IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A15-11

Aflibercept (new therapeutic indication) – Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Aflibercept (neues Anwendungsgebiet) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 11 June 2015). 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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Keywords: aflibercept, retinal vein occlusion, benefit assessment

[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
BRVO	branch retinal vein occlusion
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)
TI	therapeutic indication

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 aflibercept. 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 11 March 2015.

Research question

The aim of this report was to assess the added benefit of aflibercept in comparison with ranibizumab or grid laser therapy as appropriate comparator therapy (ACT) in adult patients with visual impairment due to macular oedema following branch retinal vein occlusion (BRVO).

The ACT specified by the G-BA as ranibizumab or grid laser therapy was followed for the present benefit assessment. This deviated from the company, which rejected grid laser therapy as ACT and specified ranibizumab as only ACT.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 6 months were to be included in the assessment.

Results

No relevant data were available for the benefit assessment of aflibercept versus the ACT. One direct comparative RCT (VIBRANT) compared aflibercept with grid laser therapy, but the use of aflibercept in the study did not comply with the approval.

Hence no relevant data were available for the assessment of the added benefit of aflibercept. There was no hint of an added benefit of aflibercept 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]

The result of the added benefit of aflibercept in the present therapeutic indication is shown in Table 2.

Table 2: Aflibercept – extent and probability of added benefit

Therapeutic indication	ACT[a]	Extent and probability of added benefit
Treatment of adults with visual impairment due to macular oedema following BRVO	**Ranibizumab** or grid laser therapy	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. The company rejected grid laser therapy as ACT in its dossier. The only ACT the company considered relevant is printed in bold. ACT: appropriate comparator therapy; BRVO: branch retinal vein occlusion; 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 this report was to assess the added benefit of aflibercept in comparison with ranibizumab or grid laser therapy as ACT in adult patients with visual impairment due to macular oedema following BRVO.

The ACT specified by the G-BA as ranibizumab or grid laser therapy was followed for the present benefit assessment. This deviates from the company, which rejected grid laser therapy as ACT and specified ranibizumab as only ACT.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier. RCTs with a minimum duration of 6 months were to be included in the assessment. This deviated from the company's inclusion criteria, which stated no minimum study duration.

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 aflibercept (studies completed up to 24 February 2015)
- bibliographical literature search on aflibercept (last search on 27 January 2015)
- search in trial registries for studies on aflibercept (last search on 29 January 2015)
- bibliographical literature search on the ACT (last search on 27 January 2015)
- search in trial registries for studies on the ACT (last search on 29 January 2015)

No relevant data were available for the benefit assessment of aflibercept versus the ACT. One direct comparative RCT (VIBRANT [3]) was available for the comparison of aflibercept with grid laser therapy, but the use of aflibercept in the study did not comply with the approval (see Section 2.7.2.3.2 of the full dossier assessment for a detailed description). This deviates from the company's approach, which would not have included this study in its benefit assessment also in case of approval-compliant use of aflibercept because it specified a different ACT.

2.4 Results on added benefit

No relevant data were available for the assessment of the added benefit of aflibercept. There was no hint of an added benefit of aflibercept in comparison with the ACT; an added benefit is therefore not proven.

The company also derived no added benefit of aflibercept versus the ACT ranibizumab it had specified. It justified this result with the lack of adequate studies for a direct or indirect comparison of the treatment alternatives.

2.5 Extent and probability of added benefit

The result of the added benefit of aflibercept in the present therapeutic indication is shown in Table 3.

Table 3: Aflibercept – extent and probability of added benefit

Therapeutic indication	**ACT**[a]	**Extent and probability of added benefit**
Treatment of adults with visual impairment due to macular oedema following BRVO	**Ranibizumab** or grid laser therapy	Added benefit not proven
a: Presentation of the respective ACT specified by the G-BA. The company rejected grid laser therapy as ACT in its dossier. The only ACT the company considered relevant is printed in bold. ACT: appropriate comparator therapy; BRVO: branch retinal vein occlusion; G-BA: Federal Joint Committee		

This concurs with the company's assessment, which also derived no added benefit of aflibercept versus the ACT it had specified.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as no studies were included in the benefit assessment.

References for English extract

Please see full dossier assessment for full reference list.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden: Version 4.2. Köln: IQWiG; 2015. URL: https://www.iqwig.de/download/IQWiG_Methoden_Version_4-2.pdf.

2. Institute for Quality and Efficiency in Health Care. Ticagrelor: benefit assessment according to § 35a Social Code Book V; extract; commission no. A11-02 [online]. 29 September 2011 [accessed 5 May 2012]. URL: https://www.iqwig.de/download/A11-02_Extract_of_dossier_assessment_Ticagrelor.pdf.

3. Campochiaro PA, Clark WL, Boyer DS, Heier JS, Brown DM, Vitti R et al. Intravitreal aflibercept for macular edema following branch retinal vein occlusion: the 24-week results of the VIBRANT study. Ophthalmology 2015; 122(3): 538-544.

The full report (German version) is published under https://www.iqwig.de/de/projekte-ergebnisse/projekte/arzneimittelbewertung/a15-11-aflibercept-neues-anwendungsgebiet-nutzenbewertung-gemaess-35a-sgb-v-dossierbewertung.6664.html.