Nonacog beta pegol (haemophilia B, patients < 12 years)

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

EXTRACT

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[1] Translation of Sections I 1 to I 6 of the dossier assessment *Nonacog beta pegol (Hämophilie B, Patientinnen und Patienten < 12 Jahre) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This document was translated by an external translator and 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.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Dragana Mitrovic.

IQWiG thanks the respondent and the Deutsche Hämophiliegesellschaft e. V. (German Haemophilia Society) for participating in the written exchange and for their support. The respondent 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 (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 nonacog beta pegol. 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 4 September 2023.

Research question

The aim of this report was to assess the added benefit of nonacog beta pegol in comparison with recombinant or human plasma-derived coagulation factor IX products as the appropriate comparator therapy (ACT) in patients < 12 years with haemophilia B (congenital factor IX deficiency).

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

Table 2: Research question of the benefit assessment of nonacog beta pegol

Therapeutic indication	**ACT**[a]
Treatment and prophylaxis of bleeding in patients aged < 12 years with haemophilia B (congenital factor IX deficiency)[b]	**Recombinant** or human plasma-derived **coagulation factor IX products**
a. Presented is the respective 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. It is assumed that the patient population in the present therapeutic indication is haemophilia patients requiring factor IX substitution. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification and selected the recombinant coagulation factor IX products from among the presented options.

The assessment is 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 for the derivation of any added benefit. For the prophylactic treatment, RCTs with a minimum duration of 6 months were used. A study duration of at least 50 exposure days is required for an assessment of the episodic treatment.

Results

Concurring with the company, the check for completeness of the study pool identified no RCTs for the direct comparison of nonacog beta pegol versus the ACT.

However, the company presents as supplementary information the single-arm approval studies Paradigm 5 and Paradigm 6. As these studies do not allow a comparison with the ACT, they are unsuitable for assessing the added benefit of nonacog beta pegol.

Results on added benefit

For nonacog beta pegol in the treatment and prophylaxis of patients aged < 12 years with haemophilia B (congenital factor IX deficiency), no suitable data are available for assessing any added benefit in comparison with the ACT. This results in no hint of an added benefit of nonacog beta 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 nonacog beta pegol.

Table 3: Nonacog beta pegol – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Treatment and prophylaxis of bleeding in patients aged < 12 years with haemophilia B (congenital factor IX deficiency)[b]	**Recombinant** or human plasma-derived **coagulation factor IX products**	Added benefit not proven
a. Presented is the respective 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. It is assumed that the patient population in the present therapeutic indication is haemophilia patients requiring factor IX substitution. 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 was to assess the added benefit of nonacog beta pegol in comparison with recombinant or human plasma-derived coagulation factor IX products as the ACT in patients < 12 years with haemophilia B (congenital factor IX deficiency).

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

Table 4: Research question of the benefit assessment of nonacog beta pegol

Therapeutic indication	**ACT**[a]
Treatment and prophylaxis of bleeding in patients aged < 12 years with haemophilia B (congenital factor IX deficiency)[b]	**Recombinant** or human plasma-derived **coagulation factor IX products**
a. Presented is the respective 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. It is assumed that the patient population in the present therapeutic indication is haemophilia patients requiring factor IX substitution. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

The company followed the G-BA's specification and selected the recombinant coagulation factor IX products from among the presented options.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs were used for the derivation of any added benefit. For the prophylactic treatment, RCTs with a minimum duration of 6 months were used. A study duration of at least 50 exposure days is required for an assessment of the episodic treatment. This deviates from the inclusion criteria used by the company, which did not differentiate between prophylactic treatment versus episodic treatment and defined a study duration of at least 6 months irrespective 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 nonacog beta pegol (status: 7 July 2023)
- bibliographical literature search on nonacog beta pegol (last search on 7 July 2023)
- search in trial registries / trial results databases for studies on nonacog beta pegol (last search on 7 July 2023)
- search on the G-BA website for nonacog beta pegol (last search on 7 July 2023)

To check the completeness of the study pool:

- search in trial registries for studies on nonacog beta pegol (last search on 20 September 2023); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check of completeness of the study pool identified no RCTs for the direct comparison of nonacog beta pegol versus the ACT.

However, in Appendix 4 G of Module 4 A, the company presents as supplementary information 2 single-arm approval studies on nonacog beta pegol (Paradigm 5 [NN7999-3774] [3] and Paradigm 6 [NN7999-3895] [4]), but it does not use their results to derive added benefit.

The Paradigm 5 study enrolled treatment-experienced male patients aged ≤ 12 years with a body weight of ≥ 10 kg, while the Paradigm 6 study included treatment-naive male patients aged < 6 years. At the time of study enrolment, patients had to have haemophilia B with a factor-IX-activity of ≤ 2%. In both studies, treatment with nonacog beta pegol as prophylactic treatment was supplemented by episodic treatment due to bleeding or prior to surgery. The studies were divided into a main and an extension phase, with the main phase having to comprise at least 52 weeks (Paradigm 5) or 50 days of exposure (Paradigm 6). However, since both of these studies offer no comparison with the ACT, they are unsuitable for assessing added benefit.

I 4 Results on added benefit

For nonacog beta pegol in the treatment and prophylaxis of patients aged < 12 years with haemophilia B (congenital factor IX deficiency), no suitable data are available for assessing any added benefit in comparison with the ACT. This results in no hint of an added benefit of nonacog beta pegol in comparison with 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 for nonacog beta pegol in comparison with the ACT.

Table 5: Nonacog beta pegol – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Treatment and prophylaxis of bleeding in patients aged < 12 years with haemophilia B (congenital factor IX deficiency)[b]	**Recombinant** or human plasma-derived **coagulation factor IX products**	Added benefit not proven

a. Presented is the respective 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. It is assumed that the patient population in the present therapeutic indication is haemophilia patients requiring factor IX substitution.

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

The assessment described above deviates from that by the company, which had derived a hint of a non-quantifiable added benefit on the basis of the product characteristics of nonacog beta pegol and its proven efficacy and safety.

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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The full report (German version) is published under https://www.iqwig.de/en/projects/a23-90.html.