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
Atogepant (prophylaxis of migraine)

of 21 August 2025

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 decides 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 atogepant on 1 March 2025 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 1 VerfO on 26 February 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 June 2025 on the G-BA website (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 atogepant 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. 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 atogepant.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have come to 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 Atogepant (Aquipta) in accordance with the product information

AQUIPTA is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month.

Therapeutic indication of the resolution (resolution of 21.08.2025):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics

Appropriate comparator therapy for atogepant

- Amitriptyline or Clostridium botulinum toxin type A (only suitable for chronic migraine) or erenumab or flunarizine (only suitable if treatment with beta-receptor blockers is contraindicated or has not shown sufficient effect) or metoprolol or propranolol

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

b) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol)

Appropriate comparator therapy for atogepant:

- Eptinezumab or erenumab or fremanezumab or galcanezumab

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 it determines 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 addition to atogepant, the active ingredients amitriptyline, metoprolol, propranolol and topiramate, the calcitonin gene-related peptide (CGRP) and/or CGRP receptor antibodies eptinezumab, erenumab, fremanezumab and galcanezumab as well as the CGRP receptor antagonist rimegepant are approved for the present therapeutic indication. In addition, the active ingredient flunarizine is approved for prophylaxis of migraine if treatment with beta-receptor blockers is contraindicated or has not shown sufficient effect. Clostridium botulinum toxin type A is indicated for patients with chronic migraine who have had an inadequate response or were intolerant to prophylactic migraine medication.

On 2. In the context of statutory health insurance, a non-medicinal treatment within the patient group defined by the therapeutic indication is not considered as an appropriate comparator therapy.

On 3. Resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available for erenumab (resolution of 2 May 2019), galcanezumab (resolution of 19 September 2019), fremanezumab (resolution of 7 November 2019) and eptinezumab (resolution of 16 February 2023). In addition, there is a resolution on the reassessment of erenumab due to new scientific knowledge (resolution of 21 October 2021).
For valproic acid, there are resolutions from 20 March 2020 and 18 August 2022 regarding prophylaxis of migraine in adulthood (see Annex VI to Section K of the Pharmaceuticals Directive - Prescribability of approved medicinal products in non-approved therapeutic indications).

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 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.

Overall, it is to be noted that the robust evidence on therapeutic options in the present therapeutic indication is limited and no general superiority of one of the active ingredients mentioned can be deduced. Therefore, of the medicinal therapy options approved in Germany, no active ingredient can be explicitly emphasised as a therapeutic standard in prophylaxis of migraine.

On the basis of the aggregated evidence, different treatment situations are to be distinguished in prophylaxis of migraine, so that different patient populations are to be considered taking into account the present therapy recommendations.

Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics

Patient population a includes untreated and pretreated adults who are generally eligible for conventional migraine prophylactics. The following therapy options can be subsumed under the term conventional prophylaxis of migraine: Amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol, topiramate and valproic acid. Valproic acid does not have a marketing authorisation for use as a migraine prophylactic, but is listed for prophylaxis of migraine in adulthood in Part A of Annex VI to Section K of the Pharmaceuticals Directive. No prescribable medicinal products containing valproic acid are available for prophylaxis of migraine in the German healthcare context due to the current absence of any declaration from pharmaceutical companies on the recognition of the intended use (liability of the pharmaceutical company). Against this background, valproic acid cannot be considered as an appropriate comparator therapy.

