Gemeinsamer Bundesausschuss

Justification

to the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive: Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Lecanemab (Early Alzheimer's disease)

of 19 February 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical studies the pharmaceutical company have conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application,
7. number of study participants who participated in the clinical studies at study sites within the scope of SGB V, and total number of study participants.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decide on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient lecanemab on 1 September 2025 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. Pursuant to Section 4, paragraph 3, No. 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, No. 1 Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 26 August 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 December 2025 on the G-BA website at (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of lecanemab compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of lecanemab.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made the following assessment:

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

2.1.1 Approved therapeutic indication of Lecanemab (Leqembi) in accordance with the product information

Leqembi 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 Alzheimer's disease) who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology.

Therapeutic indication of the resolution (resolution of 19.02.2026):

See the approved therapeutic indication.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

Appropriate comparator therapy for lecanemab:

Best supportive care

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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

Appropriate comparator therapy for lecanemab:

Donepezil *or* galantamine *or* rivastigmine

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1: In the present therapeutic indication, the acetylcholinesterase inhibitors (AChEIs) donepezil, galantamine and rivastigmine are approved for the symptomatic treatment of mild to moderate Alzheimer's dementia.

The active ingredient donanemab is approved for the treatment of adults with a clinical diagnosis of mild cognitive impairment and mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology.

A dry extract from Ginkgo biloba leaves is approved for improving age-related cognitive impairment and quality of life in cases of mild dementia.

On 2. Occupational therapy, e.g. brain power training, is considered a measure in accordance with the Remedies Directive and the catalogue of remedies.

On 3. For the treatment of patients with Alzheimer's disease, there are no resolutions from the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present therapeutic indication.
The S3 Guideline on Dementias[2] is particularly relevant for the German healthcare context.

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V.

Based on the evidence, there are different therapy recommendations depending on the stage of Alzheimer's disease. In accordance with the marketing authorisation, different therapy options are available for different stages of the disease: Symptomatic antidementia drugs are not approved for the treatment of mild cognitive impairment, whereas AChEIs have been granted marketing authorisation for the treatment of mild to moderate Alzheimer's dementia.

During the written statement procedure, it was pointed out that Alzheimer's disease is a progressive condition and that transitions from mild cognitive impairment to dementia are common.

According to the S3 guideline, the clinical differentiation between these stages is based on an assessment of the extent of everyday skills. In accordance with the authorisation status, the S3 guideline also states that there are different therapy recommendations for the stage of mild cognitive impairment and mild dementia.

[2] DGN e. V. & DGPPN e. V. (ed.) S3 Guideline on Dementias, Version 5.2, 17.07.2025, available at: https://register.awmf.org/de/leitlinien/detail/038-013

Against this background, patient group differentiation by mild cognitive impairment or mild dementia due to Alzheimer's disease is made.

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

No symptomatic pharmacotherapy is approved for the treatment of mild cognitive impairment. Based on the S3 Guideline on Dementias and other evidence, no recommendations can be made regarding the pharmacological treatment of mild cognitive impairment. Based on the evidence, no superiority of AChEIs over placebo can be inferred in patients with mild cognitive impairment. Against this background, the S3 Guideline on Dementias does not recommend treatment with AChEIs for patients with mild cognitive impairment.

Ginkgo biloba leaf extract is approved for improving age-related cognitive impairment and quality of life in mild dementia and, based on the evidence, has a minor therapeutic significance.
The active ingredient memantine is only approved for the treatment of patients with moderate to severe Alzheimer's dementia and is only recommended for these patients based on the available evidence.
Similar to lecanemab, the active ingredient donanemab is a new treatment option in the present therapeutic indication. Donanemab has only recently been approved and is now available in Germany. Based on the evidence, there are currently no recommendations regarding the use of this active ingredient for the treatment of Alzheimer's disease.
In summary, Ginkgo biloba leaf extract, memantine and donanemab are not considered an appropriate comparator therapy for patient group a, taking into account their respective marketing authorisation and the generally accepted state of medical knowledge. The explanations also apply to the appropriate comparator therapy for patient group b (see below).

According to the S3 guideline, cognitive training or cognitive stimulation is recommended to improve cognition in patients with mild cognitive impairment. These therapies can be provided as non-medicinal measures within the meaning of the Remedies Directive or the catalogue of remedies (occupational therapy, e.g. brain power training).

In the overall assessment, based on the generally accepted state of medical knowledge at this point in time, no recommendations can be made regarding pharmacological treatment of mild cognitive impairment due to Alzheimer's disease. Against this background and taking into account the recommendations for non-medicinal measures, best supportive care is determined to be the appropriate comparator therapy for patient population a.

Best supportive care is defined as the therapy that provides the best possible, patient-individually optimised, supportive treatment to alleviate symptoms and improve quality of life.

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

AChEIs (donepezil, galantamine and rivastigmine) are approved for the symptomatic treatment of mild to moderate Alzheimer's dementia. Based on the available evidence, the use of AChEIs is recommended for the treatment of patients in the mild to moderate stage of Alzheimer's dementia. This recommendation has the highest level of recommendation in the S3 Guideline on Dementias.

