# Elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide (HIV-1 infection [children ≥ 2 to < 6 years and with a body weight of ≥ 14 kg]) –

## Benefit assessment according to §35a SGB V[1]

**EXTRACT**

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[1] Translation of Sections I 2 to I 7 of the dossier assessment *Elvitegravir/Cobicistat/Emtricitabin/ Tenofoviralafenamid (HIV-1-Infektion [Kinder ≥ 2 bis < 6 Jahre und ≥ 14 kg Körpergewicht]) – Nutzenbewertung gemäß § 35a SGB V*. 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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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 available for the present dossier assessment.

**Patient and family involvement**

No feedback was received in the framework of the present dossier assessment.

**IQWiG employees involved in the dossier assessment**

- Helmut Hörn
- Simone Heß
- Christopher Kunigkeit
- Ana Liberman
- Annette Pusch-Klein
- Min Ripoll
- Anke Schulz

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# Part I: Benefit assessment

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

# I List of abbreviations

| Abbreviation | Meaning |
|---|---|
| ACT | appropriate comparator therapy |
| EVG/COBI/FTC/TAF | elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide |
| G-BA | Gemeinsamer Bundesausschuss (Federal Joint Committee) |
| HIV-1 | human immunodeficiency virus-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) |

## I 2 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 fixed drug combination elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF). 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 31 October 2022.

### Research question

The aim of the present report is to assess the added benefit of EVG/COBI/FTC/TAF in comparison with the appropriate comparator therapy (ACT) in patients aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with human immunodeficiency virus-1 (HIV-1) infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

The research questions shown in Table 2 are derived from the ACT specified by the G-BA.

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

| Research question | Therapeutic indication | ACT[a, b] |
|---|---|---|
| 1 | Treatment-naive children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Abacavir + lamivudine or abacavir + emtricitabine, each in combination with<br>▪ dolutegravir or<br>▪ lopinavir/ritonavir or<br>▪ raltegravir or<br>▪ nevirapine or<br>▪ atazanavir/ritonavir or<br>▪ darunavir/ritonavir |
| 2 | Pretreated children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Individual antiretroviral therapy chosen from the approved drugs; under consideration of prior treatment(s) and 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. Presented is the respective ACT specified by the G-BA.
b. The use of the drugs in compliance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
c. The HIV must not have any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; EVG/COBI/FTC/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus-1

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

The assessment is 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 are used for the derivation of added benefit.

**Results**

In agreement with the company, no relevant study was identified for the assessment of the added benefit of EVG/COBI/FTC/TAF in comparison with the ACT for either of the 2 research questions (see Table 2).

Since no relevant study is available for the benefit assessment, there is no hint of an added benefit of EVG/COBI/FTC/TAF in comparison with the ACT for either research question; 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 the probability and extent of added benefit of EVG/COBI/FTC/TAF.

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

| **Research question** | **Therapeutic indication** | **ACT[a, b]** | **Probability and extent of added benefit** |
|---|---|---|---|
| 1 | Treatment-naive children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Abacavir + lamivudine or abacavir + emtricitabine, each in combination with<br>▪ dolutegravir or<br>▪ lopinavir/ritonavir or<br>▪ raltegravir or<br>▪ nevirapine or<br>▪ atazanavir/ritonavir or<br>▪ darunavir/ritonavir | Added benefit not proven |
| 2 | Pretreated children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Individual antiretroviral therapy chosen from the approved drugs; under consideration of prior treatment(s) and 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. Presented is the respective ACT specified by the G-BA.
b. The use of the drugs in compliance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
c. The HIV must not have any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; EVG/COBI/FTC/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus-1

The G-BA decides on the added benefit.

## I 3 Research question

The aim of the present report is to assess the added benefit of EVG/COBI/FTC/TAF in comparison with the ACT in patients aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

The research questions shown in Table 4 are derived from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of the drug combination EVG/COBI/FTC/TAF

| Research question | Therapeutic indication | ACT[a, b] |
|---|---|---|
| 1 | Treatment-naive children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Abacavir + lamivudine or abacavir + emtricitabine, each in combination with<br>▪ dolutegravir or<br>▪ lopinavir/ritonavir or<br>▪ raltegravir or<br>▪ nevirapine or<br>▪ atazanavir/ritonavir or<br>▪ darunavir/ritonavir |
| 2 | Pretreated children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Individual antiretroviral therapy chosen from the approved drugs; under consideration of prior treatment(s) and 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. Presented is the respective ACT specified by the G-BA.
b. The use of the drugs in compliance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
c. The HIV must not have any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; EVG/COBI/FTC/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus-1

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

The assessment is 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 are used for the derivation of added benefit. This concurs with the company’s inclusion criteria.

## I 4 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 lists on EVG/COBI/FTC/TAF (status: 3 August 2022)
- bibliographical literature search on EVG/COBI/FTC/TAF (last search on 3 August 2022)
- search in trial registries/trial results databases for studies on EVG/COBI/FTC/TAF (last search on 3 August 2022)

To check the completeness of the study pool:

- search in trial registries for studies on EVG/COBI/FTC/TAF (last search on 22 November 2022); for search strategies, see I Appendix A of the full dossier assessment

The check did not identify any relevant studies for either research question 1 (treatment-naive children) or research question 2 (pretreated children).

The company concurred by reporting not to have identified any relevant studies for the present research questions. It presented the results of the uncontrolled approval study GS-US-292-0106 [3] in Module 4 A as supplementary information, but did not use this study to derive an added benefit. The company's approach is appropriate.

## I 5 Results on added benefit

Since no relevant study is available for the benefit assessment, there is no hint of an added benefit of EVG/COBI/FTC/TAF in comparison with the ACT for either research question; an added benefit is therefore not proven.

## I 6 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

| Research question | Therapeutic indication | ACT[a, b] | Probability and extent of added benefit |
|---|---|---|---|
| 1 | Treatment-naive children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Abacavir + lamivudine or abacavir + emtricitabine, each in combination with<br>▪ dolutegravir or<br>▪ lopinavir/ritonavir or<br>▪ raltegravir or<br>▪ nevirapine or<br>▪ atazanavir/ritonavir or<br>▪ darunavir/ritonavir | Added benefit not proven |
| 2 | Pretreated children aged ≥ 2 to < 6 years and with a body weight of ≥ 14 kg with HIV-1 infection[c] | Individual antiretroviral therapy chosen from the approved drugs; under consideration of prior treatment(s) and 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. Presented is the respective ACT specified by the G-BA.
b. The use of the drugs in compliance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
c. The HIV must not have any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; EVG/COBI/FTC/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus-1

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

The G-BA decides on the added benefit.

## I 7 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. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 6.1 [online]. 2022 [Accessed: 27.01.2022]. URL: https://www.iqwig.de/methoden/allgemeine-methoden-v6-1.pdf.

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3. Gilead Sciences. Study to Evaluate the Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in HIV-1 Infected Antiretroviral Treatment-Naive Adolescents and Virologically Suppressed Children [online]. 2022 [Accessed: 16.11.2022]. URL: https://clinicaltrials.gov/ct2/show/NCT01854775.

*The full report (German version) is published under https://www.iqwig.de/en/projects/a22-116.html.*