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
Donanemab (Early Alzheimer's disease)

of 16 April 2026

At their session on 16 April 2026, 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. In Annex XII, information on the active ingredient Donanemab shall be added in alphabetical order as follows:

Donanemab

Resolution of: 16 April 2026
Entry into force on: 16 April 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 24 September 2025):

Donanemab is indicated for the treatment of adult patients with a clinical diagnosis of mild cognitive impairment and mild dementia due to Alzheimer's disease (Early symptomatic Alzheimer's disease) who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology.

Therapeutic indication of the resolution (resolution of 16 April 2026):

See therapeutic indication according to marketing authorisation.

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

a) Adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

Appropriate comparator therapy:

Best supportive care

Extent and probability of the additional benefit of donanemab compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

Appropriate comparator therapy:

Donepezil *or* galantamine *or* rivastigmine

Extent and probability of the additional benefit of donanemab compared to acetylcholinesterase inhibitors (AChEI):

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
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 ∅: No data available. n.a.: not assessable		

b) Adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

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 differences for the benefit assessment.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↓	Disadvantage in the endpoint of therapy discontinuation due to AE.
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 ∅: No data available. n.a.: not assessable		

[1] Data from the dossier assessment of the IQWiG (A25-134) and from the addendum (A26-29), unless otherwise indicated.

AACI study:
Randomised, controlled phase III study, donanemab versus placebo (each in combination with an AChEI)

The results presented are based on two sub-populations of the study, defined according to the following criteria:

• ApoE ε4 heterozygotes and non-carriers • No memantine treatment • **Existing AChEI therapy at the time of screening**
Clinical Dementia Rating Scale – Global Score (CDR-GS): 1 or 2 (hereinafter referred to as the "CDR-GS sub-population") | **Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB)**: 4.5 to 9 (hereinafter referred to as the "CDR-SB sub-population")

Mortality

Endpoint	**Donanemab + AChEI**		**Placebo + AChEI**		**Donanemab + AChEI vs Placebo + AChEI**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Overall mortality[a]					
CDR-GS sub-population					
	120	6 (5.0)	110	1 (0.9)	5.50 [0.67; 44.96]; 0.122
CDR-SB sub-population					
	117	6 (5.1)	107	1 (0.9)	5.49 [0.67; 44.84]; 0.122

Morbidity

Endpoint	Donanemab + AChEI		Placebo + AChEI		Donanemab + AChEI vs Placebo + AChEI
	N	Median time to event (weeks) [95% CI] Patients with event n (%)	N	Median time to event (weeks) [95% CI] Patients with event n (%)	HR [95% CI]; p value
Symptomatology as assessed by the CDR-SB; time to permanent deterioration[b, c]					
CDR-GS sub-population					
	122	77.3 [77.00; n.c.] 36 (29.5)	110	77.0 [75.71; n.c.] 45 (40.9)	0.80 [0.51; 1.25]; 0.320
CDR-SB sub-population					
	119	79.0 [77.00; n.c.] 33 (27.7)	107	77.0 [75.71; n.c.] 42 (39.3)	0.75 [0.47; 1.19]; 0.218
Cognition as assessed by the ADAS-Cog13; time to permanent deterioration[b, d]					
CDR-GS sub-population					
	122	n.r. [78.14; n.c.] 20 (16.4)	110	79.9 [76.71; n.c.] 33 (30.0)	0.60 [0.34; 1.06]; 0.079
CDR-SB sub-population					
	119	n.r. [78.14; n.c.] 19 (16.0)	107	n.r. [76.71; n.c.] 30 (28.0)	0.56 [0.31; 0.9997]; 0.0499

Health-related quality of life

There are no assessable data.

Side effects

Endpoint	Donanemab + AChEI		Placebo + AChEI		Donanemab + AChEI vs Placebo + AChEI
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Total adverse events (presented additionally)					
CDR-GS sub-population					
	120	*107 (89.2)*	*110*	*90 (81.8)*	–
CDR-SB sub-population					
	117	*105 (89.7)*	*107*	*84 (78.5)*	-
Serious adverse events (SAEs)					
CDR-GS sub-population					
	120	27 (22.5)	110	17 (15.5)	1.46 [0.84; 2.52]; 0.184
CDR-SB sub-population					
	117	25 (21.4)	107	16 (15.0)	1.43 [0.81; 2.53]; 0.231
Therapy discontinuation due to adverse events					
CDR-GS sub-population					
	120	20 (16.7)	110	6 (5.5)	3.06 [1.27; 7.33]; 0.011
CDR-SB sub-population					
	117	19 (16.2)	107	5 (4.7)	3.48 [1.34; 8.98]; 0.008
Specific adverse events					
Symptomatic ARIA events					
CDR-GS sub-population					
Symptomatic ARIA events, combined[e]	No data available				
Symptomatic ARIA-E	120	4 (3.3)		0 (0)	8.26 [0.45; > 100]; 0.123
Symptomatic ARIA-H	No data available				
Serious ARIA-E	120	0 (0)	110	0 (0)	–
Serious ARIA-H	120	1 (0.8)	110	0 (0)	2.75 [0.11; 66.86]; > 0.999