A Direct Healthcare Professional Communication ("Rote-Hand-Brief") dated 2 November 2023, which provides information on further known safety risks associated with the use of topiramate during pregnancy in addition to its known teratogenic potential, is available for the active ingredient topiramate. Against this background, particular caution is required when treating women of reproductive age. In the overall assessment, and particularly in view of the fact that women of reproductive age make up a significant percentage of the target population in the present therapeutic indication, topiramate cannot be considered equally appropriate compared to the other available therapy options.
According to the marketing authorisation, the active ingredient flunarizine is only to be used if treatment with beta-receptor blockers is contraindicated or has not shown sufficient effect. Clostridium botulinum toxin type A is only approved for chronic migraine. However, not all patients are as a rule eligible for the active ingredient even if they have chronic migraine.
By resolution of 20 May 2021, the G-BA carried out a new benefit assessment for the active ingredient erenumab, based on an application due to new scientific knowledge in accordance with Section 14 VerfO. For patient group a, erenumab was able to give a hint for a considerable additional benefit compared to topiramate. Therefore, erenumab is also considered an equally appropriate therapy option for this patient population.

In the overall assessment, amitriptyline or Clostridium botulinum toxin type A or erenumab or flunarizine or metoprolol or propranolol (taking into account the respective marketing authorisations) is determined as the appropriate comparator therapy for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics.

The appropriate comparator therapy determined here includes several therapy options. In this context, individual therapy options only represent a comparator therapy for the part of the patient population that has the patient and disease characteristics specified in brackets. The therapeutic alternatives are only to be considered equally appropriate in the therapeutic indication, where the patient populations have the same characteristics.
Any therapy option that is not restricted by the bracketed patient and disease characteristics can be used for demonstrating the additional benefit for the total population. If the appropriate comparator therapy comprises several therapy option alternatives without any restriction, the additional benefit for the total population can be demonstrated in comparison with one of these therapeutic alternatives.

In contrast, the sole comparison with a therapy option that only represents a comparator therapy for part of the patient population is generally insufficient to demonstrate the additional benefit for the total population.

Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol)

Patient population b includes adults who have at least 4 migraine days per month and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol). With the antibodies eptinezumab, erenumab, fremanezumab and galcanezumab, further medicinal products have been approved in the present therapeutic indication in recent years. Within the scope of the benefit assessment according to Section 35a SGB V, a hint for a considerable additional benefit of erenumab, galcanezumab and fremanezumab compared to best supportive care was derived for patient population b. In addition, the antibodies are considered to be established in healthcare in the present treatment setting. Eptinezumab is the latest of the available CGRP (receptor) antibodies. An additional benefit thereof compared to fremanezumab for patient population b could not be proven in the benefit assessment according to Section 35a SGB V by resolution of 16 February 2023. However, based on the available evidence, including the guideline recommendations and taking into account the explanations in the written statements of the scientific-medical societies on the reality of care, eptinezumab is considered equally appropriate compared to the other CGRP (receptor) antibodies for the patient group b and thus, considered as the therapy standard for this patient population.
Rimegepant, which is also approved for prophylaxis of migraine, has only recently become available in Germany (1 June 2025). At the time of adoption of this resolution, benefit assessment in accordance with Section 35a SGB V is not yet available for this active ingredient. On the basis of the generally recognised state of medical knowledge and against the background of its currently only minor significance in healthcare, rimegepant is not determined as the appropriate comparator therapy in the present case.

In the overall assessment, a therapy with eptinezumab, erenumab, fremanezumab or galcanezumab is determined as the appropriate comparator therapy for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol).

The appropriate comparator therapy determined here includes several therapy options. These therapeutic alternatives are equally appropriate for the comparator therapy. The additional benefit can be demonstrated compared to one of the therapeutic alternatives mentioned.

Change in the appropriate comparator therapy for patient group b

To date, the CGRP (receptor) antibodies erenumab or fremanezumab or galcanezumab have been considered as the appropriate comparator therapy for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol).

The additional benefit of eptinezumab compared to the appropriate comparator therapy was not proven in the benefit assessment according to Section 35a SGB V by resolution of 16 February 2023.

However, according to the available evidence, including the guideline recommendations and taking into account the explanations in the written statements of the scientific-medical societies on the reality of care, all CGRP (receptor) antibodies approved in Germany assume comparable significance as prophylaxis of migraine for the patient group b and represent the therapy standard for this patient population. Against this background, eptinezumab is considered equally appropriate compared to the other CGRP (receptor) antibodies for the patient population b.

