IQWiG Reports – Commission No. A20-37

Cobicistat (HIV infection in adolescents) –

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

Extract

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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
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 cobicistat. 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 02 April 2020.

Due to the working conditions during the coronavirus pandemic, the present assessment was conducted without the use of strictly confidential data presented in Module 5 of the company's dossier.

Research question

The aim of this report is to assess the added benefit of cobicistat as a pharmacokinetic enhancer (i.e. booster) of atazanavir 300 mg once daily or darunavir 800 mg once daily as part of antiretroviral combination therapy in comparison with ritonavir as the appropriate comparator therapy (ACT) in human immunodeficiency virus type 1 (HIV-1) infected adolescents 12 years and older weighing ≥ 35 kg (if co-administered with atazanavir) or ≥ 40 kg (if co-administered with darunavir).

The ACT specified by the G-BA served as the basis for the research question presented in Table 2 for this benefit assessment.

Table 2: Research questions of the benefit assessment of cobicistat

Research question	Therapeutic indication	ACT[a]
1	HIV-1-infected adolescents aged 12 years and older[b]	Ritonavir

a. Presentation of ACT specified by the G-BA.
b. Body weight of ≥ 35 kg if co-administered with atazanavir or ≥ 40 kg if co-administered with darunavir.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1

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

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.

Results

In its dossier, the company did not present any data for the assessment of added benefit of cobicistat in comparison with the ACT in HIV-1-infected adolescents aged 12 years and older.

Consequently, there is no hint of added benefit of cobicistat 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 presents a summary of the probability and extent of added benefit of cobicistat.

Table 3: Cobicistat – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
HIV-1-infected adolescents aged 12 years and older[b]	Ritonavir	Added benefit not proven

a. Presentation of ACT specified by the G-BA.
b. Body weight of ≥ 35 kg if co-administered with atazanavir or ≥ 40 kg if co-administered with darunavir.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1

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 this report is to assess the added benefit of cobicistat as a pharmacokinetic enhancer (i.e. booster) of atazanavir 300 mg once daily or darunavir 800 mg once daily as part of antiretroviral combination therapy in comparison with ritonavir as the appropriate comparator therapy (ACT) in HIV-1 infected adolescents 12 years and older weighing ≥ 35 kg (if co-administered with atazanavir) or ≥ 40 kg (if co-administered with darunavir).

The ACT specified by the G-BA served as the basis for the research question presented in Table 4 for this benefit assessment.

Table 4: Research questions of the benefit assessment of cobicistat

Research question	Therapeutic indication	ACT[a]
1	HIV-1-infected adolescents aged 12 years and older[b]	Ritonavir

a. Presentation of ACT specified by the G-BA.
b. Body weight of ≥ 35 kg if co-administered with atazanavir or ≥ 40 kg if co-administered with darunavir.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1

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

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 cobicistat (status: 19 February 2020)
- Bibliographic literature search on cobicistat (most recent search on 19 February 2020)
- Search in trial registries for studies on cobicistat (most recent search on 19 February 2020)

To check the completeness of the study pool:

- Search in trial registries for studies on cobicistat (most recent search on 16 April 2020)

Concurring with the company, the check of completeness of the study pool did not show any RCT with HIV-1-infected adolescents aged 12 years and older comparing cobicistat with the ACT.

The company presented the data of the ongoing, 1-arm approval study GS-US-216-0128 [3]. Since the study involves no comparison, the company considers this study irrelevant for the benefit assessment and therefore did not use it in its dossier assessment. This approach is appropriate.

2.4 Results on added benefit

In its dossier, the company did not present any data for the assessment of added benefit of cobicistat in comparison with the ACT in HIV-1-infected adolescents aged 12 years and older. Consequently, there is no hint of added benefit of cobicistat in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

Since the company did not present any data for the assessment of the added benefit of cobicistat in comparison with the ACT in HIV-1-infected adolescents 12 years of age and older, an added benefit is not proven.

Table 5 presents a summary of the results regarding the benefit assessment of cobicistat in comparison with the ACT.

Table 5: Cobicistat – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
HIV-1-infected adolescents aged 12 years and older[b]	Ritonavir	Added benefit not proven
a. Presentation of ACT specified by the G-BA. b. Body weight of ≥ 35 kg if co-administered with atazanavir or ≥ 40 kg if co-administered with darunavir. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HIV-1: human immunodeficiency virus type 1		

The above-described assessment of the extent and probability of added benefit agrees with that of the company.

The G-BA decides on the added benefit.

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: 01.07.2019]. 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 2016; 58(1): 43-58.

3. Gilead Sciences. A phase 2/3, multicenter, open-label, multicohort, two-part study evaluating pharmacokinetics (PK), safety, and efficacy of cobicistat-boosted atazanavir (ATV/co) or cobicistat-boosted darunavir (DRV/co), administered with a background regimen (BR) in HIV-1 infected, treatment-experienced, virologically suppressed pediatric subjects: interim 1 clinical study report; GS-US-216-0128. 2019.

The full report (German version) is published under *https://www.iqwig.de/en/projects-results/projects/drug-assessment/a20-37-cobicistat-hiv-infection-benefit-assessment-according-to-35a-social-code-book-v.13065.html*.