During the written statement procedure, it was pointed out that not all patients with mild Alzheimer's dementia receive treatment with AChEIs in healthcare. Contraindications and side effects were cited as reasons for this. However, this contrasts with the strong recommendation in the S3 guideline for the use of AChEIs, which is based on high-quality evidence in the form of systematic reviews and meta-analyses and also takes the German healthcare context into account. Against this background, it can be assumed that, according to generally accepted state of medical knowledge, AChEIs are considered the recommended therapy standard and therefore represent the appropriate therapy for patients with mild Alzheimer's dementia.

With regard to the active ingredients Ginkgo biloba, memantine and donanemab, please refer to the above explanations. These active ingredients are not considered to be the appropriate comparator therapy for patient group b.

In the overall assessment of the body of evidence, the AChEIs donepezil, galantamine or rivastigmine are considered as the appropriate comparator therapy for adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology. The highest tolerable dose should be aimed for.

The appropriate comparator therapy determined for patient group b comprises several therapeutic alternatives. These therapeutic alternatives are equally appropriate for the comparator therapy. The additional benefit can be demonstrated compared to one of the treatment options mentioned.

Taking into account the S3 guideline recommendation for the use of cognitive procedures in mild dementia, it is also pointed out for patient population b that non-medicinal measures within the meaning of the Remedies Directive or the catalogue of remedies (occupational therapy, e.g. brain power training) can contribute to alleviation of symptoms.

The relevant findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

Change in the appropriate comparator therapy for patient group a

Until now, monitoring wait-and-see approach has been considered the appropriate comparator therapy for adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology.

As explained above, non-medicinal measures within the meaning of the Remedies Directive or the catalogue of remedies (occupational therapy, e.g. brain power training) assume

relevant significance in this context, which is reflected in the guideline recommendation of cognitive training or cognitive stimulation for patients with mild cognitive impairment.

Since the application of non-medicinal measures goes beyond the monitoring wait-and-see approach, the G-BA consider it appropriate to determine best supportive care as the appropriate comparator therapy for patient group a in the present case.

The relevant findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of lecanemab is assessed as follows:

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

   The additional benefit is not proven for adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology.

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

   The additional benefit is not proven for adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology.

Justification:

For the benefit assessment, the pharmaceutical company submitted evaluations of the double-blind, randomised controlled trial CLARITY AD.

Patients 50 to 90 years of age with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's dementia were enrolled in the study. Patients had to show positive biomarker evidence of amyloid pathology, which could be determined either by assessment of a positron emission tomography (PET) scan with an amyloid tracer (amyloid PET) or by measuring total tau/ amyloid β in cerebrospinal fluid. Further inclusion criteria are based, among other things, on the Clinical Dementia Rating Scale (CDR) and the Mini Mental Status Test (MMST).
If patients were already receiving symptomatic medication for the treatment of Alzheimer's disease (e.g. AChEI or memantine), the dose had to have been stable for at least 12 weeks prior to baseline. Patients who had not previously received symptomatic medication for the treatment of Alzheimer's disease were also eligible to participate in the study.

A total of 1,795 patients were randomised to receive treatment with lecanemab in the intervention arm or placebo in the comparator arm. The duration of the double-blind treatment phase was 18 months. In addition to lecanemab or placebo, patients who had previously been treated with symptomatic antidementia drugs in both study arms should continue their respective medication as unchanged as possible. Where medically necessary,

adjustment to existing antidementia medication and the initiation of antidementia therapy in previously untreated patients were permitted.

On the relevant sub-populations for the benefit assessment

In the dossier, the pharmaceutical company submitted evaluations of the total population of the CLARITY AD study. The evaluations based on the total population are not used for the present benefit assessment since the total study population neither takes into account the restrictions of the marketing authorisation with regard to ApoE ε4 carrier status and the use of anticoagulants, nor the appropriate comparator therapy determined differentially for patient groups a and b.

In the Annex, the pharmaceutical company also presented analyses of different sub-populations. Data that allows comparison with the appropriate comparator therapy is relevant for the benefit assessment. In addition, the marketing authorisation requirements for the medicinal product to be assessed must be taken into account.

Consequently, in accordance with patient groups a and b, the evaluations here are considered relevant for the following sub-populations of the CLARITY AD study:

- Patient group a: Patients with mild cognitive impairment due to Alzheimer's disease, who were not receiving symptomatic antidementia drugs at the start of the study, who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes, and who were not receiving anticoagulants at baseline (N = 252 [lecanemab] versus N = 245 [placebo]); hereinafter referred to as study sub-population a
- Patient group b: Patients with mild Alzheimer's dementia, who were receiving AChEI therapy at the start of the study, who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes, and who were not receiving anticoagulants at baseline (N = 139 [lecanemab] versus N = 138 [placebo]); hereinafter referred to as study sub-population b

Due to the study design, which provides for the administration of AChEIs as possible concomitant therapy in both study arms, only data on lecanemab as add-on therapy to AChEIs are available for patient group b (mild Alzheimer's dementia), but not on lecanemab used as monotherapy.

On the limitations of the CLARITY AD study

Missing information on the use of non-medicinal measures

The use of non-medicinal therapies was generally permitted during the study, but these were not systematically offered as part of the study. Overall, it can be assumed that non-medicinal therapies were used whenever medically indicated and available.
However, no information is available on the percentage and type of non-medicinal therapies used during the study.

