Gemeinsamer Bundesausschuss

Brolucizumab (New Therapeutic Indication: Diabetic Macular Oedema)

Resolution of: 20 October 2022 Valid until: unlimited
Entry into force on: 20 October 2022
Federal Gazette, BAnz AT 21 11 2022 B2

New therapeutic indication (according to the marketing authorisation of 28 March 2022):

Beovu is indicated in adults for the treatment of visual impairment due to diabetic macular oedema (DME).

Therapeutic indication of the resolution (resolution of 20 October 2022):

See new therapeutic indication according to marketing authorisation.

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 brolucizumab 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 differences for the benefit assessment.
Morbidity	↔	No relevant differences for the benefit assessment.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↔	No relevant differences for the benefit assessment.

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-50) unless otherwise indicated.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: 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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

KESTREL study: RCT brolucizumab vs aflibercept (data at week 52)

KITE study: RCT brolucizumab vs aflibercept (data at week 52)

and the meta-analysis of the two studies

Mortality

Endpoint Study	Brolucizumab		Aflibercept		Brolucizumab vs Aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Overall mortality					
KESTREL	189	5 (2.6)	187	2 (1.1)	2.47 [0.49; 12.59]; 0.275
KITE	179	3 (1.7)	181	2 (1.1)	1.52 [0.26; 8.97]; 0.646
Total[a]					2.00 [0.61; 6.58]; 0.255

Morbidity

Endpoint/ scale study	Brolucizumab		Aflibercept		Brolucizumab vs Aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
BCVA (improvement by ≥ 10 ETDRS letters[b])					
KESTREL	189	99 (52.4)	187	107 (57.2)	0.92 [0.76; 1.10]; 0.347
KITE	179	110 (61.5)	181	106 (58.6)	1.05 [0.89; 1.24]; 0.576
Total[a]					0.98 [0.87; 1.11]; 0.771
BCVA (improvement by ≥ 15 ETDRS letters[b])					
KESTREL	189	70 (37.0)	187	74 (39.6)	0.94 [0.72; 1.21]; 0.613
KITE	179	83 (46.4)	181	68 (37.6)	1.23 [0.97; 1.58]; 0.092
Total[a]					1.08 [0.90; 1.29]; 0.405

Health-related quality of life

Endpoint/ scale study	Brolucizumab		Aflibercept		Brolucizumab vs Aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
NEI VFQ-25[c] component score (improvement by ≥ 15 points[d])					
KESTREL	188	46 (24.5)	187	43 (23.0)	1.06 [0.74; 1.53]; 0.737
KITE	178	37 (20.8)	181	33 (18.2)	1.14 [0.75; 1.74]; 0.542
Total[a]					1.10 [0.83; 1.44]; 0.510

Side effects[e]

Endpoint Study	Brolucizumab		Aflibercept		Brolucizumab vs Aflibercept
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
AE (additionally)					
KESTREL	189	155 (82.0)	187	148 (79.1)	---
KITE	179	136 (76.0)	181	146 (80.7)	---
SAE					
KESTREL	189	37 (19.6)	187	43 (23.0)	0.85 [0.58; 1.26]; 0.419
KITE	179	34 (19.0)	181	40 (22.1)	0.86 [0.57; 1.29]; 0.467
Total[a]					0.86 [0.65; 1.13]; 0.277
Discontinuation due to AEs					
KESTREL	189	4 (2.1)	187	7 (3.7)	0.57 [0.17; 1.90]; 0.356
KITE	179	10 (5.6)	181	8 (4.4)	1.26 [0.51; 3.13]; 0.612
Total[a]					0.94 [0.46; 1.91]; 0.856
Intraocular inflammation[f, g] (AE)					
KESTREL	189	7 (3.7)	187	1 (0.5)	6.93 [0.86; 55.74]; 0.069
KITE	179	4 (2.2)	181	3 (1.7)	1.35 [0.31; 5.94]; 0.693
Total[a]					2.75 [0.88; 8.60]; 0.081
Intraocular inflammation[f, h] (SAE)					
KESTREL	189	0 (0.0)	187	0 (0.0)	n.a.
KITE	179	1 (0.6)	181	1 (0.6)	1.01 [0.06; 16.04]; 0.994
Total[a]					1.01 [0.06; 16.04]; 0.994

