IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A18-01

Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (HIV-infected children) –

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/Cobicistat/Emtricitabin/Tenofovir-alafenamid (HIV-Infektion bei Kindern) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 12 April 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.

Publishing details

Publisher:

Institute for Quality and Efficiency in Health Care

Topic:

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (HIV-infected children) – Benefit assessment according to §35a Social Code Book V

Commissioning agency:

Federal Joint Committee

Commission awarded on:

5 January 2018

Internal Commission No.:

A18-01

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

Medical and scientific advice:

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

IQWiG employees involved in the dossier assessment:

- Claudia Selbach
- Elena Bardach
- Simone Johner
- Vjollcë Olluri
- Min Ripoll
- Dorothea Sow
- Beate Wieseler

Keywords: elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide, HIV infections, child, benefit assessment

Table of contents

List of tables[2]

Page

[2] Table numbers start with "2" as numbering follows that of the full dossier assessment.

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
COBI	cobicistat
EVG	elvitegravir
FTC	emtricitabine
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HIV	human immunodeficiency virus
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)
TAF	tenofovir alafenamide

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 alafenamide (EVG/COBI/FTC/TAF). 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 5 January 2018.

Research question

The aim of the present report was the assessment of the added benefit of EVG/COBI/FTC/TAF in comparison with the appropriate comparator therapy (ACT) in children aged 6 to < 12 years and with body weight of ≥ 25 kg infected with human immunodeficiency virus type 1 (HIV-1) for whom alternative regimens are unsuitable due to toxicities. The HIV must not have any known mutations associated with resistance to the integrase inhibitor class, FTC or tenofovir.

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

Table 2: Research questions of the benefit assessment of EVG/COBI/FTC/TAF

Research question	Subindication	ACT[a, b]
1	Treatment-naive children from 6 to < 12 years	ART of 2 NRTIs (ABC or 3TC or FTC or AZT) and 1 NNRTI (EFV or NVP) or 1 protease inhibitor (LPV/r or ATV/r or DRV/r)
2	Antiretroviral treatment-experienced children from 6 to < 12 years	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 side effects
a: Presentation of the respective ACT specified by the G-BA. b: The combination of FTC and 3TC is contraindicated. 3TC: lamivudine; ABC: abacavir; ART: antiretroviral therapy; ATV: atazanavir; AZT: zidovudine; COBI: cobicistat; DRV: darunavir; EFV: efavirenz; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; LPV: lopinavir; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; NVP: nevirapine; r: ritonavir; TAF: tenofovir alafenamide		

The company mostly 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 were available either for research question 1 or for research question 2 for the assessment of the added benefit of EVG/COBI/FTC/TAF in comparison with the ACT. This concurs with the company's assessment. Hence, there was no hint of an added benefit of EVG/COBI/FTC/TAF 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/TAF in comparison with the ACT is assessed as follows:

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

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

Subindication	**ACT[a, b]**	**Probability and extent of added benefit**
Treatment-naive children from 6 to < 12 years	ART of 2 NRTIs (ABC or 3TC or FTC or AZT) and 1 NNRTI (EFV or NVP) or 1 protease inhibitor (LPV/r or ATV/r or DRV/r)	Added benefit not proven
Antiretroviral treatment-experienced children from 6 to < 12 years	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 side effects	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. b: The combination of FTC and 3TC is contraindicated. 3TC: lamivudine; ABC: abacavir; ART: antiretroviral therapy; ATV: atazanavir; AZT: zidovudine; COBI: cobicistat; DRV: darunavir; EFV: efavirenz; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; LPV: lopinavir; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; NVP: nevirapine; r: ritonavir; TAF: tenofovir alafenamide		

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 the assessment of the added benefit of EVG/COBI/FTC/TAF in comparison with the ACT in children aged 6 to < 12 years and with body weight of ≥ 25 kg infected with HIV-1 for whom alternative regimens are unsuitable due to toxicities. The HIV must not have any known mutations associated with resistance to the integrase inhibitor class, FTC or tenofovir.

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 EVG/COBI/FTC/TAF

Research question	Subindication	ACT[a, b]
1	Treatment-naive children from 6 to < 12 years	ART of 2 NRTIs (ABC or 3TC or FTC or AZT) and 1 NNRTI (EFV or NVP) or 1 protease inhibitor (LPV/r or ATV/r or DRV/r)
2	Antiretroviral treatment-experienced children from 6 to < 12 years	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 side effects
a: Presentation of the respective ACT specified by the G-BA. b: The combination of FTC and 3TC is contraindicated. 3TC: lamivudine; ABC: abacavir; ART: antiretroviral therapy; ATV: atazanavir; AZT: zidovudine; COBI: cobicistat; DRV: darunavir; EFV: efavirenz; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; LPV: lopinavir; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; NVP: nevirapine; r: ritonavir; TAF: tenofovir alafenamide		

The company mostly followed the ACT specified by the G-BA (see Section 2.7.1 of the full dossier assessment).

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/TAF (status: 20 November 2017)
- bibliographical literature search on EVG/COBI/FTC/TAF (last search on 20 November 2017)
- search in trial registries for studies on EVG/COBI/FTC/TAF (last search on 20 November 2017)

To check the completeness of the study pool:

- search in trial registries for studies on EVG/COBI/FTC/TAF (last search on 18 January 2018)

The check identified no relevant study for research question 1 (treatment-naive children) or research question 2 (children with antiretroviral pretreatment).

The company also identified no relevant study for the present benefit assessment. For reasons of completeness, transparency and clinical relevance, it presented the results of the single-arm approval study GS-US-292-0106 in Module 4 A, but did not use it explicitly for the assessment of the added benefit.

2.4 Results on added benefit

The company presented no data for research question 1 or for research question 2 for the assessment of the added benefit of EVG/COBI/FTC/TAF in comparison with the ACT for the treatment of children aged 6 to < 12 years and with body weight of ≥ 25 kg infected with HIV-1 without any known mutations associated with resistance to the integrase inhibitor class, FTC or tenofovir for whom alternative regimens are unsuitable due to toxicities. Hence, there was no hint of an added benefit of EVG/COBI/FTC/TAF 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/TAF in comparison with the ACT is summarized in Table 5.

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

Subindication	**ACT**[a, b]	**Probability and extent of added benefit**
Treatment-naive children from 6 to < 12 years	ART of 2 NRTIs (ABC or 3TC or FTC or AZT) and 1 NNRTI (EFV or NVP) or 1 protease inhibitor (LPV/r or ATV/r or DRV/r)	Added benefit not proven
Antiretroviral treatment-experienced children from 6 to < 12 years	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 side effects	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. b: The combination of FTC and 3TC is contraindicated. 3TC: lamivudine; ABC: abacavir; ART: antiretroviral therapy; ATV: atazanavir; AZT: zidovudine; COBI: cobicistat; DRV: darunavir; EFV: efavirenz; EVG: elvitegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; LPV: lopinavir; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; NVP: nevirapine; r: ritonavir; TAF: tenofovir alafenamide		

The assessment described above concurs with that of the company, which also derived no added benefit for ECG/COBI/FTC/TAF 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/a18-01-elvitegravir-cobicistat-emtricitabine-tenofovir-alafenamide-hiv-infected-children-benefit-assessment-according-to-35a-social-code-book-v.8882.html.