Missing information on the use of AChEI treatment

The pharmaceutical company submitted information on the medicinal concomitant treatments used in the study at the start of the study and during the course of the study, but not on the dosage and timing of AChEI therapy adjustments. However, these would be necessary in order to verify the marketing authorisation compliance of the application for the active ingredients of the appropriate comparator therapy for patient group b:
According to the requirements of the relevant product information, AChEIs should be titrated to the highest tolerable dose within a defined time interval, taking into account clinical response and tolerability.

Overall, there is no indication that AChEIs were not used in accordance with the product information in patients of the study sub-population b. However, the relevant information for verification is missing.

Missing requirements on how to deal with lack of efficacy or progression to the next stage

According to the product information, treatment with lecanemab should be discontinued in the event of disease progression to the moderate stage. Discontinuation of treatment with lecanemab upon progression to the moderate stage was not planned in the study. Continued treatment with lecanemab in patients with disease progression to the moderate stage during the study therefore does not comply with the requirements of the marketing authorisation. No information is available on the percentage of patients affected by this in the study.

Furthermore, regular evaluation of cognitive function and clinical symptoms is indicated for both lecanemab and AChEIs in order to assess whether treatment should be discontinued in the absence of clinical efficacy. The study was designed to record therapeutic effects, but not to provide an overall assessment by doctors concerning possible lack of efficacy with corresponding requirements for discontinuation of lecanemab or AChEIs.

With regard to treatment with AChEIs, there are also uncertainties concerning the initiation of appropriate treatment in cases of progression from mild cognitive impairment to mild dementia. Overall, there is a lack of information on the reasons for the adjustments made to concomitant medication during the study.

For both study sub-populations relevant to the benefit assessment, uncertainties remain as to whether the treatments were discontinued in accordance with the product information in the event of lack of efficacy and whether adequate therapies were used during progression to the next stage of the disease.

Despite the described limitations of the CLARITY AD study, the treatment in the intervention arm and the respective appropriate comparator therapy for both patient groups are considered to have been adequately implemented. Consequently, the results based on the CLARITY AD study are used in the present benefit assessment.

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

<u>Extent and probability of the additional benefit</u>

<u>Mortality</u>

The results on overall mortality are based on the data on fatal adverse events (AEs).
For the endpoint of overall mortality, there was no statistically significant difference between the treatment arms.

<u>Morbidity</u>

As part of the written statement procedure, evaluations stratified by sub-population, baseline AChEI intake, ApoE ε4 status and region were subsequently submitted for the endpoints on morbidity and health-related quality of life based on responder analyses. For methodological reasons, these are preferred over the unstratified evaluations presented in the dossier and are used accordingly in the benefit assessment.

Symptoms using the Clinical Dementia Rating (CDR)

The CDR is a measurement tool for assessing the severity of symptoms in patients with Alzheimer's disease, based on a semi-structured interview with both the patient and a caregiver.
It is a complex scale with a total of 6 domains: 3 cognitive domains (memory, orientation, judgement and problem solving) and 3 functional domains (community living, household and hobbies, personal care). The patient is only questioned about the 3 cognitive domains, while the caregiver is questioned exclusively about the 3 functional domains.

Based on the 6 domain scores, two different total scores can be calculated:

The CDR Sum of Boxes (CDR-SB) is calculated by adding the 6 domain scores together to produce a summary score, with the CDR-SB showing a scale range of 0 to 18.

The CDR Global Score (CDR-GS) is calculated using an algorithm in which, among other things, the memory domain is weighted more heavily than the other 5 domains, and takes point values on an ordinal scale from 0 to 3 points (0 points: no dementia, 0.5 points: questionable dementia, 1 point: mild dementia, 2 points: moderate dementia, 3 points: severe dementia). This means that changes in the course of the disease may occur in several domains, but these are not reflected in the CDR-GS total score.

The pharmaceutical company submitted evaluations for both total scores. Overall, the CDR-SB shows higher sensitivity than the CDR-GS, particularly in early Alzheimer's disease, and is better than the CDR-GS at distinguishing between mild cognitive impairment and mild dementia. Against this background, evaluations based on the CDR-SB are used to assess symptoms in the present benefit assessment.

Responder analyses for deterioration at month 18 based on the CDR-SB

There are evaluations - based on the CDR-SB - of the deterioration by at least 3 points (2.7 points correspond to 15% of the scale range) at month 18 for the study sub-population a. These are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

Time-to-event analyses of the time to deterioration based on the CDR-SB

In the written statement procedure, time-to-event analyses of the time to first deterioration and the time to confirmed deterioration based on the above-mentioned response criterion (deterioration of the CDR-SB by at least 3 points) were subsequently submitted. These are not used in the present benefit assessment for the following reasons:

Even though time-to-event analyses of the time to first deterioration may be appropriate in principle, depending on the specific data basis, evaluations of a confirmed or permanent deterioration are to be preferred over those of a first deterioration in the present therapeutic indication. This is because a deterioration that persists over a longer period of time is more relevant and reflects the progressive course of the disease more accurately than isolated deteriorations at individual points in time.

The submitted evaluations of the time to first deterioration also have methodological limitations, which arise in particular from unclear or missing information on censoring. According to the information provided by the pharmaceutical company, patients who showed no deterioration up to month 18 were censored. It is not clear why censoring is indicated for month 21 in the submitted evaluations and to what extent patients with an event shortly after

month 18 (but within the visit window) were included in the analysis. Overall, it remains unclear whether events in the lecanemab arm, particularly in the evaluations of study sub-population b, were not taken into account in the presented analyses of the first deterioration. Particularly in light of the methodological limitations mentioned above, the evaluations of the time to first deterioration are considered insufficiently reliable for interpretation in the overall assessment.

In the evaluations of the time to confirmed deterioration, an event was defined as a deterioration in the CDR-SB by at least 3 points on two consecutive visits. Missing values were not replaced, and a one-time deterioration without a follow-up survey was considered an unconfirmed deterioration.
Consequently, patients with a first deterioration at month 18 and those with a one-time deterioration after which no follow-up survey was conducted (e.g. due to study discontinuation) were not counted as patients with an event. This may lead to a risk of bias of the analyses, particularly given the high percentage of patients with first deterioration at month 18 and the differential, lower return rates in the lecanemab arm. Suitable sensitivity analyses are not available. The presented analyses of the time to confirmed deterioration are therefore unsuitable and are not used for the present benefit assessment.
Continuous analyses of change from baseline at month 18 based on the CDR-SB

In addition, evaluations of the change in CDR-SB at month 18, based on the mixed model for repeated measures (MMRM), are available. The change in CDR-SB at month 18 represents the primary endpoint of the CLARITY AD study and has been widely cited in publications. The responder analyses of deterioration at month 18 are used for the benefit assessment. The continuous analyses are presented additionally here for reasons of transparency.

Based on continuous analyses, no statistically significant difference was detected between the treatment arms for patient population a.

Cognition using the Alzheimer's Disease Assessment Scale – Cognitive Subscale 14 (ADAS-Cog14)

The ADAS-Cog14 is a function test developed to assess the severity of cognitive impairment in Alzheimer's dementia.

The assessment is conducted in the form of an interview with the patient. The items include tasks to be performed by the patient themselves (e.g. for temporal and spatial orientation) as well as subjective assessments by the interviewer (e.g. for language comprehension). The scores for all items are added together to produce a summary score; the ADAS-Cog14 scale ranges from 0 to 90 points.

Evaluations - based on ADAS-Cog14 - of deterioration by at least 13.5 points (corresponding to 15% of the scale range) at month 18 are available for the study sub-population a and are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

Health status using the visual analogue scale (VAS) of the EQ-5D

Health status was assessed using the VAS of the EQ-5D, on which patients answer the question about their own health status at the survey time point. 0 stands for the worst imaginable health status and 100 for the best imaginable health status. The VAS of the EQ-5D is considered in the morbidity category for the benefit assessment.

Evaluations - based on EQ-5D VAS - of deterioration by at least 15 points (corresponding to 15% of the scale range) at month 18 are available for the study sub-population a and are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

About the Alzheimer's Disease Composite Score (ADCOMS) measurement tool

The ADCOMS was designed to assess clinical deterioration in patients with prodromal Alzheimer's disease or mild Alzheimer's dementia. It is not a stand-alone tool, but a composite scale composed of items or domains from the following tools:

- ADAS-Cog12: 4 items
- MMST: 2 items
- CDR-SB: all 6 domains

The result of the CDR-SB is thus fully incorporated into the ADCOMS; likewise, the 4 items from the ADAS-Cog12 that are included in the ADCOMS are also contained in the ADAS-Cog14. The ADCOMS is therefore redundant in relation to the CDR-SB and the ADAS-Cog14. The evaluations - based on ADCOMS - presented in the dossier are therefore not used for the benefit assessment.

Activities of daily living using the Alzheimer's Disease Cooperative Study Mild Cognitive Impairment Activities of Daily Living Inventory (ADCS-MCI-ADL)

The dossier contains evaluations of activities of daily living based on the ADCS-MCI-ADL. This is a measurement tool that uses external assessment to survey the impairment of activities of daily living in patients with mild cognitive impairment. The survey is conducted in the form of an interview with a cohabitant of the patient or a person who spends time with them regularly (e.g. the patient's partner).

Activities of daily living are generally considered to be patient-relevant in the therapeutic indication of Alzheimer's disease. However, the ADCS-MCI-ADL measurement tool is not considered valid and suitable for assessment of the activities of daily living in the present indication. This is due to missing information on content validity, in particular regarding the involvement of patients in the therapeutic indication during the development of the tool. Furthermore, the ADCS-MCI-ADL is surveyed exclusively by external assessment, although it can be assumed that patients with early Alzheimer's disease are still largely capable of assessing impairments in activities of daily living themselves. Furthermore, the sources provided do not indicate that the ADCS-MCI-ADL is designed for patients with mild dementia due to Alzheimer's disease in addition to patients with mild cognitive impairment.

Against this background, the evaluations based on the ADCS-MCI-ADL are not used for the present benefit assessment.

Biomarker-associated endpoints

Several biomarker-associated endpoints on amyloid and tau pathology were presented in the dossier. The survey was conducted using imaging procedures and cerebrospinal fluid diagnostics. The symptoms noticeable to patients associated with the change in amyloid and tau pathology or the resulting impairment of health-related quality of life are relevant for the benefit assessment pursuant to Section 35a SGB V. A surrogate validation with a biomarker-associated endpoint as a surrogate for a patient-relevant endpoint was not presented. Against this background, the biomarker-associated endpoints are not used for the present benefit assessment.

Quality of life

The Quality of Life in Alzheimer's Disease Scale (QOL-AD) is a tool for assessing the health-related quality of life of patients with Alzheimer's disease. The tool comprising a total of 13 items assesses health-related quality of life separately through self-assessment (using a structured interview) and external assessment (using a questionnaire for relatives or caregivers). The scores for all 13 items (each on a scale of 1 to 4) are added together to produce a summary score, so that the scale ranges from 13 to 52.

In the CLARITY AD study, QOL-AD was assessed both in patient-reported and peer-reported forms. Based on the validation study and taking into account the baseline characteristics, it is assumed that the patients in the CLARITY AD study were predominantly able to complete the QOL-AD themselves. Against this background, the patient-reported version of the QOL-AD is used for the present benefit assessment.

In this regard, evaluations of deterioration by at least 5.85 points (corresponding to 15% of the scale range) at month 18 are available for the study sub-population a and are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

Side effects

There are evaluations of adverse events that occurred during treatment or within 30 days after the last dose of the study medication.

With regard to serious adverse events (SAEs), the overall rate excluding disease-related events is used for the present benefit assessment.

For the overall rates of SAEs and adverse events leading to discontinuation of the study medication, there was no statistically significant difference between the treatment arms in the evaluations based on the study sub-population a.

In detail, there was a statistically significant disadvantage of lecanemab in the endpoint of symptomatic ARIA events. There is a discrepancy between the 95% confidence interval, which covers the zero effect, and the p value (< 0.05).
In addition, there was also a statistically significant disadvantage of lecanemab in the endpoint of infusion-related reactions.

Overall assessment

Data from the CLARITY AD study are available for the benefit assessment of lecanemab for the treatment of adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's

disease (Early Alzheimer's disease) who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology. This is a double-blind, randomised study comparing lecanemab with placebo over a treatment period of 18 months, if applicable in addition to continued treatment with symptomatic antidementia drugs.

To assess the additional benefit of lecanemab for patient population a, data based on a study sub-population are used to enable a comparison of lecanemab versus best supportive care.

With regard to mortality, there were no statistically significant differences between the treatment arms.

In the morbidity endpoint category, based on the responder analyses for the endpoints of symptoms using CDR-SB, cognition using ADAS-Cog14 and health status using EQ-5D VAS, there was no statistically significant difference between the treatment arms.

For the endpoint category of health-related quality of life, there was no statistically significant difference between the treatment arms in the evaluations based on QOL-AD.

In the endpoint category of side effects, there was no statistically significant difference between the treatment arms in the overall rates of serious adverse events and therapy discontinuation due to adverse events.
In detail, there was a statistically significant disadvantage of lecanemab in the endpoints of symptomatic ARIA events and infusion-related reactions.
Overall, no relevant differences for the benefit assessment were derived in the category of side effects.

In the overall assessment, based on the CLARITY AD study, no relevant differences for the benefit assessment were identified for the patient sub-population a in the endpoint categories of mortality, morbidity, health-related quality of life and side effects. An additional benefit of lecanemab for the treatment of adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology is therefore not proven.

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

Extent and probability of the additional benefit

The patient-relevant endpoints used in the benefit assessment are identical for patient groups a and b. In this regard, please refer to the above explanations. The results are described below based on the endpoints used.

Mortality

For the endpoint of overall mortality, there was no statistically significant difference between the treatment arms.

Morbidity

Symptoms using the Clinical Dementia Rating (CDR)

Evaluations - based on the CDR-SB - of deterioration by at least 3 points (2.7 points correspond to 15% of the scale range) at month 18 for the study sub-population b. These are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

In addition, evaluations of the change in CDR-SB at month 18 (MMRM analyses) are available. The responder analyses of deterioration at month 18 are used for the benefit assessment. The continuous analyses are presented additionally here for reasons of transparency.

Based on the continuous analyses, there was a statistically significant advantage of lecanemab over AChEIs for patient population b. The 95% confidence interval of the standardised mean difference (SMD) is however not completely outside the irrelevance range from - 0.2 to 0.2, so that it cannot be concluded that the effect is clinically relevant.

Cognition using the Alzheimer's Disease Assessment Scale – Cognitive Subscale 14 (ADAS-Cog14)

Evaluations - based on ADAS-Cog14 - of deterioration by at least 13.5 points (corresponding to 15% of the scale range) at month 18 are available for the study sub-population b and are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

Health status using the visual analogue scale (VAS) of the EQ-5D

Evaluations - based on EQ-5D VAS - of deterioration by at least 15 points (corresponding to 15% of the scale range) at month 18 are available for the study sub-population b and are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

Quality of life

Evaluations - based on QOL-AD - of deterioration by at least 5.85 points (corresponding to 15% of the scale range) at month 18 are available for the study sub-population b and are used for the benefit assessment.

No statistically significant difference was detected between the treatment arms based on these analyses.

Side effects

For the overall rates of SAEs and AEs leading to discontinuation of the study medication, there was no statistically significant difference between the treatment arms for the study sub-population b.

In detail, there was a statistically significant disadvantage of lecanemab in the endpoint of symptomatic ARIA events. There is a discrepancy between the 95% confidence interval, which covers the zero effect, and the p value (< 0.05).
In addition, there was also a statistically significant disadvantage of lecanemab in the endpoint of infusion-related reactions. For the endpoint of urinary tract infections, there was a statistically significant advantage of lecanemab.

Overall assessment

Data from the CLARITY AD study are available for the benefit assessment of lecanemab for the treatment of adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who

are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology. This is a double-blind, randomised study comparing lecanemab with placebo over a treatment period of 18 months, if applicable in addition to continued treatment with symptomatic antidementia drugs.

To assess the additional benefit of lecanemab for patient population b, data based on a study sub-population are used to enable a comparison of lecanemab versus donepezil or galantamine or rivastigmine.

With regard to mortality, there were no statistically significant differences between the treatment arms.

In the morbidity endpoint category, based on the responder analyses for the endpoints of symptoms using CDR-SB, cognition using ADAS-Cog14 and health status using EQ-5D VAS, there was no statistically significant difference between the treatment arms.

For the endpoint category of health-related quality of life, there was no statistically significant difference between the treatment arms in the evaluations based on QOL-AD.

In the endpoint category of side effects, there was no statistically significant difference between the treatment arms in the overall rates of serious adverse events and therapy discontinuation due to adverse events.
In detail, there was a statistically significant disadvantage of lecanemab in the endpoints of symptomatic ARIA events and infusion-related reactions. For the endpoint of urinary tract infections, there was a statistically significant advantage of lecanemab.
Overall, no relevant differences for the benefit assessment were derived in the category of side effects.

In the overall assessment, based on the CLARITY AD study, no relevant differences for the benefit assessment were identified for the patient sub-population b in the endpoint categories of mortality, morbidity, health-related quality of life and side effects. An additional benefit of lecanemab for the treatment of adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology is therefore not proven.

2.1.4 Summary of the assessment

The present benefit assessment refers to the medicinal product Leqembi with the active ingredient lecanemab for use in the following therapeutic indication:

"Leqembi 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 Alzheimer's disease) who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology."

The following patient populations were distinguished for the benefit assessment:

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

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

Patient population a)

Best supportive care was determined as the appropriate comparator therapy for lecanemab.

Data from a study sub-population of the double-blind, randomised CLARITY AD study, which allows a comparison of lecanemab versus best supportive care over a treatment period of 18 months, are used for the assessment of the additional benefit in this patient population.

With regard to mortality, there was no relevant difference for the benefit assessment between the treatment arms.

In the morbidity endpoint category, based on the responder analyses for the endpoints of symptoms using CDR-SB, cognition using ADAS-Cog14 and health status using EQ-5D VAS, there was no statistically significant difference between the treatment arms.

For the endpoint category of health-related quality of life, there was no statistically significant difference between the treatment arms, based on QOL-AD.

In the endpoint category of side effects, there was no statistically significant difference between the treatment arms in the overall rates of serious adverse events and therapy discontinuation due to adverse events.
In detail, there was a statistically significant disadvantage of lecanemab in the endpoints of symptomatic ARIA events and infusion-related reactions.
Overall, no relevant differences for the benefit assessment were derived in the category of side effects.

In the overall assessment, based on the CLARITY AD study, no relevant differences for the benefit assessment were identified for the patient sub-population a in the endpoint categories of mortality, morbidity, health-related quality of life and side effects. An additional benefit of lecanemab for the treatment of adults with a clinical diagnosis of mild cognitive impairment due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology is therefore not proven.

Patient population b)

Donepezil, galantamine or rivastigmine were determined to be the appropriate comparator therapy for lecanemab.

Data from a study sub-population of the double-blind, randomised CLARITY AD study, which compares lecanemab with donepezil, galantamine or rivastigmine over a treatment period of 18 months, are used for the assessment of the additional benefit in this patient population.

With regard to mortality, there was no relevant difference for the benefit assessment.

In the morbidity endpoint category, based on the responder analyses for the endpoints of symptoms using CDR-SB, cognition using ADAS-Cog14 and health status using EQ-5D VAS, there was no statistically significant difference between the treatment arms.

For the endpoint category of health-related quality of life, there was no statistically significant difference between the treatment arms, based on QOL-AD.

In the endpoint category of side effects, there was no statistically significant difference between the treatment arms in the overall rates of serious adverse events and therapy discontinuation due to adverse events.
In detail, there was a statistically significant disadvantage of lecanemab in the endpoints of symptomatic ARIA events and infusion-related reactions. For the endpoint of urinary tract infections, there was a statistically significant advantage of lecanemab.

Overall, no relevant differences for the benefit assessment were derived in the category of side effects.

In the overall assessment, based on the CLARITY AD study, no relevant differences for the benefit assessment were identified for the patient sub-population b in the endpoint categories of mortality, morbidity, health-related quality of life and side effects. An additional benefit of lecanemab for the treatment of adults with a clinical diagnosis of mild dementia due to Alzheimer's disease who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology is therefore not proven.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The number of patients is based on the target population in statutory health insurance (SHI).

The information provided by the pharmaceutical company in the benefit assessment dossier on lecanemab has limitations, particularly with regard to the estimation of dementia prevalence based on a literature-based derivation approach as well as limitations beyond the therapeutic indication with regard to available treatment capacities and patient preferences/ doctor decisions. Overall, the dossier information on lecanemab is an underestimation.

This resolution is based on information from dossier assessment A25-134[3] on donanemab, which is based on a calculation by the IQWiG and on information provided in the benefit assessment dossier on donanemab.

These are based, among other things, on a prevalence estimate based on a routine SHI data analysis and on a restriction to ApoE ε4 non-carriers and heterozygotes in accordance with the marketing authorisation. In the dossier on donanemab, further steps were taken to determine the percentage of patients who are eligible for treatment with donanemab using Appropriate Use Criteria (AUC) or Appropriate Use Recommendations (AUR) based on the inclusion and exclusion criteria of approval studies for lecanemab and aducanumab. According to the explanations made by the pharmaceutical company, this takes into account, among other things, comorbidities and monitoring guidelines for adverse events (AEs), e.g. ARIA. Overall, this step leads to a restriction of the target population that does not result from the approved therapeutic indication.

The information used in the resolution is based on the derivation of the figures in the dossier on donanemab and is obtained without taking the limitation to AUC or AUR into account.
The resulting data represent the best approximation of the SHI target population to date, particularly due to the more appropriate estimation of dementia prevalence compared to the lecanemab procedure. It should be noted that a smaller number of patients can be expected, taking into account contraindications, e.g. treatment with anticoagulants, as well as other requirements (e.g. prior registration in the Controlled Access Programme [CAP]). Limitations in the derivation also arise, among other things, in relation to determining the percentage of patients with dementia due to Alzheimer's disease.

Overall, the information is subject to uncertainty.

[3] https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1278/#nutzenbewertung

2.3 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 Leqembi (active ingredient: lecanemab) at the following publicly accessible link (last access: 5 January 2026):

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

Treatment with lecanemab 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 have timely access to Magnetic Resonance Imaging (MRI) diagnostics.

Prior to initiating treatment with lecanemab, testing for ApoE ε4 status must be performed and the presence of amyloid beta (Aβ) pathology must be confirmed using an appropriate test.

During treatment with lecanemab, cognitive function should be reviewed and clinical symptoms assessed approximately every 6 months.
Treatment with lecanemab should be discontinued as soon as the patient has progressed to moderate Alzheimer's disease.
In accordance with Annex III No. 10a of the Pharmaceuticals Directive, the prevention of progression to moderate Alzheimer's disease must therefore be reviewed every 6 months for the continued prescription of lecanemab. The type, duration and outcome of the use of lecanemab must be documented.

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

Prior to initiating treatment with lecanemab, a current (no older than 6 months) baseline brain MRI should be obtained to assess for pre-existing ARIA. Furthermore, an MRI scan must be performed before the 3rd, 5th, 7th and 14th infusion. A clinical assessment, including MRI, should be performed if a patient develops symptoms indicative of ARIA at any time during treatment.

Treatment with lecanemab should not be initiated in patients receiving ongoing therapy with anticoagulants.

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 card.
The training material contains, in particular, information on the above-mentioned requirements for treatment with lecanemab and warnings about the risks of ARIA.

Treatment should be initiated for all patients via a mandatory central registration system as part of a Controlled Access Programme (CAP).

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 December 2025). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is different from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or co-morbidities) are not taken into account when calculating the annual treatment costs.

The treatment costs for best supportive care are different from patient to patient. Because best supportive care has been determined as the appropriate comparator therapy for patient group a), this is also reflected in the medicinal product to be assessed. The type and scope of best supportive care can vary depending on the medicinal product to be assessed and the comparator therapy.

Treatment period:

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

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Lecanemab	Continuously, 1 x every 14 days	26.1	1	26.1
Best supportive care	Different from patient to patient			
Appropriate comparator therapy				
Best supportive care	Different from patient to patient			

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

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Lecanemab	Continuously, 1 x every 14 days	26.1	1	26.1
Appropriate comparator therapy				
Donepezil or galantamine or rivastigmine				
Donepezil	Continuously, 1 x daily	365.0	1	365.0
Galantamine	Continuously, 1 x daily	365.0	1	365.0
Rivastigmine	Continuously, 2 x daily	365.0	1	365.0

Consumption:

As it is not always possible to achieve the exact calculated dose per day with the commercially available dosage strengths, in these cases rounding up or down to the next higher or lower available dose that can be achieved with the commercially available dose potencies as well as the scalability of the respective dosage form.

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were used as a basis (average body weight 77.7 kg)[4].

