IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Turoctocog alfa – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 10 April 2014). 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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[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)
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 turoctocog 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 15 January 2014.

Research question

The aim of the present report is to assess the added benefit of turoctocog alfa compared with the appropriate comparator therapy (ACT) in the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).

The G-BA specified the ACT for the therapeutic indication as follows:

- recombinant or human plasma-derived coagulation factor VIII products

The company chose the recombinant coagulation factor octocog alfa as one of the options specified as ACT by the G-BA, but limited its selection to a third-generation octocog alfa (Advate). This approach was not accepted. According to the G-BA's specification, all products containing the drug octocog alfa would have to be considered. The ACT specified by the G-BA is therefore used for the assessment.

The assessment was conducted based on patient-relevant outcomes.

Results

No relevant study was identified for the present benefit assessment to assess the added benefit of turoctocog alfa versus the ACT. This concurs with the company's assessment. The company therefore based its conclusions on added benefit on further deliberations, for which it presented various publications and statistics. It described an "improvement in the provision of health care" and a "better integration of patients with haemophilia into a normal social life", which, from the company's point of view, already arise through market entry of turoctocog alfa. This rationale was not followed.

No added benefit can be derived solely from the approval and market entry of a new product and the associated "improvement in the provision of health care" claimed by the company.

Furthermore, the company postulated an advantage of turoctocog alfa in comparison with the third-generation octocog alfa from the fact that turoctocog alfa can temporarily be stored at temperatures of up to 30 °C, in contrast to 25 °C for octocog alfa. This advantage is supposed to be particularly beneficial during the summer months and during travels to warmer countries

and thus enable a "better integration of patients with haemophilia into a normal social life". It is not denied that the integration of patients with haemophilia into a normal social life is an important treatment goal. However, in order to classify such an advantage versus the comparator therapy postulated by the company with certainty, comparative, sufficiently interpretable data on patient-relevant outcomes are needed first, because an added benefit in the aspects "morbidity" (such as bleeding) or "health-related quality of life" is not obvious from the 5 °C difference in storability. However, the company presented no comparative data on patient-relevant outcomes at all.

The deliberations presented by the company are overall not suited to allow the assessment of patient-relevant beneficial and harmful effects of turoctocog alfa versus the appropriate comparator therapy.

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 turoctocog alfa compared with the ACT is assessed as follows:

Table 2: Turoctocog alfa: extent and probability of added benefit

Therapeutic indication	ACT[a]	Extent and probability of added benefit
Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)	**Recombinant**[b] 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**.

b: Choice on the basis of the company's information in the dossier: octocog alfa.

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), see [1]. 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), see [2].

2.2 Research question

The aim of the present report is to assess the added benefit of turoctocog alfa compared with the ACT in the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency) [3].

The G-BA specified the ACT for the therapeutic indication as follows:

- recombinant or human plasma-derived coagulation factor VIII products

The company chose the recombinant coagulation factor octocog alfa as one of the options specified as ACT by the G-BA, but limited its selection to a third-generation octocog alfa (Advate [4]). According to the G-BA's specification however, all products containing the drug octocog alfa would have to be considered. Overall, the company's limitation had no consequence on the present result of the assessment, however.

The ACT specified by the G-BA was used for the assessment. The assessment was conducted based on patient-relevant outcomes.

Further information about the research question can be found in Module 3, Section 3.1, and Module 4, Section 4.2.1 of the dossier, and in Sections 2.7.1 and 2.7.2.1 of the full dossier assessment.

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 turoctocog alfa (studies completed up to 12 November 2013)
- search in trial registries for studies on turoctocog alfa (last search on 18 October 2013)

No relevant study was identified from the steps of information retrieval mentioned. This concurs with the search results of the company, which also identified no studies that would allow a direct or indirect comparison of turoctocog alfa with the ACT specified by the G-BA.

Further documents

The company based its assessment solely on further deliberations. The company argued that, from its point of view, an "improvement in the provision of health care" and a "better integration of patients with haemophilia into a normal social life" arise through market entry. It derived the latter because storability differed from other factor products (temporary storability at up to 30 °C). The deliberations presented were unsuitable for the assessment of the added benefit (see Section 2.7.2.7 of the full dossier assessment).

Further information on the inclusion criteria for studies in this benefit assessment and the methods of information retrieval can be found in Module 4, Sections 4.2.2 and 4.2.3 of the dossier, and in Sections 2.7.2.1 and 2.7.2.3 of the full dossier assessment.

2.4 Results on added benefit

No relevant data were available for the assessment of the added benefit of turoctocog alfa versus the ACT. Hence the added benefit of turoctocog alfa versus the ACT is not proven.

This deviates from the company's result, which derived an added benefit of turoctocog alfa.

2.5 Extent and probability of added benefit

The result of the assessment of the added benefit of turoctocog alfa in comparison with the ACT is shown in Table 3.

Table 3: Turoctocog alfa: extent and probability of added benefit

Therapeutic indication	**ACT**[a]	**Extent and probability of added benefit**
Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)	**Recombinant**[b] 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**. b: Choice on the basis of the company's information in the dossier: octocog alfa. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

This assessment deviates from that of the company, which derived a hint of a non-quantifiable added benefit of turoctocog alfa.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as the company did not present any studies in the dossier from which an added benefit versus the ACT specified by the G-BA could be derived.

References for English extract

Please see full dossier assessment for full reference list.

1. Institute for Quality and Efficiency in Health Care. General Methods: version 4.1 [online]. 28 November 2013 [accessed: 7 February 2014]. URL: https://www.iqwig.de/download/IQWiG_General_Methods_Version_%204-1.pdf.

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