Bictegravir/emtricitabine/tenofovir alafenamide (HIV infection in children and adolescents)

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

EXTRACT

Project: A22-134 Version: 1.0 Status: 24 March 2023

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Bictegravir/Emtricitabin/Tenofoviralafenamid (HIV-Infektion bei Kindern und Jugendlichen) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This document was translated by an external translator and 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

Bictegravir/emtricitabine/tenofovir alafenamide (HIV infection in children and adolescents) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

20 December 2022

Internal Project No.

A22-134

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.

Patient and family involvement

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

IQWiG employees involved in the dossier assessment

- Ulrike Mikulić
- Ulrich Grouven
- Tatjana Hermanns
- Christopher Kunigkeit
- Prateek Mishra
- Regine Potthast
- Min Ripoll

Keywords

Bictegravir, Emtricitabine, Tenofovir Alafenamide, HIV Infections, Child, Adolescent, Benefit Assessment

Part I: Benefit assessment

I Table of contents

I List of tables[2]

Page

[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
BIC	bictegravir
FTC	emtricitabine
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)
TAF	tenofovir alafenamide

I 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 bictegravir/emtricitabine/tenofovir alafenamide (BIC/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 20 December 2022.

Research question

The aim of this report was to assess the added benefit of BIC/FTC/TAF compared with the appropriate comparator therapy (ACT) for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in children and adolescents at least 2 years of age and weighing at least 14 kg. There must be neither present nor past evidence of HI virus 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 BIC/FTC/TAF

Research question	**Therapeutic indication**	**ACT[a]**
1	HIV-1 infection[b] in treatment-naive children 2 to < 6 years of age weighing at least 14 kg	▪ Abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ lopinavir/ritonavir or ▫ raltegravir or ▫ nevirapine or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir
2	HIV-1 infection[b] in treatment-naive children 6 to < 12 years of age weighing at least 14 kg	▪ Abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir
3	HIV-1 infection[b] in treatment-naive adolescents 12 to < 18 years of age weighing at least 14 kg	▪ Tenofovir alafenamide + emtricitabine or ▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir or ▫ elvitegravir/cobicistat
4	HIV-1 infection[b] in treatment-experienced children 2 to < 18 years of age weighing at least 14 kg	Individualized antiretroviral therapy chosen from the approved drugs, taking into account prior treatment(s) and the reason for the treatment switch, 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. There must be neither present nor past evidence of resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; BIC: bictegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1; TAF: tenofovir alafenamide

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 were used for deriving the added benefit.

Results

Concurring with the company, no relevant studies were found for any of the 4 research questions in the assessment of added benefit of BIC/FTC/TAF in comparison with the ACT for the treatment of HIV-1 in children and adolescents at least 2 years of age and weighing at least 14 kg. This results in no hint of an added benefit of BIC/FTC/TAF in comparison 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 the probability and extent of added benefit of BIC/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: BIC/FTC/TAF – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	HIV-1 infection[b] in treatment-naive children 2 to < 6 years of age weighing at least 14 kg	▪ Abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ lopinavir/ritonavir or ▫ raltegravir or ▫ nevirapine or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir	Added benefit not proven
2	HIV-1 infection[b] in treatment-naive children 6 to < 12 years of age weighing at least 14 kg	▪ Abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir	Added benefit not proven
3	HIV-1 infection[b] in treatment-naive adolescents 12 to < 18 years of age weighing at least 14 kg	▪ Tenofovir alafenamide + emtricitabine or ▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir or ▫ elvitegravir/cobicistat	Added benefit not proven
4	HIV-1 infection[b] in treatment-experienced children 2 to < 18 years of age weighing at least 14 kg	Individualized antiretroviral therapy chosen from the approved drugs, taking into account prior treatment(s) and the reason for the treatment switch, 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. There must be neither present nor past evidence of resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; BIC: bictegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1; TAF: tenofovir alafenamide

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report was to assess the added benefit of BIC/FTC/TAF compared with the ACT in children and adolescents 2 years of age and older and weighing at least 14 kg who are infected with HIV-1. There must be neither present nor past evidence of HI virus 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 BIC/FTC/TAF

