Concizumab (haemophilia A)

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

EXTRACT

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Concizumab, Hemophilia A, Adolescent, Adult, Benefit Assessment

Medical and scientific advice

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IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Günter Auerswald and one other person.

IQWiG thanks the respondents and the patient organization 'Deutsche Hämophiliegesellschaft e. V.' for participating in the written exchange and for their support. The respondents and the 'Deutsche Hämophiliegesellschaft e. V.' were not involved in the actual preparation of the 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
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 concizumab. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the 'company'). The dossier was sent to IQWiG on 29 April 2025.

Research question

The aim of this report is to assess the added benefit of concizumab compared with emicizumab as the appropriate comparator therapy (ACT) for routine prophylaxis of bleeding in patients 12 years of age or more with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors.

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

Table 2: Research question for the benefit assessment of concizumab

Therapeutic indication	**ACT**[a]
Routine prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors[b] and of 12 years of age or more	emicizumab
a. Presented is the ACT specified by the G-BA. b. It is assumed that the patient population for the therapeutic indication in question is patients with haemophilia requiring factor VIII replacement therapy. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

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

Results

A review of the completeness of the study pool did not reveal any relevant studies for assessing the added benefit of concizumab in comparison with the ACT.

Results on added benefit

Since no relevant study was available for the benefit assessment, there is no hint of an added benefit of concizumab 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 the added benefit of concizumab.

Table 3: Concizumab – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Routine prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors[b] and of 12 years of age or more	emicizumab	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. It is assumed that the patient population for the therapeutic indication in question is patients with haemophilia requiring factor VIII replacement therapy.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

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].

I 2 Research question

The aim of this report is to assess the added benefit of concizumab compared with emicizumab as the ACT for routine prophylaxis of bleeding in patients 12 years of age or more with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors.

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

Table 4: Research question for the benefit assessment of concizumab

Therapeutic indication	**ACT**[a]
Routine prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors[b] and of 12 years of age or more	emicizumab
a. Presented is the ACT specified by the G-BA. b. It is assumed that the patient population for the therapeutic indication in question is patients with haemophilia requiring factor VIII replacement therapy. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

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 24 weeks 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 concizumab (status: 19 February 2025)
- Bibliographical literature search on concizumab (last search on 19 February 2025)
- Search of trial registries/trial results databases for studies on concizumab (last search on 19 February 2025)
- Search on the G-BA website for concizumab (last search on 19 February 2025)
- Bibliographical literature search on the ACT (last search on 19 February 2025)
- Search of trial registries/trial results databases for studies on the ACT (last search on 19 February 2025)
- Search on the G-BA website for the ACT (last search on 19 February 2025)

To check the completeness of the study pool:

Search of trial registries for studies on concizumab (last search on 13 May 2025); for search strategies, see I Appendix A of the full dossier assessment

Direct comparison

Concurring with the company, the review of the completeness of the study pool did not identify any relevant studies for the assessment of the added benefit of concizumab versus the ACT.

Supplementary evidence presented by the company – the explorer7 study

Regardless of the results of its information retrieval, in Module 4 A of the dossier the company presented results on the RCT explorer7 [3], conducted on the relevant therapeutic indication, as supplementary data. Explorer7 is an open-label RCT comparing concizumab with on-demand treatment with bypassing agents. In Module 4 A, the company presented results from analyses of the subpopulation of patients with haemophilia A with inhibitors for the primary data cut date from 27 December 2021 and, based on this supplementary data, derived a hint of non-quantifiable added benefit.

The treatment in the control arm of explorer7 did not correspond to the ACT, so this study did not provide any data for comparing concizumab with the comparator therapy specified by the G-BA.

Indirect comparison

As no study of direct comparison relevant for the benefit assessment was identified, the company conducted an information retrieval on studies that could be considered for an indirect comparison between concizumab and emicizumab via a common comparator. It identified the above-mentioned explorer7 study for concizumab as well as the HAVEN 1 study, which compared emicizumab with episodic treatment with bypassing agents [4]. The company considered explorer7 and HAVEN 1 to be unsuitable for conducting an indirect comparison, as they were not sufficiently similar. The company stated that one of the reasons for this was that no patients with a documented inhibitor titre < 5 Bethesda units were enrolled in HAVEN 1, whereas the exclusion criterion for explorer7 was < 0.6 Bethesda units. In addition, the company saw differences in the number of target joints and in the age and weight of the patients, and indicated differences with regard to bleeding episodes in the control arms of the studies. Despite this substantive justification, the company stated that it would not conduct the indirect comparison for formal reasons.

I 4 Results on added benefit

No suitable data were available for the assessment of concizumab in comparison with the ACT emicizumab for the routine prophylaxis of bleeding in patients aged 12 years or more with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors. There is no hint of an added benefit of concizumab 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 concizumab in comparison with the ACT is summarized in Table 5.

Table 5: Concizumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Routine prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors[b] and of 12 years of age or more	emicizumab	Added benefit not proven
a. Presented is the ACT specified by the G-BA. b. It is assumed that the patient population for the therapeutic indication in question is patients with haemophilia requiring factor VIII replacement therapy. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The assessment described above deviates from that of the company, which derived a hint of non-quantifiable added benefit of concizumab in comparison with emicizumab for the routine prophylaxis of bleeding in patients aged 12 years or more with haemophilia A (congenital factor VIII deficiency) and factor VIII inhibitors.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 02.09.2024]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a25-55.html.