Eftrenonacog alfa (haemophilia B)

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

EXTRACT

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No advisor on medical and scientific questions was involved in the present dossier assessment.

Patient and family involvement

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
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 (SGB) V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug eftrenonacog alfa. 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 August 2023.

Research question

The aim of this report was to assess the added benefit of eftrenonacog alfa in comparison with recombinant or human plasma-derived coagulation factor IX products as the appropriate comparator therapy (ACT) in patients with haemophilia B.

The research question presented in Table 2 has been derived from the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of eftrenonacog alfa

Therapeutic indication	**ACT**[a]
Treatment and prophylaxis of bleeding in patients of all age groups with haemophilia B (congenital factor IX deficiency)	**Recombinant**[b] or human plasma-derived **coagulation factor IX products**
a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in bold. b. The company has limited the selection of recombinant coagulation factor IX products to those with an extended half-life. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the ACT specified by the G-BA only in part. It has limited the selection of recombinant FIX products to those with an extended half-life and identified the 2 drugs nonacog beta pegol and albutrepenonacog alfa as the ACT. These 2 drugs are included in the ACT specified by the G-BA. The described deviation by the company has no consequences for the benefit assessment.

The present benefit assessment was conducted in comparison with the ACT specified by the G-BA.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

In the present therapeutic indication, randomized controlled trials (RCTs) were used for the derivation of any added benefit. For prophylactic treatment, RCTs with a minimum study duration of 24 weeks are used; for the evaluation of on-demand treatment, a study duration of at least 50 exposure days must be ensured.

Results

No suitable data are available for assessing the added benefit of eftrenonacog alfa compared with the ACT in patients with haemophilia B. This results in no hint of an added benefit of eftrenonacog alfa versus 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 added benefit of eftrenonacog alfa.

Table 3: Eftrenonacog alfa – extent and probability of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Treatment and prophylaxis of bleeding in patients of all age groups with haemophilia B (congenital factor IX deficiency)	**Recombinant**[b] or human plasma-derived **coagulation factor IX products**	Added benefit not proven

a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in bold.
b. The company has limited the selection of recombinant coagulation factor IX products to those with an extended half-life.

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

The G-BA decides on the added benefit.

Supplementary note

The result of the assessment deviates from the result of the G-BA's assessment conducted in the context of the market launch in 2016. In said assessment, the G-BA had determined a non-quantifiable added benefit of eftrenonacog alfa. However, in said assessment, the added

[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].

benefit had been regarded as proven by the marketing authorization irrespective of the underlying data because of the special situation for orphan drugs.

I 2 Research question

The aim of this report was to assess the added benefit of eftrenonacog alfa in comparison with recombinant or human plasma-derived coagulation factor IX products as the ACT in patients with haemophilia B.

The research question presented in Table 4 has been derived from the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of eftrenonacog alfa

Therapeutic indication	**ACT**[a]
Treatment and prophylaxis of bleeding in patients of all age groups with haemophilia B (congenital factor IX deficiency)	**Recombinant**[b] or human plasma-derived **coagulation factor IX products**
a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in bold. b. The company has limited the selection of recombinant coagulation factor IX products to those with an extended half-life. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the ACT specified by the G-BA only in part. It has limited the selection of recombinant FIX products to those with an extended half-life and identified the 2 drugs nonacog beta pegol and albutrepenonacog alfa as the ACT. These 2 drugs are included in the ACT specified by the G-BA. The described deviation by the company has no consequences for the benefit assessment.

The present benefit assessment was conducted in comparison with the ACT specified by the G-BA.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

In the present therapeutic indication, RCTs were used for the derivation of any added benefit. For prophylactic treatment, RCTs with a minimum study duration of 24 weeks are used; for the evaluation of on-demand treatment, a study duration of at least 50 exposure days must be ensured. This deviates from the company's inclusion criteria, which took into account RCTs with a minimum study duration of 24 weeks regardless of the treatment situation.

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 eftrenonacog alfa (status: 15 May 2023)
- bibliographical literature search on eftrenonacog alfa (last search on 5 May 2023)
- search in trial registries / trial results databases for studies on eftrenonacog alfa (last search on 4 May 2023)
- search on the G-BA website for eftrenonacog alfa (last search on 5 May 2023)

To check the completeness of the study pool:

- search in trial registries for studies on eftrenonacog alfa (last search on 15 August 2023); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, no relevant studies on the direct comparison of eftrenonacog alfa versus the ACT were identified from the check of the completeness of the study pool.

The company's Module 4 A presents as supportive evidence 4 non-randomized, non-controlled studies on eftrenonacog alfa: B-LONG [3,4], Kids B-LONG [5], PUPs B-LONG [6] and B-YOND [7]. Each of the 4 studies enrolled male patients with severe haemophilia B (defined by ≤ 2 IU/dL endogenous factor IX activity).

The company has presented the results of these studies only as supplementary information, without using them for the derivation of added benefit.

I 4 Results on added benefit

No suitable data are available for assessing the added benefit of eftrenonacog alfa compared with the ACT in patients with haemophilia B. This results in no hint of an added benefit of eftrenonacog alfa versus 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 eftrenonacog alfa in comparison with the ACT.

Table 5: Eftrenonacog alfa – extent and probability of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Treatment and prophylaxis of bleeding in patients of all age groups with haemophilia B (congenital factor IX deficiency)	**Recombinant**[b] or human plasma-derived **coagulation factor IX products**	Added benefit not proven

a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company is printed in bold.
b. The company has limited the selection of recombinant coagulation factor IX products to those with an extended half-life.

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

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

The G-BA decides on the added benefit.

Supplementary note

The result of the assessment deviates from the result of the G-BA's assessment in the context of the market launch in 2016. In said assessment, the G-BA had determined a non-quantifiable added benefit of eftrenonacog alfa, but the added benefit had been regarded as proven by the marketing authorization irrespective of the underlying data because of the special situation for orphan drugs.

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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The full report (German version) is published under https://www.iqwig.de/en/projects/a23-77.html.