The G-BA therefore considers it appropriate to change the appropriate comparator therapy at this point in time and to adapt it to the current state of medical knowledge. Accordingly, eptinezumab or erenumab or fremanezumab or galcanezumab is determined as the appropriate comparator therapy for patient group b.

The change in the appropriate comparator therapy has no impact on the present benefit assessment.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

a) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics

The additional benefit is not proven for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics.

Justification:

The pharmaceutical company did not present data for the assessment of the additional benefit of atogepant compared to the appropriate comparator therapy for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics.

b) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal

therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol)

The additional benefit is not proven for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol).

Justification:

The pharmaceutical company submitted adjusted indirect comparisons for the assessment of atogepant versus erenumab or fremanezumab via the bridge comparator placebo for the patient population to be assessed. The results of the ADVANCE, ELEVATE and PROGRESS studies were used for this purpose on the intervention side, while the LIBERTY (erenumab) and FOCUS (fremanezumab) studies were used on the comparator side.

The ADVANCE, ELEVATE and PROGRESS studies are double-blind, randomised, controlled studies comparing atogepant with placebo. Adults with episodic migraine were enrolled in the ADVANCE and ELEVATE studies, while adults with chronic migraine were enrolled in the PROGRESS study. The studies each comprise a 4-week screening phase, a 12-week double-blind, placebo-controlled treatment phase and a 4-week follow-up phase. Migraine days/month was collected as the primary endpoint of all three studies, operationalised as the change in the number of monthly migraine days over 12 weeks compared to baseline.

The LIBERTY and FOCUS studies are double-blind, randomised, controlled studies comparing erenumab and fremanezumab respectively with placebo. Both studies were already the subject of the benefit assessments of erenumab and fremanezumab respectively. Adults with episodic migraine were enrolled in the LIBERTY study, while adults with chronic or episodic migraine were enrolled in the FOCUS study. The duration of the controlled treatment phases in the studies was 12 weeks in each case.
Migraine days/month was collected as the primary endpoint of the studies, operationalised as reduction in migraine days/month by ≥ 50% at week 12 (LIBERTY) or as a change in the average monthly migraine days compared to baseline (FOCUS).

For all studies, the pharmaceutical company submitted evaluations for study sub-populations, which are relevant according to patient population b and include patients, who previously did not respond, were intolerant to at least two of the following active ingredients, or these were contraindicated: Beta-blockers (metoprolol/ propranolol), flunarizine, topiramate, amitriptyline or valproic acid (valproic acid not applicable to the FOCUS study; Clostridium botulinum toxin type A only for the PROGRESS study). Overall, data from 216 patients treated with atogepant and 202 patients treated with placebo were included in the indirect comparison on the intervention side, and data from 86 patients treated with erenumab, 388 patients treated with fremanezumab and 299 patients treated with placebo were included on the comparator side.
These study sub-populations presented by the pharmaceutical company are relevant for the present research question for patient group b and are accordingly used for the benefit assessment.

On the indirect comparison
The ELEVATE, ADVANCE, PROGRESS, LIBERTY and FOCUS studies presented are based on a similar study design. The patient populations of the studies show differences with regard to the underlying disease characteristic of migraine type (episodic or chronic migraine) and associated characteristics (e.g. with regard to the monthly migraine days at baseline and with

regard to the percentage of patients with medication overuse). Overall, these differences however do not call into question the sufficient similarity of the studies and thus, the performance of an indirect comparison via the placebo bridge comparator, taking into account all 5 studies.

In the dossier, the pharmaceutical company used separate indirect comparisons of atogepant versus erenumab and atogepant versus fremanezumab as the main analyses for the assessment. In deviation from this approach, analyses on the indirect comparison of atogepant versus erenumab or fremanezumab, taking into account all 5 studies on episodic and/or chronic migraine, are primarily considered relevant for the present assessment.