a. IQWiG's own calculation, meta-analysis with Mantel-Haenszel fixed effect model; test for homogeneity based on effect measure RR
b. Percentage of patients with an increase of BCVA by ≥ 10 ETDRS letters (or ≥ 15 ETDRS letters respectively) compared to the start of the study at week 52 with a scale range from 0 to 100. Higher (increasing) values mean an improvement of symptomatology.
c. For the subscales, the pharmaceutical company only presents continuous evaluations. None of these also shows any statistically significant and relevant difference between the treatment arms.
d. Percentage of patients with an increase of the NEI VFQ-25 component score by ≥ 15 points (≥ 15% of the scale range) compared to the start of the study at week 52 with a scale range from 0 to 100. Higher (increasing) values mean an improvement of health-related quality of life.
e. Contains events of the underlying disease (PT diabetic retinal oedema); evaluation nevertheless suitable for the benefit assessment as this event occurred only sporadically
f. Collected via pre-specified PT list of the pharmaceutical company
g. In the KESTREL study, the PTs iritis, uveitis, ocular inflammation and retinal vasculitis occurred; in the KITE study, the PTs iridocyclitis, uveitis and anterior chamber flickering occurred.
h. No events occurred in the KESTREL study, PT uveitis occurred in the KITE study.

BCVA: best corrected visual acuity; ETDRS: Early Treatment Diabetic Retinopathy Study; CI: confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; NEI: National Eye Institute; PT: preferred term; PC: pharmaceutical company; RCT: randomised controlled trial; RR: relative risk; SAE: serious adverse event; AE: adverse event; VFQ-25: Function Questionnaire-25

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 – 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 Beovu (active ingredient: brolucizumab) at the following publicly accessible link (last access: 16 August 2022):

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

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

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient (for one eye)
Medicinal product to be assessed:	
Brolucizumab	1st year: € 6,125.76 - € 7,146.72
	Subsequent years: € 4,390.13 - € 6,636.24
Intravitreal injection	1st year: € 545.52 – € 1,327.27
	Subsequent years: € 390.96 – € 1,232.47
Postoperative treatment	1st year: € 112.86 - € 183.75
	Subsequent years: € 80.88 – € 170.63
Additionally required SHI services	non-quantifiable[2]
Total	1st year: € 6,784.14 - € 8,657.74
	Subsequent years: € 4,861.97 - € 8,039.33
Appropriate comparator therapy:	
Aflibercept	1st year: € 8,298.96
	Subsequent years: € 0 - € 6,224.22
Intravitreal injection	1st year: € 727.36 – € 1,516.88
	Subsequent years: € 0 - € 1,137.66
Postoperative treatment	1st year: € 150.48 – € 210.00
	Subsequent years: € 0 – € 157.50
Additionally required SHI services	non-quantifiable[Fehler! Textmarke nicht definiert.]
Total	1st year: € 9,176.80 - € 10,025.84
	Subsequent years: € 0 – € 7,519.38
Ranibizumab	1st year: € 7,153.02 - € 14,306.04
	Subsequent years: € 0 – € 14,306.04
Intravitreal injection	1st year: € 545.52 – € 2,275.32
	Subsequent years: € 0 – € 2,275.32
	1st year: € 112.86 – € 315.00

[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.

Designation of the therapy	Annual treatment costs/ patient (for one eye)
Postoperative treatment	Subsequent years: € 0 – € 315.00
Additionally required SHI services	non-quantifiable[Fehler! Textmarke nicht definiert.]
Total	1st year: € 7,811.40 - € 16,896.36
	Subsequent years: € 0 – € 16,896.36

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 October 2022)