IQWiG Reports – Commission No. A17-03

Lonoctocog alfa (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 *Lonoctocog alfa (Hämophilie A) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 25 April 2017). 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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Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Medical and scientific advice:

- Bernd Pötzsch, Bonn University Hospital, Germany

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.

IQWiG employees involved in the dossier assessment[2]:

- Gregor Moritz
- Judith Gibbert
- Wolfram Groß
- Thomas Kaiser
- Marco Knelangen
- Fabian Lotz
- Katrin Nink

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[2] Due to legal data protection regulations, employees have the right not to be named.

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[3] 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)
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 lonoctocog alfa. 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 1 February 2017.

Research question

The aim of the present report was to assess the added benefit of lonoctocog alfa compared with the appropriate comparator therapy (ACT) in the treatment and prophylaxis of bleeding in patients 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 question of the benefit assessment of lonoctocog alfa

Research question	Therapeutic indication	ACT[a]
1	Treatment and prophylaxis of bleeding in patients 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 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 suitable data for the assessment of the added benefit of lonoctocog alfa 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 lonoctocog alfa with the ACT, neither for prophylaxis nor for on-demand treatment.

Further investigations

The company identified 2 single-arm studies for lonoctocog alfa. Both studies investigated the efficacy and safety of lonoctocog alfa in pretreated patients with severe haemophilia A of different age groups. Both studies started with an assessment of pharmacokinetics. This was followed by a treatment phase with lonoctocog alfa in different treatment regimens (prophylaxis or on-demand treatment) and an extension phase so that the patients included were treated up to 24 months.

Both studies were unsuitable for the derivation of an added benefit because, as single-arm 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

Overall, the company presented no suitable data for the assessment of the added benefit of lonoctocog alfa. Hence there was no hint of an added benefit of lonoctocog alfa in comparison with the ACT; an added benefit is therefore not proven.

Extent and probability of added benefit, patient groups with therapeutically important added benefit[4]

On the basis of the results presented, the extent and probability of the added benefit of the drug lonoctocog alfa compared with the ACT is assessed as follows:

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

Therapeutic indication	**ACT**[a]	**Extent and probability of added benefit**
Treatment and prophylaxis of bleeding in children and adults 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 G-BA decides on the added benefit.

[4] 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, no added benefit, or less benefit). For further details see [1,2].

2.2 Research question

The aim of the present report was to assess the added benefit of lonoctocog alfa compared with the ACT in the treatment and prophylaxis of bleeding in patients 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 question of the benefit assessment of lonoctocog alfa

Research question	Therapeutic indication	ACT[a]
1	Treatment and prophylaxis of bleeding in patients 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		

In its choice of the ACT, the company followed the G-BA's specification.

The 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 lists on lonoctocog alfa (status: 2 December 2016)
- bibliographical literature search on lonoctocog alfa (last search on 5 December 2016)
- search in trial registries for studies on lonoctocog alfa (last search on 29 November 2016)

To check the completeness of the study pool:

- search in trial registries for studies on lonoctocog alfa (last search on 16 February 2017)

Direct comparison

From its information retrieval, the company identified no randomized or non-randomized study of direct comparison on the comparison of lonoctocog alfa 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 identified 2 single-arm studies for lonoctocog alfa: CSL627_1001 [3] and CSL627_3002 [4]. Both studies investigated the efficacy and safety of lonoctocog alfa in pretreated patients with severe haemophilia A of different age groups. Both studies started with an assessment of pharmacokinetics after a single administration of the study medication. In this phase of the CSL627_1001 study, the single administration of lonoctocog alfa was compared with octocog alfa in a crossover design after a four-day wash-out phase. In the CSL627_3002 study, participation in the pharmacokinetics phase of the study was optional and exclusively consisted of the single administration of lonoctocog alfa. In both studies, this was followed by a treatment phase with lonoctocog alfa in different treatment regimens (prophylaxis or on-demand treatment) and an extension phase so that the patients included were treated up to 24 months.

Both studies were unsuitable for the derivation of an added benefit because, as single-arm 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 (see Section 2.7.2.3.1 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 lonoctocog alfa in its dossier. This resulted in no hint of an added benefit of lonoctocog alfa in comparison with the ACT; an added benefit is therefore not proven.

2.5 Extent and probability of added benefit

The result of the assessment of the added benefit of lonoctocog alfa in comparison with the ACT is shown in Table 5.

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

Therapeutic indication	**ACT**[a]	**Extent and probability of added benefit**
Treatment and prophylaxis of bleeding in children and adults 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		

This deviates from the approach of the company, which derived a hint of a non-quantifiable added benefit for lonoctocog alfa.

The G-BA decides on the added benefit.

2.6 List of included studies

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

References for English extract

Please see full dossier assessment for full reference list.

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Citations marked with * are unedited citations provided by the company.

The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a17-03-lonoctocog-alfa-haemophilia-a-benefit-assessment-according-to-35a-social-code-book-v.7844.html.