With regard to the methodology for conducting the adjusted indirect comparison, a fixed-effects model using the inverse variance method was selected for the meta-analytic summary of the study results on the intervention and comparator sides. In view of the aforementioned differences with regard to the underlying disease characteristic of migraine type (episodic or chronic migraine) and other associated disease characteristics in the study sub-populations used, the performance of the indirect comparison with a method that takes random effects into account is considered adequate in the present case. However, the pharmaceutical company's approach in the present data basis has no consequences for the conclusion of the benefit assessment since the indirect comparison analyses presented by the pharmaceutical company did not show a statistically significant and relevant effect for any of the endpoints, even when using a fixed-effects model (see below).

Extent and probability of the additional benefit

Mortality

In the ELEVATE, ADVANCE and PROGRESS studies on the intervention side and the LIBERTY and FOCUS studies on the comparator side, no deaths occurred in the relevant sub-populations for the benefit assessment in each case.

Morbidity

Symptomatology (migraine days per month)

The information was recorded daily by the patients in all 5 studies in their electronic patient diary. Given the symptom burden of the patients in the studies, reduction in migraine days/month by ≥ 50% is an appropriate response criterion, regardless of whether episodic migraine or chronic migraine is present.

No evaluations across all 5 studies are possible for the reduction of migraine days/month by ≥ 75% or 100%, as only evaluations for different operationalisations are available for the two studies on the comparator side.

The reduction in migraine days/month by ≥ 50% in month 3 compared to baseline is therefore used to derive the additional benefit. The continuous evaluations of the change in migraine days/month in month 3 compared to baseline are presented additionally.

In the written statement procedure, the pharmaceutical company subsequently submitted evaluations of migraine days/month for the PROGRESS study and for the ADVANCE study (responder analyses with non-responder imputations), including the indirect comparison based on these evaluations.

Overall, the adjusted indirect comparison of atogepant versus erenumab or fremanezumab showed no statistically significant and relevant differences for the reduction in migraine days/month by ≥ 50% in month 3 compared to baseline.

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

In the studies, health status was assessed in a patient-reported manner using the visual analogue scale (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.

For the endpoint of health status, assessed using EQ-5D VAS, the adjusted indirect comparison of atogepant versus erenumab or fremanezumab showed no statistically significant difference.

Quality of life

Migraine-Specific Quality of Life Questionnaire (MSQoL)

There are evaluations of the MSQoL, which measures the influence of migraine on health-related quality of life within the past 4 weeks and is made up of three domains: Role Function-Restrictive, Role Function-Preventive and Emotional Function. Higher values indicate a better health-related quality of life. This endpoint was not assessed in the LIBERTY study.

In the Role Function-Restrictive and Role Function-Preventive domains, the adjusted indirect comparison showed statistically significant differences in favour of atogepant in each case. However, the respective 95% confidence interval of the standardised mean differences (SMD) is not completely outside the irrelevance range between −0.2 and 0.2. Thus, it cannot be inferred with sufficient certainty that the effects are clinically relevant.

The adjusted indirect comparison showed no statistically significant difference for the Emotional Function domain.

General impairment due to headache (HIT-6)

For health-related quality of life, evaluations based on the HIT-6 are also available. This is a validated instrument to assess headache-related impairment over the past month. The manifestation of the impairment due to headache is assessed on a Likert scale; depending on the answer, the questions are weighted and a total score is calculated, which can range from 36 to 78. Higher values correspond to more pronounced impairment due to headache.

For the endpoint of general impairment due to headache (HIT-6), assessed using EQ-5D VAS, the adjusted indirect comparison of atogepant versus erenumab or fremanezumab showed a statistically significant difference in favour of atogepant. However, the 95% confidence interval of the standardised mean difference (SMD) is not completely outside the irrelevance range between −0.2 and 0.2. Thus, it cannot be inferred with sufficient certainty that the effect is clinically relevant.

