

IQWiG Reports – Commission No. A15-49

**Aflibercept (new therapeutic  
indication) –  
Benefit assessment according to  
§35a Social Code Book V<sup>1</sup>**

**Extract**

---

<sup>1</sup> Translation of Sections 2.1 to 2.6 of the dossier assessment *Aflibercept (neues Anwendungsgebiet) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 26 February 2016). 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.

# Publishing details

**Publisher:**

Institute for Quality and Efficiency in Health Care

**Topic:**

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

**Commissioning agency:**

Federal Joint Committee

**Commission awarded on:**

24 November 2015

**Internal Commission No.:**

A15-49

**Address of publisher:**

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](mailto:berichte@iqwig.de)

Internet: [www.iqwig.de](http://www.iqwig.de)

**Medical and scientific advice:**

No advisor on medical and scientific questions was involved in the present dossier assessment.

**IQWiG employees involved in the dossier assessment<sup>2</sup>:**

- Raphaela Gorris
- Dorothea Gechter
- Corinna ten Thoren
- Beate Wieseler
- Min Zhou

**Keywords:** aflibercept, myopia – degenerative, choroidal neovascularization, benefit assessment

---

<sup>2</sup> Due to legal data protection regulations, employees have the right not to be named.

# Table of contents

	<b>Page</b>
<b>List of tables .....</b>	<b>iv</b>
<b>List of abbreviations.....</b>	<b>v</b>
<b>2 Benefit assessment .....</b>	<b>1</b>
<b>2.1 Executive summary of the benefit assessment.....</b>	<b>1</b>
<b>2.2 Research question .....</b>	<b>3</b>
<b>2.3 Information retrieval and study pool.....</b>	<b>3</b>
<b>2.4 Results on added benefit.....</b>	<b>4</b>
<b>2.5 Extent and probability of added benefit .....</b>	<b>4</b>
<b>2.6 List of included studies .....</b>	<b>4</b>
<b>References for English extract .....</b>	<b>5</b>

**List of tables<sup>3</sup>**

	<b>Page</b>
Table 2: Aflibercept – extent and probability of added benefit .....	2
Table 3: Research question and ACT for aflibercept.....	3
Table 4: Aflibercept – extent and probability of added benefit .....	4

---

<sup>3</sup> Table numbers start with “2” as numbering follows that of the full dossier assessment.

**List of abbreviations**

<b>Abbreviation</b>	<b>Meaning</b>
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)
mCNV	myopic choroidal neovascularization
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 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 24 November 2015.

#### **Research question**

The aim of this report was to assess the added benefit of aflibercept in comparison with ranibizumab as appropriate comparator therapy (ACT) in adults with visual impairment due to myopic choroidal neovascularization (mCNV).

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier.

#### **Results**

The company presented no studies in its dossier that are suitable to compare aflibercept with the ACT in patients with mCNV. Hence an added benefit of aflibercept in comparison with the ACT ranibizumab is not proven for patients with mCNV.

#### **Extent and probability of added benefit, patient groups with therapeutically important added benefit<sup>4</sup>**

Since no relevant studies for the assessment of the added benefit of aflibercept in patients with mCNV were presented, an added benefit in comparison with the ACT ranibizumab specified by the G-BA is not proven. Hence there are also no patient groups for whom a therapeutically important added benefit can be derived.

Table 2 presents a summary of the extent and probability of the added benefit of aflibercept.

---

<sup>4</sup> 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].

Table 2: Aflibercept – extent and probability of added benefit

Therapeutic indication	ACT <sup>a</sup>	Extent and probability of added benefit
Treatment of adults with visual impairment due to mCNV	Ranibizumab	Added benefit not proven
a: Presentation of the appropriate comparator therapy specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; mCNV: myopic choroidal neovascularization		

The result concurs with the company's assessment, which also derived no added benefit of aflibercept in the treatment of adults with visual impairment due to mCNV. The G-BA decides on the added benefit.



## 2.2 Research question

The aim of this report was to assess the added benefit of aflibercept in comparison with the ACT in adults with visual impairment due to mCNV.

