Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Faricimab (Diabetic macular oedema)

of 6 April 2023

At its session on 6 April 2023, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient Faricimab as follows:

Faricimab

Resolution of: 6 April 2023
Entry into force on: 6 April 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 15 September 2022):

Vabysmo is indicated for the treatment of adult patients with:

- neovascular (wet) age-related macular degeneration (nAMD),
- visual impairment due to diabetic macular oedema (DME).

Therapeutic indication of the resolution (resolution of 6 April 2023):

Vabysmo is indicated for the treatment of adult patients with visual impairment due to diabetic macular oedema (DME).

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adults with visual impairment due to diabetic macular oedema (DME)

Appropriate comparator therapy:

– Ranibizumab or aflibercept

Extent and probability of the additional benefit of faricimab compared to aflibercept:

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults with visual impairment due to diabetic macular oedema (DME)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment
Morbidity	↔	No relevant difference for the benefit assessment
Health-related quality of life	↔	No relevant difference for the benefit assessment
Side effects	↔	No relevant difference for the benefit assessment
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-109) unless otherwise indicated.

↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable

RHINE study: Faricimab vs aflibercept

YOSEMITE study: Faricimab vs aflibercept

and the meta-analysis of the two studies

Mortality

Endpoint Study	Faricimab		Aflibercept		Faricimab vs aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value
Overall mortality					
RHINE	319	0 (0)	314	5 (1.6)	0 [0; n.c.]; 0.024[b]
YOSEMITE	313	9 (2.9)	311	4 (1.3)	2.24 [0.70; 7.18]; 0.212[b]
Total					0.99 [0.40; 2.47][c]; 0.981[d]

Morbidity

Endpoint/ scale study	Faricimab		aflibercept		Faricimab vs aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value
BCVA[e] (improvement by ≥ 10 ETDRS letters[f])					
RHINE	294	155 (52.7)	279	151 (54.1)	0.97 [0.84; 1.12]; 0.791[b]
YOSEMITE	276	161 (58.3)	276	159 (57.6)	1.03 [0.90; 1.18]; 0.916[b]
Total					1.00 [0.91; 1.10]; 0.916[d]
BCVA[e] (improvement by ≥ 15 ETDRS letters[f])					
RHINE	294	83 (28.2)	279	85 (30.5)	0.97 [0.76; 1.23]; 0.600[b]
YOSEMITE	276	98 (35.5)	276	88 (31.9)	1.10 [0.88; 1.37]; 0.053[b]
Total					1.04 [0.88; 1.22]; 0.799[d]

Endpoint/ scale study	Faricimab			aflibercept			Faricimab vs aflibercept
	N[g]	Values at the start of the study MV (SD)	Change at week 52 MV[h] (SE)	N[g]	Values at the start of the study MV (SD)	Change at week 52 MV[h] (SE)	RR [95% CI][h]; p value
NEI VFQ-25[i] (general health status subscale)							
RHINE	275	45.38 (21.54)	4.64 (1.09)	259	44.25 (21.34)	6.52 (1.12)	-1.18 [-4.95; 1.19] n.d.
YOSEMITE	256	47.02 (19.22)	3.44 (1.17)	248	46.19 (19.86)	4.80 (1.18)	-1.36 [-4.61; 1.90] n.d.
Total							-1.65 [-3.88; 0.59][j]; n.d.

Health-related quality of life

Endpoint/ scale study	Faricimab			aflibercept			Faricimab vs aflibercept
	N[g]	Values at the start of the study MV (SD)	Change at week 52 MV[h] (SE)	N[g]	Values at the start of the study MV (SD)	Change at week 52 MV[h] (SE)	RR [95% CI][h]; p value
NEI VFQ-25[i] (sum score[m])							
RHINE	275	74.33 (17.47)	7.07 (0.66)	259	74.67 (18.54)	7.51 (0.68)	-0.44 [-2.31; 1.43] n.d.
YOSEMITE	256	72.83 (18.15)	7.96 (0.71)	248	73.97 (17.70)	7.93 (0.71)	-0.03 [-1.94; 2.00] n.d.
Total							-0.20 [-1.55; 1.16][j]; n.d.

Side effects

Endpoint Study	Faricimab		aflibercept		Faricimab vs aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value
AE[k] (additional)					
RHINE	319	234 (73.4)	314	246 (78.3)	-
YOSEMITE	313	255 (81.5)	311	245 (78.8)	-
SAE[k]					
RHINE	319	52 (16.3)	314	58 (18.5)	0.88 [0.63; 1.24]; 0.533[b]
YOSEMITE	313	77 (24.6)	311	58 (18.6)	1.32 [0.97; 1.79]; 0.072[b]

Endpoint Study	Faricimab		aflibercept		Faricimab vs aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value
Total					1.10 [0.88; 1.38]; 0.408[d]
Discontinuation due to AEs					
RHINE[k]	319	4 (1.3)	314	3 (1.0)	1.31 [0.30; 5.82]; 0.804[b]
YOSEMITE	313	8 (2.6)	311	3 (1.0)	2.65 [0.71; 9.89]; 0.140[b]
Total					1.98 [0.75; 5.24]; 0.162[d]
Ocular AE[e k]					
RHINE	319	116 (36.4)	314	109 (34.7)	1.05 [0.85; 1.29]; 0.712[b]
YOSEMITE	313	105 (33.5)	311	103 (33.1)	1.01 [0.81; 1.26]; 0.937[b]
Total					1.98 [0.75; 5.24]; 0.162[d]
Ocular SAE[e k]					
RHINE	319	9 (2.8)	314	6 (1.9)	1.48 [0.53; 4.10]; 0.533[b]
YOSEMITE	313	9 (2.9)	311	2 (0.6)	4.47 [0.97; 20.53]; 0.038[b,l]
Total					2.23 [0.97; 5.08]; 0.051[d]