Research question	**Therapeutic indication**	**ACT[a]**
1	HIV-1 infection[b] in treatment-naive children 2 to < 6 years of age weighing at least 14 kg	▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ lopinavir/ritonavir or ▫ raltegravir or ▫ nevirapine or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir
2	HIV-1 infection[b] in treatment-naive children 6 to < 12 years of age weighing at least 14 kg	▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir
3	HIV-1 infection[b] in treatment-naive adolescents 12 to < 18 years of age weighing at least 14 kg	▪ tenofovir alafenamide + emtricitabine or ▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir or ▫ elvitegravir/cobicistat
4	HIV-1 infection[b] in treatment-experienced children 2 to < 18 years of age weighing at least 14 kg	Individualized antiretroviral therapy chosen from the approved drugs, taking into account prior treatment(s) and the reason for the treatment switch, 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. There must be neither present nor past evidence of resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; BIC: bictegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1; TAF: tenofovir alafenamide

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 were used for deriving the added benefit. This concurs with the company's inclusion criteria.

I 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 BIC/FTC/TAF (status: 24 October 2022)
- bibliographical literature search on BIC/FTC/TAF (last search on 24 October 2022)
- search in trial registries for studies on BIC/FTC/TAF (last search on 24 October 2022)
- search on the G-BA website for BIC/FTC/TAF (last search on 24 October 2022)

Completeness of the study pool was checked by means of:

- search in trial registries for studies on BIC/FTC/TAF (last search on 20 January 2023); for search strategies, see I Appendix A of the full dossier assessment

The check did not identify any relevant studies for assessing the added benefit of BIC/FTC/TAF in comparison with the ACT. This concurs with the company's assessment.

In Module 4A, the company presents data from the single-arm approval study GS1474 [3,4], which enrolled children and adolescents 2 to < 18 years of age weighing ≥ 14 kg with virologically suppressed HIV-1 infection. The company presents the results of this study as supplementary information, disregarding it in its derivation of added benefit. The company’s approach is appropriate.

I 4 Results on added benefit

No suitable data were available for the 4 research questions in the assessment of added benefit of BIC/FTC/TAF in comparison with the ACT for HIV-1 infection in children and adolescents aged 2 years and older and weighing at least 14 kg. This results in no hint of an added benefit of BIC/FTC/TAF in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

Table 5 summarizes the result of the assessment of added benefit of BIC/FTC/TAF in comparison with the ACT.

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

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	HIV-1 infection[b] in treatment-naive children 2 to < 6 years of age weighing at least 14 kg	▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ lopinavir/ritonavir or ▫ raltegravir or ▫ nevirapine or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir	Added benefit not proven
2	HIV-1 infection[b] in treatment-naive children 6 to < 12 years of age weighing at least 14 kg	▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir	Added benefit not proven
3	HIV-1 infection[b] in treatment-naive adolescents 12 to < 18 years of age weighing at least 14 kg	▪ tenofovir alafenamide + emtricitabine or ▪ abacavir + lamivudine or ▪ abacavir + emtricitabine each in combination with ▫ dolutegravir or ▫ atazanavir/ritonavir or ▫ darunavir/ritonavir or ▫ elvitegravir/cobicistat	Added benefit not proven
4	HIV-1 infection[b] in treatment-experienced children 2 to < 18 years of age weighing at least 14 kg	Individualized antiretroviral therapy chosen from the approved drugs, taking into account prior treatment(s) and the reason for the treatment switch, 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. There must be neither present nor past evidence of resistance to the integrase inhibitor class, emtricitabine or tenofovir.

ACT: appropriate comparator therapy; BIC: bictegravir; FTC: emtricitabine; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1; TAF: tenofovir alafenamide

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

The G-BA decides on the added benefit.

I 6 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.

2. Skipka G, Wieseler B, Kaiser T et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2016; 58(1): 43-58. https://dx.doi.org/10.1002/bimj.201300274.

3. ClinicalTrials.gov. NCT02881320 - Titel: B/F/TAF FDC in HIV-1 Infected Adolescents and Children [online]. 2022. URL: https://ClinicalTrials.gov/show/NCT02881320.

4. Gaur AH, Cotton MF, Rodriguez CA et al. Fixed-dose combination bictegravir, emtricitabine, and tenofovir alafenamide in adolescents and children with HIV: week 48 results of a single-arm, open-label, multicentre, phase 2/3 trial. Lancet Child Adolesc Health 2021; 5(9): 642-651. https://dx.doi.org/10.1016/s2352-4642(21)00165-6.

The full report (German version) is published under https://www.iqwig.de/en/projects/a22-134.html.