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Lecanemab	10 mg/kg BW 777 mg	777 mg	2 x 500 mg	26.1	52.2 x 500 mg

[4] Federal health reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Best supportive care	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				

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

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Lecanemab	10 mg/kg BW = 777 mg	777 mg	2 x 500 mg	26.1	52.2 x 500 mg
Appropriate comparator therapy					
Donepezil or galantamine or rivastigmine					
Donepezil	5 mg – 10 mg	5 mg – 10 mg	1 x 5 mg – 1 x 10 mg	365.0	365 x 5 mg – 365 x 10 mg
Galantamine	16 mg – 24 mg	16 mg – 24 mg	1 x 16 mg – 1 x 24 mg	365.0	365 x 16 mg – 365 x 24 mg
Rivastigmine	3 mg – 6 mg	6 mg – 12 mg	2 x 3 mg – 2 x 6 mg	365.0	730 x 3 mg – 730 x 6 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

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

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

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Lecanemab 500 mg	1 CII	€ 788.86	€ 1.77	€ 43.05	€ 744.04
Appropriate comparator therapy					
Donepezil 5 mg	98 FCT	€ 63.17	€ 1.77	€ 4.10	€ 57.30
Donepezil 10 mg	98 FCT	€ 66.26	€ 1.77	€ 4.35	€ 60.14
Galantamine 16 mg	84 SRC	€ 57.72	€ 1.77	€ 3.67	€ 52.28
Galantamine 24 mg	84 SRC	€ 59.02	€ 1.77	€ 3.77	€ 53.48
Rivastigmine 3 mg	112 HC	€ 69.90	€ 1.77	€ 4.63	€ 63.50
Rivastigmine 6 mg	112 HC	€ 73.02	€ 1.77	€ 4.88	€ 66.37
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CII = concentrate for injection or infusion solution; SRC = sustained-release hard capsules					

LAUER-TAXE® last revised: 15 December 2025

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

The calculation of the additionally required SHI services is based on the fee structure items (FSI) as of the 3rd quarter of 2025 of the uniform value scale (UVS 2025/Q3).

Prior to treatment and before the 3rd, 5th, 7th and 14th infusion, magnetic resonance imaging (MRI) examinations must be performed in accordance with the product information. In addition, an additional MRI examination should be performed if a patient develops symptoms indicative of ARIA.

Designation of the therapy	Designation of the service	Number	Costs per unit	Costs per patient per year
Lecanemab	MRI examination of the neurocranium (FSI 34410)	5	€ 130.50	€ 652.50

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

2.5 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

According to Section 35a, paragraph 3, sentence 4, the G-BA designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c,

sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from

a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA have decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

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.

Justification for the findings on designation in the present resolution:

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

References:
Product information for lecanemab (Leqembi); LEQEMBI® 100 mg/ml; last revised: September 2025

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

No medicinal product with new active ingredients that can be used in a combination therapy, for which the requirements of Section 35a, paragraph 3, sentence 4 SGB V are fulfilled.

References:
Product information for lecanemab (Leqembi); LEQEMBI® 100 mg/ml; last revised: September 2025

2.6 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 Leqembi is a medicinal product placed on the market from 1 January 2025. In accordance with Section 35a, paragraph 3, sentence 5 SGB V, the G-BA must determine whether a relevant percentage of the clinical studies on the medicinal product were conducted within the scope of SGB V. This is the case if the percentage of study participants who have participated in the clinical studies on the medicinal product to be

assessed in the therapeutic indication to be assessed at study sites within the scope of SGB V is at least five per cent of the total number of study participants.

The calculation is based on all studies that were submitted as part of the benefit assessment dossier in the therapeutic indication to be assessed in accordance with Section 35a, paragraph 1, sentence 3 SGB V in conjunction with Section 4, paragraph 6 AM-NutzenV.

Approval studies include all studies submitted to the regulatory authority in section 2.7.3 (Summary of Clinical Efficacy) and 2.7.4 (Summary of Clinical Safety) of the authorisation dossier in the therapeutic indication for which marketing authorisation has been applied for. In addition, studies, which were conducted in whole or in part within the therapeutic indication described in this document, and in which the company was a sponsor or is otherwise financially involved, must also be indicated.

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% (0.96%) of the total number of study participants according to the information provided by the pharmaceutical company.

In the dossier, the pharmaceutical company provided information on a total of 8 studies in the present therapeutic indication, with a total percentage of 0.96% study participants at German study sites.

In relation to one of the studies (BAN2401-G000-303 study), there are uncertainties regarding the information on the number of study participants across all study sites based on an estimate. Furthermore, it is unclear whether recruitment for this study has already been completed.

Regardless of whether the BAN2401-G000-303 study is taken into account, the percentage of study participants at study sites within the scope of SGB V is less than 5%.

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

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At their session on 24 January 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. The Subcommittee on Medicinal Products newly determined the appropriate comparator therapy at their session on 6 May 2025.

On 26 August 2025, the pharmaceutical company submitted a dossier for the benefit assessment of lecanemab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 26 August 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient lecanemab.

The dossier assessment by the IQWiG was submitted to the G-BA on 27 November 2025, and the written statement procedure was initiated with publication on the G-BA website on 1 December 2025. The deadline for submitting written statements was 22 December 2025.

The oral hearing was held on 12 January 2026.

By letter dated 13 January 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 30 January 2026.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the subcommittee session on 10 February 2026, and the draft resolution was approved.

At their session on 19 February 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	24 January 2023	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	6 May 2025	New determination of the appropriate comparator therapy
Working group Section 35a	6 January 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	12 January 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	20 January 2026 3 February 2026	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	10 February 2026	Concluding discussion of the draft resolution
Plenum	19 February 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 19 February 2026

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

Prof. Hecken