The G-BA defined ranibizumab as ACT for adults with visual impairment due to mCNV. In its dossier, the company followed the G-BA's specification of the ACT.

The following research question resulted from this for the benefit assessment:

Table 3: Research question and ACT for aflibercept

Research question	Therapeutic indication	ACT
1	Adults with visual impairment due to mCNV	Ranibizumab
ACT: appropriate comparator therapy; mCNV: myopic choroidal neovascularization		

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier.

## 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 (status: 24 September 2015)
- bibliographical literature search on aflibercept (last search on 13 October 2015)
- search in trial registries for studies on aflibercept (last search on 15 October 2015)
- bibliographical literature search on the ACT (last search on 13 October 2015)
- search in trial registries for studies on the ACT (last search on 15 October 2015)

To check the completeness of the study pool:

- search in trial registries for studies on aflibercept (last search on 9 December 2015)
- search in trial registries for studies on the ACT (last search on 9 December 2015)

No additional relevant study was identified from the check.

From the steps of information retrieval mentioned, the company identified only the placebo-controlled approval study of aflibercept in the present therapeutic indication (study MYRROR [3]). There were no studies with patients with visual impairment due to mCNV in which aflibercept was directly compared with the ACT ranibizumab. It is therefore not possible to assess the added benefit of aflibercept on the basis of studies of direct comparisons.

When no studies of direct comparisons are available, it is possible to investigate the added benefit on the basis of adjusted indirect comparisons. The company described in the dossier that it had conducted a search for studies for an indirect comparison of aflibercept and ranibizumab. It had not identified any adequate studies for such a comparison of both drugs, however. Hence it was not possible to assess the added benefit of aflibercept using an adjusted indirect comparison.

The company presented no further documents (non-randomized comparative studies or further investigations) to investigate the added benefit of aflibercept.

In summary, the company presented no studies in the dossier that are suitable to investigate the added benefit of aflibercept in mCNV in comparison with the ACT.

## 2.4 Results on added benefit

The company presented no studies in its dossier that are suitable to compare aflibercept with the ACT in patients with mCNV. Hence an added benefit of aflibercept in comparison with the ACT ranibizumab is not proven for patients with mCNV.

## 2.5 Extent and probability of added benefit

Since no relevant studies for the assessment of the added benefit of aflibercept in patients with mCNV were presented, an added benefit in comparison with the ACT ranibizumab specified by the G-BA is not proven. Hence there are also no patient groups for whom a therapeutically important added benefit can be derived.

The result of the assessment of the added benefit of aflibercept in comparison with the ACT is summarized in Table 4.

Table 4: Aflibercept – extent and probability of added benefit

Therapeutic indication	ACT <sup>a</sup>	Extent and probability of added benefit
Treatment of adults with visual impairment due to mCNV	Ranibizumab	Added benefit not proven
a: Presentation of the appropriate comparator therapy specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; mCNV: myopic choroidal neovascularization		

This concurs with the company's approach, which also derived no added benefit of aflibercept in mCNV. The company described that it considered the added benefit to be unprovable because studies of direct comparisons as well as adequate studies for an indirect comparison were missing. 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. Institute for Quality and Efficiency in Health Care. General Methods: version 4.2 [online]. 22 April 2015 [accessed: 20 October 2015]. URL: [https://www.iqwig.de/download/IQWiG\\_General\\_Methods\\_Version\\_%204-2.pdf](https://www.iqwig.de/download/IQWiG_General_Methods_Version_%204-2.pdf).
2. Skipka G, Wieseler B, Kaiser T, Thomas S, Bender R, Windeler J et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. *Biom J* 2015; 58(1): 43-58
3. Ikuno Y, Ohno-Matsui K, Wong TY, Korobelnik JF, Vitti R, Li T et al. Intravitreal Aflibercept Injection in Patients with Myopic Choroidal Neovascularization: The MYRROR Study. *Ophthalmology* 2015; 122(6): 1220-1227.

*The full report (German version) is published under <https://www.iqwig.de/de/projekte-ergebnisse/projekte/arzneimittelbewertung/a15-49-aflibercept-neues-anwendungsgebiet-nutzenbewertung-gemaess-35a-sgb-v.7150.html>.*