a. RR and CI from regression model; for morbidity endpoints stratified by BCVA on day 1 (< 64 vs ≥ 64 ETDRS letters), pretreatment with intravitreal anti-VEGF therapies (yes vs no) and region (USA/Canada vs Asia/Rest of World), for pooled analysis additionally stratified by study in each case
b. Own calculation, unconditional exact test (CSZ method)
c. Despite statistically significant heterogeneity (p = 0.003 [likelihood ratio test]), the joint effect estimator is presented in the present data situation.
d. Calculation from IPD meta-analysis with factor study as fixed effect (for model, see footnote "a"); p-value: Cochran-Mantel-Haenszel test
e. refers to the eye under study
f. Percentage of patients with an increase in BCVA of ≥ 10 ETDRS letters (or, presented additionally, ≥ 15 ETDRS letters) compared to the start of the study averaged over weeks 48, 52 and 56 (scale range from 0 to 100); observations after a COVID-19-related event were not included in the analysis
g. Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at start of study can be based on other patient numbers.
h. Unless otherwise stated: MMRM with covariates treatment, visit, interaction between treatment and visit and baseline value, adjusted for stratification factors of randomisation (BCVA on day 1 [< 64 vs ≥ 64 ETDRS letters], pretreatment with intravitreal anti-VEGF therapies [yes vs no] and region [USA/Canada vs Asia/Rest of World]), each additionally stratified by study for pooled analysis; effect refers to difference in mean change at week 52; observations after a COVID-19-related event were not included in the analysis
i. Higher (increasing) values mean better symptomatology/ health-related quality of life; positive effects (intervention minus control) mean an advantage for the intervention (scale range 0 to 100).
j. Calculation from IPD meta-analysis with factor study as fixed effect (for model, see footnote "h")
k. contains events of the underlying disease
l. Discrepancy between CI and p value due to different calculation methods
m. The following subscales were recorded: General vision, eye pain, near vision, distance vision, social functioning, psychological well-being, performance of social roles, dependence on others, problems with driving a car, problems with colour vision, peripheral vision. There are no statistically significant differences.

Abbreviations used:

Endpoint Study	Faricimab		aflibercept		Faricimab vs aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value
BCVA = best corrected visual acuity; COVID-19 = coronavirus disease 2019; ETDRS = Early Treatment Diabetic Retinopathy Study; IPD = individual patient data; n.d.: no data available; CI = confidence interval; MMRM = mixed model for repeated measures; MD = mean difference; MV = mean value; N = number of patients evaluated. n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; NEI VFQ-25 = National Eye Institute Function Questionnaire-25; RR = relative risk; SD = standard deviation; SE = standard error; SAE = serious adverse event; AE = adverse event; VEGF = vascular endothelial growth factor; vs = versus					

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with visual impairment due to diabetic macular oedema (DME)

Approx. 190,000 to 241,000 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Vabysmo (active ingredient: faricimab) at the following publicly accessible link (last access: 17 January 2023):

https://www.ema.europa.eu/en/documents/product-information/vabysmo-epar-product-information_en.pdf

Treatment with faricimab should only be initiated and monitored by doctors experienced in the therapy of diabetic macular oedema.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for patients. In particular, the training material contains information and warnings about infective endophthalmitis and intraocular inflammation.

4. Treatment costs

Annual treatment costs:

Adults with visual impairment due to diabetic macular oedema (DME)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Faricimab	1st year: € 7,194.04 - € 13,360.36
	Subsequent years: € 3,391.48 - € -13,360.36
Intravitreal injection	1st year: € 625.80 - € 2,487.29

Designation of the therapy	Annual treatment costs/ patient
	Subsequent years: € 295.02 - € 2,487.29
Postoperative treatment	1st year: € 134.33 - € 348.14
	Subsequent years: € 63.33 - € 348.14
Additionally required SHI services	non-quantifiable[2]
Total	1st year: € 7,954.17 - € 16,195.79
	Subsequent years: € 3,749.83 - € 16,195.79
Appropriate comparator therapy:	
aflibercept	1st year: € 6,958.70 - € 7,952.80
	Subsequent years: € 0 - € 5,964.60
Intravitreal injection	1st year: € 625.80 - € 1,530.64
	Subsequent years: € 0 - € 1,147.98
Postoperative treatment	1st year: € 134.33 - € 214.24
	Subsequent years: € 0 - € 160.68
Additionally required SHI services	Non-quantifiable[2]
Total	1st year: € 7,718.83 - € 9,697.68
	Subsequent years: € 0 - € 7,273.26
Ranibizumab	1st year: € 6,854.58 - € 13,709.16
	Subsequent years: € 0 - € 13,709.16
Intravitreal injection	1st year: € 536.40 - € 2,295.96
	Subsequent years: € 0 - € 2,295.96
Postoperative treatment	1st year: € 115.14 - € 321.36
	Subsequent years: € 0 - € 321.36
Additionally required SHI services	Non-quantifiable[2]
Total	1st year: € 7,506.12 - € 16,326.48
	Subsequent years: € 0 - € 16,326.48

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 March 2023)

5. Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with faricimab

Medicinal products with the new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients that can be used in a combination therapy with faricimab for the treatment of vision impairments due

[2] Due to the individual determination of the type and frequency of check-ups by the attending physician, the costs incurred for all treatment options cannot be quantified.

to diabetic macular oedema in adults on the basis of the marketing authorisation granted under Medicinal Products Act:

Adults with visual impairment due to diabetic macular oedema (DME)

- No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 6 April 2023.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 6 April 2023

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken