Dolutegravir/abacavir/lamivudine (HIV infection in children)

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

EXTRACT

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[1] Translation of Sections I 1 to I 6 of the dossier assessment *Dolutegravir/Abacavir/Lamivudin (HIV-Infektion bei Kindern) – 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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No advisor on medical and scientific questions was involved in the present dossier assessment.

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No patients or families were involved in the present dossier assessment.

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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
DTG/ABC/3TC	dolutegravir/abacavir/lamivudine
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HIV	human immunodeficiency virus
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 1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book, 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 dolutegravir/abacavir/lamivudine (DTG/ABC/3TC). 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 1 March 2023.

Research question

The aim of this report is to assess the added benefit of DTG/ABC/3TC compared with the appropriate comparator therapy (ACT) in human immunodeficiency virus (HIV)-infected children < 12 years of age and weighing at least 14 kg.

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 DTG/ABC/3TC

Research question	Therapeutic indication	ACT[a]
1	Treatment-naive children with HIV-1 infection[b] aged 2 to < 6 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ lopinavir/ritonavir or ▪ raltegravir or ▪ nevirapine or ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir
2	Treatment-naive children with HIV-1 infection[b] aged 6 to < 12 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir
3	Treatment-experienced children with HIV-1 infection[b] aged 2 to < 12 years	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. The use of the drugs in accordance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
b. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

DTG/ABC/3TC: dolutegravir/abacavir/lamivudine; G-BA: Federal Joint Committee; HIV: human immunodeficiency virus; HLA: human leukocyte antigen

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

No suitable data are available for any of the 3 research questions in the assessment of added benefit of DTG/ABC/3TC in comparison with the ACT for HIV-infected children < 12 years of age and weighing at least 14 kg. This results in no hint of an added benefit of DTG/ABC/3TC 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 probability and extent of the added benefit of DTG/ABC/3TC.

[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: DTG/ABC/3TC – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Treatment-naive children with HIV-1 infection[b] aged 2 to < 6 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ lopinavir/ritonavir or ▪ raltegravir or ▪ nevirapine or ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir	Added benefit not proven
2	Treatment-naive children with HIV-1 infection[b] aged 6 to < 12 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir	Added benefit not proven
3	Treatment-experienced children with HIV-1 infection[b] aged 2 to < 12 years	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. The use of the drugs in accordance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
b. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

DTG/ABC/3TC: dolutegravir/abacavir/lamivudine; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1; HLA: human leukocyte antigen

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report is to assess the added benefit of DTG/ABC/3TC compared with the ACT in HIV-infected children < 12 years of age and weighing at least 14 kg.

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 DTG/ABC/3TC

Research question	Therapeutic indication	ACT[a]
1	Treatment-naive children with HIV-1 infection[b] aged 2 to < 6 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ lopinavir/ritonavir or ▪ raltegravir or ▪ nevirapine or ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir
2	Treatment-naive children with HIV-1 infection[b] aged 6 to < 12 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir
3	Treatment-experienced children with HIV-1 infection[b] aged 2 to < 12 years	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. The use of the drugs in accordance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
b. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

DTG/ABC/3TC: dolutegravir/abacavir/lamivudine; G-BA: Federal Joint Committee; HIV: human immunodeficiency virus; HLA: human leukocyte antigen

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 DTG/ABC/3TC (status: 3 January 2023)
- bibliographical literature search on DTG/ABC/3TC (last search on 3 January 2023)
- search in trial registries/trial results databases for studies on DTG/ABC/3TC (last search on 3 January 2023)
- search on the G-BA website for DTG/ABC/3TC (last search on 3 January 2023)

To check the completeness of the study pool:

- search in trial registries for studies on DTG/ABC/3TC (last search on 15 March 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 DTG/ABC/3TC in comparison with the ACT. This concurs with the company's assessment.

In Module 4 A, the company presented data from the single-arm IMPAACT 2019 study [3], which included HIV-1-infected children up to an age of < 12 years and weighing between 6 and < 40 kg. The company presented the results of this study only as supplementary information, without using it for the derivation of added benefit.

I 4 Results on added benefit

No suitable data are available for any of the 3 research questions in the assessment of added benefit of DTG/ABC/3TC in comparison with the ACT for HIV-infected children < 12 years of age and weighing at least 14 kg. This results in no hint of an added benefit of DTG/ABC/3TC in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of DTG/ABC/3TC in comparison with the ACT is summarized in Table 5.

Table 5: DTG/ABC/3TC – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Treatment-naive children with HIV-1 infection[b] aged 2 to < 6 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ lopinavir/ritonavir or ▪ raltegravir or ▪ nevirapine or ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir	Added benefit not proven
2	Treatment-naive children with HIV-1 infection[b] aged 6 to < 12 years	Abacavir + lamivudine or abacavir + emtricitabine, each in combination with ▪ atazanavir/ritonavir or ▪ darunavir/ritonavir	Added benefit not proven
3	Treatment-experienced children with HIV-1 infection[b] aged 2 to < 12 years	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. The use of the drugs in accordance with the approval must be observed. Here, in particular, the age-appropriate use of the drugs.
b. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

DTG/ABC/3TC: dolutegravir/abacavir/lamivudine; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1; HLA: human leukocyte antigen

The assessment described above deviates from the company's, which generally argued with high efficacy, good tolerability and a child-friendly formulation, and derived a hint of non-quantifiable added benefit for each of the 3 research questions.

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.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a23-17.html.