1 (adult patients in need of systemic medicinal therapy) or for research question 2 (adult patients with inadequate response to other systemic treatments or with contraindication or intolerance to such treatments). The company also identified no relevant studies for the benefit assessment for both research questions.

In Module 4 A, the company presented results of the BRIDGE study [3] for both research questions. This study was a multi-centre, randomized, double-blind study on the comparison of dimethyl fumarate with fumaric acid esters (preparation: Fumaderm) and placebo in patients with moderate to severe plaque psoriasis. Treatment in the BRIDGE study was conducted for 16 weeks. A minimum duration of 24 weeks is considered necessary for the chronic disease under assessment, however (see Section 2.2). Hence, the BRIDGE study is unsuitable for the assessment of the added benefit of dimethyl fumarate.

The company itself explicitly did not include the study for the assessment of the added benefit of dimethyl fumarate in comparison with the ACT, also because treatment duration was too short. Instead, the study results were presented only to describe the medical benefit of dimethyl fumarate.

Concurring with the company, the BRIDGE study was unsuitable for the assessment of the added benefit because of the short treatment duration (see Section 2.7.2.3.2 of the full dossier assessment).

2.4 Results on added benefit

The company presented no suitable data for the assessment of the added benefit of dimethyl fumarate for the treatment of moderate to severe plaque psoriasis in adult patients in need of systemic medicinal therapy for research question 1 or for research question 2.

There was no hint of an added benefit of dimethyl fumarate in comparison with the ACT specified by the G-BA for adult patients in need of systemic medicinal therapy (research

question 1) or for adult patients with inadequate response to other systemic treatments or with contraindication or intolerance to such treatments (research question 2); an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

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

Table 5: Dimethyl fumarate – probability and extent of added benefit

Subindication	**ACT**[a]	**Probability and extent of added benefit**
Adult patients in need of systemic medicinal therapy[b]	**Fumaric acid esters** or **ciclosporin** or **methotrexate** or **oral PUVA** or **secukinumab**[c]	Added benefit not proven
Adult patients with inadequate response to other systemic treatments (including ciclosporin, methotrexate or oral PUVA) or with contraindication or intolerance to such treatments	**Adalimumab** or **infliximab** or **ustekinumab** or **secukinumab**[c, d]	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**. b: This population includes all patients in the approved therapeutic indication except for the patients mentioned in research question 2. c: The respective approval of the drugs is to be considered. d: The company cited etanercept as additional ACT. This expansion was not followed. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; PUVA: psoralen and ultraviolet-A light.		

The assessment described above concurs with that of the company.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as the company presented no relevant data for the benefit assessment.

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 5.0 [online]. 10.07.2017 [Accessed: 04.06.2018]. URL: https://www.iqwig.de/download/General-Methods_Version-5-0.pdf.

2. Skipka G, Wieseler B, Kaiser T, Thomas S, Bender R, Windeler J et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2015; 58(1): 43-58

3. Mrowietz U, Szepietowski JC, Loewe R, Van de Kerkhof P, Lamarca R, Ocker WG et al. Efficacy and safety of LAS41008 (dimethyl fumarate) in adults with moderate-to-severe chronic plaque psoriasis: a randomised, double-blind, Fumaderm and placebo-controlled trial (BRIDGE). Br J Dermatol 2017; 176(3): 615-623.

The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a17-49-dimethyl-fumarate-psoriasis-benefit-assessment-according-to-35a-social-code-book-v.8023.html.