

Acalabrutinib (previously untreated chronic lymphocytic leukaemia, combination with venetoclax)

Benefit assessment according to §35a SGB V¹



EXTRACT

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Patient and family involvement

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

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Part I: Benefit assessment

I Table of contents

	Page
I List of tables	I.3
I List of abbreviations.....	I.4
I 1 Executive summary of the benefit assessment	I.5
I 2 Research question.....	I.7
I 3 Information retrieval and study pool.....	I.8
I 4 Results on added benefit.....	I.9
I 5 Probability and extent of added benefit	I.10
I 6 References for English extract	I.11

I List of tables²

	Page
Table 2: Research question of the benefit assessment of acalabrutinib + venetoclax	I.5
Table 3: Acalabrutinib + venetoclax – probability and extent of added benefit	I.6
Table 4: Research question of the benefit assessment of acalabrutinib + venetoclax	I.7
Table 5: Acalabrutinib + venetoclax – probability and extent of added benefit	I.10

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
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
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 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 acalabrutinib (in combination with venetoclax). 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 01 July 2025.

Research question

The aim of this report is the assessment of the added benefit of acalabrutinib in combination with venetoclax (hereinafter referred to as "acalabrutinib + venetoclax") in comparison with the appropriate comparator therapy (ACT) in adult patients with previously untreated chronic lymphocytic leukaemia (CLL).

The research question shown in Table 2 was defined in accordance with the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of acalabrutinib + venetoclax

Therapeutic indication	ACT ^a
Adult patients with previously untreated CLL ^b	<ul style="list-style-type: none"> ▪ Ibrutinib ± obinutuzumab or ▪ venetoclax in combination with obinutuzumab or ▪ venetoclax in combination with ibrutinib or ▪ acalabrutinib ± obinutuzumab or ▪ zanubrutinib
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. For this therapeutic indication, the G-BA assumes that the patients require treatment (e.g. Binet stage C). Moreover, it is assumed that allogeneic stem cell transplantation is not indicated at the time point of treatment.</p> <p>ACT: appropriate comparator therapy; CLL: chronic lymphocytic leukaemia; G-BA: Federal Joint Committee</p>	

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) were used to derive the added benefit.

Results

The check of the completeness of the information retrieval did not identify any relevant RCT for assessing the added benefit of acalabrutinib + venetoclax in comparison with the ACT.

Results on added benefit

Since no relevant study is available for the benefit assessment, there is no hint of an added benefit of acalabrutinib + venetoclax in comparison with the ACT for adult patients with previously untreated CLL; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit³

Table 3 shows a summary of the probability and extent of the added benefit of acalabrutinib + venetoclax.

Table 3: Acalabrutinib + venetoclax – probability and extent of added benefit

Therapeutic indication	ACT ^a	Probability and extent of added benefit
Adult patients with previously untreated CLL ^b	<ul style="list-style-type: none"> ▪ Ibrutinib ± obinutuzumab or ▪ venetoclax in combination with obinutuzumab or ▪ venetoclax in combination with ibrutinib or ▪ acalabrutinib ± obinutuzumab or ▪ zanubrutinib 	Added benefit not proven
<p>a. Presented is the ACT specified by the G-BA. b. For this therapeutic indication, the G-BA assumes that the patients require treatment (e.g. Binet stage C). Moreover, it is assumed that allogeneic stem cell transplantation is not indicated at the time point of treatment. ACT: appropriate comparator therapy; CLL: chronic lymphocytic leukaemia; G-BA: Federal Joint Committee</p>		

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].

1.2 Research question

The aim of this report is the assessment of the added benefit of acalabrutinib in combination with venetoclax (hereinafter referred to as “acalabrutinib + venetoclax”) in comparison with the ACT in adult patients with previously untreated CLL.

The research question shown in Table 4 was defined in accordance with the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of acalabrutinib + venetoclax

Therapeutic indication	ACT ^a
Adult patients with previously untreated CLL ^b	<ul style="list-style-type: none"> ▪ Ibrutinib ± obinutuzumab or ▪ venetoclax in combination with obinutuzumab or ▪ venetoclax in combination with ibrutinib or ▪ acalabrutinib ± obinutuzumab or ▪ zanubrutinib
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. For this therapeutic indication, the G-BA assumes that the patients require treatment (e.g. Binet stage C). Moreover, it is assumed that allogeneic stem cell transplantation is not indicated at the time point of treatment.</p> <p>ACT: appropriate comparator therapy; CLL: chronic lymphocytic leukaemia; G-BA: Federal Joint Committee</p>	

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 were used to derive the added benefit. This concurred with the company's inclusion criteria.

I 3 Information retrieval and study pool

The study pool for the assessment was compiled on the basis of the following information:

Sources used by the company in the dossier:

- Study list on acalabrutinib + venetoclax (status: 19 May 2025)
- Bibliographical literature search on acalabrutinib + venetoclax (last search on 20 May 2025)
- Search in trial registries/trial results databases for studies on acalabrutinib + venetoclax (last search on 19 May 2025)
- Search on the G-BA website for acalabrutinib + venetoclax (last search on 20 May 2025)

To check the completeness of the study pool:

- Search in trial registries for studies on acalabrutinib + venetoclax (last search on 15 July 2025); for search strategies, see Appendix A of the full dossier assessment

Concurring with the company, this review did not identify any relevant study.

For reasons of clinical relevance and to describe the medical benefit, the company presents the approval study AMPLIFY [3,4]. The study is a randomized, open-label phase III study comparing acalabrutinib + venetoclax or acalabrutinib + venetoclax + obinutuzumab with a chemoimmunotherapy (either fludarabine + cyclophosphamide + rituximab or bendamustine + rituximab). Neither of the two chemoimmunotherapies used in the AMPLIFY study is included in the ACT (see Table 4). This means that there are no data for the comparison of acalabrutinib + venetoclax with the G-BA's comparator therapy.

I 4 Results on added benefit

Since no relevant study is available for the benefit assessment, there is no hint of an added benefit of acalabrutinib + venetoclax in comparison with the ACT for adult patients with previously untreated CLL; 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 acalabrutinib + venetoclax in comparison with the ACT.

Table 5: Acalabrutinib + venetoclax – probability and extent of added benefit

Therapeutic indication	ACT ^a	Probability and extent of added benefit
Adult patients with previously untreated CLL ^b	<ul style="list-style-type: none"> ▪ Ibrutinib ± obinutuzumab or ▪ venetoclax in combination with obinutuzumab or ▪ venetoclax in combination with ibrutinib or ▪ acalabrutinib ± obinutuzumab or ▪ zanubrutinib 	Added benefit not proven
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. For this therapeutic indication, the G-BA assumes that the patients require treatment (e.g. Binet stage C). Moreover, it is assumed that allogeneic stem cell transplantation is not indicated at the time point of treatment.</p> <p>ACT: appropriate comparator therapy; CLL: chronic lymphocytic leukaemia; G-BA: Federal Joint Committee</p>		

The assessment described above concurs with the company's assessment.

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.

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