IQWiG Reports – Commission No. A18-86

Damoctocog alfa pegol (haemophilia A) –

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

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment Damoctocog alfa pegol *(Hämophilie A) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 27 March 2019). 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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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.

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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)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
IU	international unit
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 damoctocog alfa pegol. The assessment was based on a dossier compiled by the company. The dossier was sent to IQWiG on 18 December 2018.

Research question

The aim of the present report was to assess the added benefit of damoctocog alfa pegol in comparison with the appropriate comparator therapy (ACT) in the treatment and prophylaxis of bleeding in patients aged 12 years and older with haemophilia A (congenital factor VIII deficiency).

For the benefit assessment, the research question presented in Table 2 resulted from the ACT specified by the G-BA.

Table 2: Research questions of the benefit assessment of damoctocog alfa pegol

Research question	**Subindication**	**ACT[a]**
1	Treatment and prophylaxis of bleeding in pretreated patients aged 12 years and older with haemophilia A (congenital factor VIII deficiency)	**Recombinant** or **human plasma-derived coagulation factor VIII products**

a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**.

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

The company exclusively cited recombinant factor IV products as ACT. The company's ACT corresponds to one of the alternatives specified as ACT by the G-BA.

Assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. The minimum study duration for prophylactic treatment is 6 months. A study duration of at least 50 exposure days has to be guaranteed for an assessment of on-demand treatment.

Results

The company presented no relevant data for the assessment of the added benefit of damoctocog alfa pegol versus the ACT.

Direct comparison

From its information retrieval, the company identified no randomized or non-randomized study of direct comparison on the comparison of damoctocog alfa pegol with the ACT, neither for prophylaxis nor for on-demand treatment. The check of completeness also produced no study of direct comparison.

Further investigations

The company included the two non-comparative studies 13024 and 13401 in its study pool for damoctocog alfa pegol.

Both studies were unsuitable for the derivation of an added benefit because, as non-controlled studies, they allowed no comparison with the ACT. Since the company did not search for studies on the ACT, its criteria for study inclusion were not aimed at completely answering the research question on the added benefit.

Summary

The company presented no suitable data for the assessment of the added benefit of damoctocog alfa pegol in its dossier. This resulted in no hint of an added benefit of damoctocog alfa pegol 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 damoctocog alfa pegol.

Table 3: Damoctocog alfa pegol – probability and extent of added benefit

Subindication	**ACT**[a]	**Probability and extent of added benefit**
Treatment and prophylaxis of bleeding in pretreated patients aged 12 years and older with haemophilia A (congenital factor VIII deficiency)	**Recombinant** or **human plasma-derived coagulation factor VIII products**	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

[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].

The G-BA decides on the added benefit.

2.2 Research question

The aim of the present report was to assess the added benefit of damoctocog alfa pegol in comparison with the ACT in the treatment and prophylaxis of bleeding in patients aged 12 years and older with haemophilia A (congenital factor VIII deficiency).

For the benefit assessment, the research question presented in Table 4 resulted from the ACT specified by the G-BA.

Table 4: Research questions of the benefit assessment of damoctocog alfa pegol

Research question	**Subindication**	**ACT[a]**
1	Treatment and prophylaxis of bleeding in pretreated patients aged 12 years and older with haemophilia A (congenital factor VIII deficiency)	**Recombinant** or **human plasma-derived coagulation factor VIII products**
a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The company exclusively cited recombinant factor IV products as ACT. The company's ACT corresponds to one of the alternatives specified as ACT by the G-BA (see Section 2.7.1 of the full dossier assessment).

Assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. The minimum study duration for prophylactic treatment is 6 months. A study duration of at least 50 exposure days has to be guaranteed for an assessment of on-demand treatment.

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 damoctocog alfa pegol (status: 11 September 2017)
- bibliographical literature search on damoctocog alfa pegol (last search on 8 October 2018)
- search in trial registries for studies on damoctocog alfa pegol (last search on 8 October 2018)

To check the completeness of the study pool:

- search in trial registries for studies on damoctocog alfa pegol (last search on 24 January 2019)

Direct comparison

From its information retrieval, the company identified no randomized or non-randomized study of direct comparison on the comparison of damoctocog alfa pegol with the ACT, neither for prophylaxis nor for on-demand treatment. The check of completeness also produced no study of direct comparison.

Further investigations

The company included the two non-comparative studies 13024 [3] and 13401 [4] in its study pool for damoctocog alfa pegol:

- Study 13024: open-label, non-controlled, partially randomized study on pretreated male patients with severe haemophilia A (residual factor VIII activities < 1%) aged 12 to 65 years. Both on-demand treatment and 3 different prophylactic treatment regimens with damoctocog alfa pegol (30 to 40 international units (IU) per kg, twice weekly/45 to 60 IU per kg every 5 days/60 IU per kg every 7 days) were investigated in a total of 4 study arms. Allocation to the treatment arms was conducted in accordance with the patients' preferences (as on-demand treatment or preventively), the risk of bleeding in the introduction phase, and partially randomized to the particular prophylactic treatment groups. Study duration for preventive or on-demand treatment was at least 36 weeks or 50 exposure days. Thereafter, the patients could participate in a 6-month extension study. In addition, application of damoctocog alfa pegol in surgical interventions was investigated in a further cohort of study 13024.
- Study 13401: open-label, non-randomized phase 1 study on pretreated male patients with severe haemophilia A (residual factor VIII activities < 1%). The study investigated the pharmacokinetics of damoctocog alfa pegol in 2 cohorts. After a single octocog alfa dose, the patients were treated over an 8-week period, either twice weekly with 25 IU damoctocog alfa pegol, or once weekly with 60 IU damoctocog alfa pegol.

Both studies were unsuitable for the derivation of an added benefit because, as non-controlled studies, they allowed no comparison with the ACT. The company's criteria for study inclusion were not aimed at completely answering the research question on the added benefit and it did not search for studies on the ACT (see Section 2.7.3.1 of the full dossier assessment).

2.4 Results on added benefit

The company presented no suitable data for the assessment of the added benefit of damoctocog alfa pegol in its dossier. This resulted in no hint of an added benefit of damoctocog alfa pegol in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

The result of the assessment of the added benefit of nonacog beta pegol in comparison with the ACT is shown in Table 5.

Table 5: Damoctocog alfa pegol – probability and extent of added benefit

Subindication	**ACT**[a]	**Probability and extent of added benefit**
Treatment and prophylaxis of bleeding in pretreated patients aged 12 years and older with haemophilia A (congenital factor VIII deficiency)	**Recombinant** or **human plasma-derived coagulation factor VIII products**	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in **bold**. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The assessment described above deviates from that of the company, which derived a non-quantifiable added benefit for damactocog. The company did not address the probability.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as the company presented no relevant data for the benefit assessment.

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: 04.06.2018]. URL: https://www.iqwig.de/download/General-Methods_Version-5-0.pdf.

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The full report (German version) is published under
https://www.iqwig.de/en/projects-results/projects/drug-assessment/a18-86-damoctocog-alfa-haemophilia-a-benefit-assessment-according-to-35a-social-code-book-v.11272.html