CDR-SB sub-population					
Symptomatic ARIA events, combined[e]	No data available				
Symptomatic ARIA-E	117	5 (4.3)	107	0 (0.0)	10.07 [0.56; > 100]; 0.061
Symptomatic ARIA-H	No data available				
Serious ARIA-E	117	1 (0.9)	107	0 (0.0)	2.75 [0.11; 66.69]; > 0.999
Serious ARIA-H	117	1 (0.9)	107	0 (0.0)	2.75 [0.11; 66.69]; > 0.999
Infusion-related reactions[f] (PT, AE)					
CDR-GS sub-population					
	120	7 (5.8)	110	0 (0)	13.76 [0.80; > 100]; 0.015
CDR-SB sub-population					
	117	8 (6.8)	107	0 (0.0)	15.56 [0.91; > 100]; 0.007

a. The results on overall mortality are based on the data on fatal AEs.
b. A permanent deterioration was defined as the first point in time at which the relevant response criterion was met without subsequent improvement until the end of the study, or only missing values occurred after a first (or, if applicable, confirmed) deterioration.
c. An increase in the score by ≥ 2.7 points (15% of the scale range) compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 18).
d. An increase by ≥ 12.75 points (15% of the scale range) compared to the start of the study is considered as clinically relevant deterioration (scale range: 0 to 85).
e. Combined evaluations of the following events are considered: symptomatic ARIA-E, symptomatic ARIA-H, serious ARIA-E and serious ARIA-H.
f. Operationalised via the PT infusion-related reaction

Abbreviations
AChEI = acetylcholinesterase inhibitors; ADAS-Cog13 = Alzheimer's Disease Assessment Scale – Cognitive subscale 13-item version; ARIA = amyloid-related imaging abnormalities; ARIA-E = ARIA with oedema; ARIA-H = ARIA with haemosiderin deposition; CDR-SB = Clinical Dementia Rating – Sum of Boxes; CI = confidence interval; HR = hazard ratio; n = number of patients with (at least 1) event; N = number of patients evaluated; n.c. = not calculable; n.r. = not reached; PT = preferred term; RR = relative risk; SD = standard deviation; SAE = serious adverse event(s); AE = adverse event(s)

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

a) Adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

and

b) Adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

Approx. 131,000 to 440,000 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 Kisunla (active ingredient: donanemab) at the following publicly accessible link (last access: 16 March 2026):

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

Treatment with donanemab should only be initiated and monitored by specialists in neurology or specialists in psychiatry and psychotherapy who are experienced in the treatment of Alzheimer's disease and are able to promptly carry out magnetic resonance imaging (MRI) diagnostics.

Before starting treatment with donanemab, patients must be tested for ApoE ε4 status and the presence of amyloid-beta pathology must be confirmed by means of a suitable test.

Treatment with donanemab should be continued until the amyloid plaques have been removed. The maximum treatment duration of 18 months should not be exceeded, even if plaque removal is not confirmed.

The benefit-risk ratio of the treatment should be reassessed at regular intervals on a case-by-case basis, taking into account the extent of disease progression.
Discontinuing treatment before the end of the maximum treatment duration of 18 months must be considered if the patient's condition progresses to moderate Alzheimer's dementia.

Donanemab may cause amyloid-related imaging abnormalities (ARIA). In addition to ARIA, intracerebral haemorrhages with a diameter of more than 1 cm occurred in patients treated with donanemab.

Before starting treatment with donanemab, a recent (no more than 6 months old) brain MRI must be available to assess whether ARIA is already present. An MRI scan must be performed before the second infusion (in the 1st month), before the third infusion (in the 2nd month), before the fourth infusion (in the 3rd month) and before the seventh infusion (in the 6th month). Patients with ARIA risk factors should undergo an additional MRI scan after one year of treatment (before the twelfth infusion).
If a patient shows symptoms suggestive of ARIA at any point during treatment, a clinical assessment, including an MRI scan, must be carried out.

Treatment with donanemab must not be initiated in patients who are currently receiving anticoagulant therapy.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients, including patient identification card. The training material contains, in particular, information on the above-mentioned requirements for treatment with donanemab and warnings about the risks of ARIA.

Treatment with donanemab must be initiated for all patients via a central registration system that forms part of a controlled access programme.

4. Treatment costs

Annual treatment costs:

a) Adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed	
Donanemab 1. Year: Subsequent year: Additionally required SHI services: 1. Year: Subsequent year: Total[2]: 1. Year: Subsequent year:	 € 43,015.98 € 22,443.12 € 652.50 € 0 € 43,668.48 € 22,443.12
Best supportive care	Different from patient to patient
Appropriate comparator therapy	
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 February 2026)

[2] This represents the annual treatment costs for the maximum treatment duration of 18 months.

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Donanemab	Surcharges for the preparation of parenteral solutions containing monoclonal antibodies	€ 100	1	1st year 13.0 Subsequent year: 6.0	1st Year: € 1,300 Subsequent year: € 600

b) <u>Adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology</u>

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed	
Donanemab 1. Year: Subsequent year: Additionally required SHI services: 1. Year: Subsequent year: Total[2]: 1. Year: Subsequent year:	 € 43,015.98 € 22,443.12 € 652.50 € 0 € 43,668.48 € 22,443.12
Appropriate comparator therapy	
Donepezil 1st and subsequent years	€ 213.41 - € 223.99
Galantamine 1st and subsequent years	€ 227.17 - € 232.38
Rivastigmine 1st and subsequent years	€ 413.88 - € 432.59

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 February 2026)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Donanemab	Surcharges for the preparation of parenteral solutions containing monoclonal antibodies	€ 100	1	1st year 13.0 Subsequent year: 6.0	1st Year: € 1,300 Subsequent year: € 600

5. Designation of 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 the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

a) Adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

- No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) heterozygotes or non-carriers with confirmed amyloid pathology

- No medicinal product with new active ingredients 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.

6. Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Kisunla is a medicinal product placed on the market from 1 January 2025.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed

who participated at study sites within the scope of SGB V (German Social Security Code) is < 5 per cent of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant percentage within the scope of SGB V.

II. The resolution will enter into force on the day of its publication on the G-BA website on 16 April 2026.

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

Berlin, 16 April 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken