IQWiG Reports – Commission No. A20-73

Trifarotene (acne vulgaris) –

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

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Trifaroten (Acne vulgaris) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 12 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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IQWiG thanks the medical and scientific advisor for his 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.

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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)
IGA	Investigator Global Assessment
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
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 trifarotene. 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 13 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 trifarotene in comparison with a topical combination therapy of adapalene + benzoyl peroxide or a topical combination therapy of clindamycin + benzoyl peroxide as appropriate comparator therapy (ACT) in patients from 12 years of age and older with acne vulgaris of the face and/or the trunk, when many comedones, papules and pustules are present.

Table 2: Research question of the benefit assessment of trifarotene

Therapeutic indication	**ACT**[a]
Local therapy of acne vulgaris of the face and/or the trunk in patients from 12 years of age and older, when many comedones, papules and pustules are present[b]	Topical combination therapy of adapalene + benzoyl peroxide or topical combination therapy of clindamycin + benzoyl peroxide
a. Presentation of the respective ACT specified by the G-BA. b. It is assumed that the patients have a moderate form of acne vulgaris and are not yet candidates for systemic therapy. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification on the 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

In the present therapeutic indication, there is no RCT available that allows a direct comparison of trifarotene with the ACT. The dossier contained no other data for a comparison of trifarotene with the ACT.

Overall, there are no suitable data for the assessment of the added benefit of trifarotene in comparison with the ACT. This resulted in no hint of an added benefit of trifarotene 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 trifarotene.

Table 3: Trifarotene – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Local therapy of acne vulgaris of the face and/or the trunk in patients from 12 years of age and older, when many comedones, papules and pustules are present[b]	Topical combination therapy of adapalene + benzoyl peroxide or topical combination therapy of clindamycin + benzoyl peroxide	Added benefit not proven

a. Presentation of the respective ACT specified by the G-BA.
b. It is assumed that the patients have a moderate form of acne vulgaris and are not yet candidates for systemic therapy.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

2.2 Research question

The aim of the present report is the assessment of the added benefit of trifarotene in comparison with a topical combination therapy of adapalene + benzoyl peroxide or a topical combination therapy of clindamycin + benzoyl peroxide as ACT in patients from 12 years of age and older with acne vulgaris of the face and/or the trunk, when many comedones, papules and pustules are present.

For the benefit assessment, the research question presented in Table 4 resulted from the ACT specified by the G-BA.

[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 4: Research question of the benefit assessment of trifarotene

Therapeutic indication	**ACT[a]**
Local therapy of acne vulgaris of the face and/or the trunk in patients from 12 years of age and older, when many comedones, papules and pustules are present[b]	Topical combination therapy of adapalene + benzoyl peroxide or topical combination therapy of clindamycin + benzoyl peroxide
a. Presentation of the respective ACT specified by the G-BA. b. It is assumed that the patients have a moderate form of acne vulgaris and are not yet candidates for systemic therapy. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification on the 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 deviates from inclusion criteria of the company which defined a minimum study duration of 12 weeks.

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 trifarotene (status: 16 June 2020)
- bibliographical literature search on trifarotene (last search on 16 June 2020)
- search in trial registries for studies on trifarotene (last search on 17 June 2020)
- search on the G-BA website for trifarotene (last search on 17 June 2020)

To check the completeness of the study pool:

- search in trial registries for studies on trifarotene (last search on 20 August 2020)

Concurring with the company, the check of the study pool did not identify any RCT that would allow a direct comparison of trifarotene with the ACT in the present therapeutic indication.

As described above, the company did not identify any study relevant to the benefit assessment in its information retrieval, but it presented the placebo-controlled approval studies PERFECT-1 and PERFECT-2 [3], and, as supplementary information, the single-arm study SATISFY [4]. The company described that it did not carry out an indirect comparison and justified this with different cosmetic and pharmacological properties of topical vehicles in comparator arms and with a variety of different classification systems for determining the

severity of acne. As the company did not provide any data on this issue, its justification will not be discussed further.

The studies PERFECT-1 and PERFECT-2 are double-blind RCTs comparing trifarotene with the drug-free topical vehicle of trifarotene (placebo). Each of the studies included and randomized about 1200 patients from the age of 9 years with moderate acne (Investigator Global Assessment [IGA] score 3) of the face and trunk. Patients with severe forms of acne (e.g. acne conglobata, acne fulminans) or secondary forms of acne (e.g. chloracne or drug-induced acne) were excluded from the studies. The studies consisted of a 12-week treatment phase during which trifarotene or the drug-free vehicle cream was to be applied once a day to the affected areas of the face and trunk.

The SATISFY study is a single-arm 52-week study on trifarotene in the present therapeutic indication.

The company described that the RCTs PERFECT-1 and PERFECT-2 and the single-arm SATISFY study are not suitable to prove an added benefit of trifarotene due to a lack of comparison with the ACT. The drug-free vehicle cream used in the RCTs PERFECT-1 and PERFECT-2 does not correspond to any of the options of the ACT, and the SATISFY study does not include a comparator arm. The company's assessment that these 3 studies are not suitable for the assessment of the added benefit is appropriate.

Contrary to the company's assessment, a study duration of only 12 weeks is considered too short for a benefit assessment in the present therapeutic indication. For chronic diseases, and thus also for the present therapeutic indication, studies of at least 24 weeks are usually required for a benefit assessment [1,5].

Approach of the company for the derivation of the added benefit

Although the company itself described that no relevant studies were available for the benefit assessment, it ultimately derived a hint of a non-quantifiable added benefit. This is not appropriate. For the assessment of the added benefit, comparative data on the ACT would be necessary, which the company – as described above – did not provide.

2.4 Results on added benefit

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

2.5 Probability and extent of added benefit

Table 5 shows a summary of probability and extent of the added benefit of trifarotene.

Table 5: Trifarotene – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Local therapy of acne vulgaris of the face and/or the trunk in patients from 12 years of age and older, when many comedones, papules and pustules are present[b]	Topical combination therapy of adapalene + benzoyl peroxide or topical combination therapy of clindamycin + benzoyl peroxide	Added benefit not proven
a. Presentation of the respective ACT specified by the G-BA. b. It is assumed that the patients have a moderate form of acne vulgaris and are not yet candidates for systemic therapy. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The assessment described above deviates from that of the company, which derived a hint of a non-quantifiable added benefit.

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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The full report (German version) is published under https://www.iqwig.de/en/projects/a20-73.html.