IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A17-59

Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil (HIV infection in adolescents) –

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

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Elvitegravir/Cobistat/Emtricitabin/ Tenofovirdisoproxil (HIV-Infektion bei Jugendlichen) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 7 February 2018). 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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- No medical expert was available as advisor for the present benefit 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
ARV	antiretroviral
EVG/COBI/FTC/TDF	elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil (fumarate)
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HIV-1	human immunodeficiency virus type 1
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 combination elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil (fumarate) (EVG/COBI/FTC/TDF). 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 16 November 2017.

Research question

The aim of the present report was to assess the added benefit of EVG/COBI/FTC/TDF in comparison with the appropriate comparator therapy (ACT) in adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with human immunodeficiency virus type 1 (HIV-1) without known mutations involving resistances against 1 of the 3 antiretroviral (ARV) drugs and the occurrence of toxicities that rule out the application of other treatment regimens which do not contain tenofovir disoproxil (fumarate) (TDF).

Table 2: Research questions of the benefit assessment of EGV/COBI/FTC/TDF

Research question	Subindication	ACT[a]
1	Treatment of HIV-1 infection in adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with HIV-1 without known mutations involving resistances against 1 of the 3 ARV drugs and the occurrence of toxicities that rule out the application of other treatment regimens which do not contain TDF	Individual antiretroviral therapy (ART) based on prior treatment(s) and under consideration of the reason for the switch of treatment, particularly treatment failure due to virologic failure and possible accompanying development of resistance, or due to AEs)
a: Presentation of the respective ACT specified by the G-BA. AEs: adverse events; ART: antiretroviral therapy; COBI: cobicistat; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV: human immunodeficiency virus; TDF: tenofovir disoproxil (fumarate)		

The company followed 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 48 weeks were used for the derivation of the added benefit. This concurs with the company's inclusion criteria.

Results

No data for the assessment of the added benefit were available for the present research question. This concurs with the company's assessment. Hence, there was no hint of an added benefit of

EVG/COBI/FTC/TDF in comparison with the 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]

On the basis of the results presented, the probability and the extent of the added benefit of the drug combination EVG/COBI/FTC/TDF in comparison with the ACT is assessed as follows:

The result of the assessment of the added benefit of EVG/COBI/FTC/TDF in comparison with the ACT is shown in Table 3.

Table 3: EVG/COBI/FTC/TDF: probability and extent of added benefit

Subindication	ACT[a]	Probability and extent of added benefit
Treatment of HIV-1 infection in adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with HIV-1 without known mutations involving resistances against 1 of the 3 ARV drugs and the occurrence of toxicities that rule out the application of other treatment regimens which do not contain TDF	Individual ART based on prior treatment(s) and under consideration of the reason for the switch of treatment, particularly treatment failure due to virologic failure and possible accompanying development of resistance, or due to AEs	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. AEs: adverse events; ART: antiretroviral therapy; COBI: cobicistat; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV: human immunodeficiency virus; TDF: tenofovir disoproxil (fumarate)		

The G-BA decides on the added benefit.

2.2 Research question

The aim of the present report was to assess the added benefit of EVG/COBI/FTC/TDF in comparison with the ACT in adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with HIV-1 without known mutations involving resistances against 1 of the 3 ARV drugs and the occurrence of toxicities that rule out the application of other treatment regimens which do not contain TDF.

[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 questions of the benefit assessment of EGV/COBI/FTC/TDF

Research question	Subindication	ACT[a]
1	Treatment of HIV-1 infection in adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with HIV-1 without known mutations involving resistances against 1 of the 3 ARV drugs and the occurrence of toxicities that rule out the application of other treatment regimens which do not contain TDF	Individual ART based on prior treatment(s) and under consideration of the reason for the switch of treatment, particularly treatment failure due to virologic failure and possible accompanying development of resistance, or due to AEs
a: Presentation of the ACT specified by the G-BA. ART: antiretroviral therapy; COBI: cobicistat; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV: human immunodeficiency virus; TDF: tenofovir disoproxil (fumarate)		

The company followed 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 48 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 EVG/COBI/FTC/TDF (status: 4 October 2017)
- bibliographical literature search on EVG/COBI/FTC/TDF (last search on 4 October 2017)
- search in trial registries for studies on EVG/COBI/FTC/TDF (last search on 4 October 2017)

To check the completeness of the study pool:

- search in trial registries for studies on EVG/COBI/FTC/TDF (last search on 11 December 2017)

No relevant study was identified from the check.

The company also identified no relevant study for the present benefit assessment.

2.4 Results on added benefit

The company presented no data for the assessment of the added benefit of EVG/ COBI/FTC/TDF in comparison with the ACT in the treatment of adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with HIV-1 without known mutations involving resistances against 1 of the 3 ARV drugs and the occurrence of toxicities

that rule out the application of other treatment regimens which do not contain tenofovir disoproxil (fumarate) (TDF). Hence, there was no hint of an added benefit of EVG/COBI/FTC/TDF in comparison with the ACT specified by the G-BA; 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 EVG/COBI/FTC/TDF in comparison with the ACT is shown in Table 5.

Table 5: EVG/COBI/FTC/TDF: probability and extent of added benefit

Subindication	**ACT[a]**	**Probability and extent of added benefit**
Treatment of HIV-1 infection in adolescents aged 12 to < 18 years with a body weight of ≥ 35 kg who are infected with HIV-1 without known mutations involving resistances against 1 of the 3 ARV drugs and the occurrence of toxicities that rule out the application of other treatment regimens which do not contain TDF	Individual ART based on prior treatment(s) and under consideration of the reason for the switch of treatment, particularly treatment failure due to virologic failure and possible accompanying development of resistance, or due to AEs	Added benefit not proven
a: Presentation of the ACT specified by the G-BA. ART: antiretroviral therapy; COBI: cobicistat; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV: human immunodeficiency virus; TDF: tenofovir disoproxil (fumarate)		

The assessment described above concurs with that of the company, which also derived no added benefit for EVG/COBI/FTC/TDF in comparison with the ACT in the present therapeutic indication.

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

The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a17-59-elvitegravir-cobicistat-emtricitabine-tenofovir-disoproxil-hiv-1-in-adolescents-benefit-assessment-according-to-35a-social-code-book-sgb-v.8368.html.