Side effects

SAEs and discontinuation due to AEs

For the endpoints of SAEs and discontinuation due to AEs, the adjusted indirect comparison of atogepant versus erenumab or fremanezumab showed no statistically significant difference.

Overall assessment

For prophylaxis of migraine in adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol), the results of the adjusted indirect comparison of atogepant versus erenumab or fremanezumab via the placebo bridge comparator based on the ADVANCE, ELEVATE and PROGRESS studies (each comparing atogepant vs placebo) as well as LIBERTY and FOCUS studies (comparison of erenumab or fremanezumab vs placebo) are available for the benefit assessment of atogepant.
The adjusted indirect comparison is used for the benefit assessment despite methodological limitations with regard to the meta-analytic summary of the studies on the intervention and comparator sides and with regard to the similarity of the studies in terms of the course of migraine (chronic vs episodic).

In terms of mortality, no deaths occurred in any of the 5 studies used for the indirect comparison.

In the endpoint category morbidity, the adjusted indirect comparison of atogepant versus erenumab or fremanezumab showed no statistically significant differences for the endpoints of reduction in migraine days/month by ≥ 50% in month 3 compared to baseline as well as health status using the visual analogue scale of the EQ-5D.

With regard to health-related quality of life, there was a statistically significant difference in favour of atogepant compared to erenumab or fremanezumab for Role Function-Restrictive and Role Function-Preventive, each assessed using MSQoL, as well as for the endpoint of general impairment due to headache, assessed using HIT-6. Based on the standardised mean differences (SMD), it cannot nevertheless be concluded with sufficient certainty that the effects are clinically relevant. In contrast, there was no statistically significant difference for the Emotional Function domain of the MSQoL.

In the category of side effects, there were no statistically significant differences in the adjusted indirect comparison of atogepant versus erenumab or fremanezumab.

In the overall assessment, the adjusted indirect comparison of atogepant versus erenumab or fremanezumab did not show any relevant differences for the benefit assessment for the endpoint categories of morbidity, health-related quality of life and side effects.

An additional benefit of atogepant is therefore not proven for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol).

2.1.4 Summary of the assessment

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

"Aquipta is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month."

The following patient populations were distinguished for the benefit assessment:

a) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics

b) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol)

Patient population a)

Therapy with amitriptyline or Clostridium botulinum toxin type A (only suitable for chronic migraine) or erenumab or flunarizine (only suitable if treatment with beta-receptor blockers is contraindicated or has not shown sufficient effect) or metoprolol or propranolol was determined as the appropriate comparator therapy.

The pharmaceutical company did not present any data for the assessment of the additional benefit in this patient population. Thus, an additional benefit of atogepant compared with the appropriate comparator therapy is not proven for adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics.

Patient population b)

Therapy with eptinezumab or erenumab or fremanezumab or galcanezumab was determined as the appropriate comparator therapy.

An adjusted indirect comparison of atogepant vs erenumab or fremanezumab via the bridge comparator placebo on the basis of 5 studies was used for the assessment of the additional benefit.
With regard to mortality, no deaths occurred in the studies.
In the morbidity category, there were no relevant differences for the benefit assessment based on the endpoints of reduction in migraine days/month by ≥ 50% in month 3 compared to baseline as well as health status using the visual analogue scale of the EQ-5D.
In terms of the quality of life, there was a statistically significant difference in favour of atogepant compared to erenumab or fremanezumab for Role Function-Restrictive and Role Function-Preventive, each assessed using MSQoL, as well as for the endpoint of general impairment due to headache, assessed using HIT-6. Based on the standardised mean differences (SMD), it cannot nevertheless be concluded with sufficient certainty that the effects are clinically relevant. There was no statistically significant difference for the Emotional Function domain of the MSQoL.
For the side effects category, no relevant differences for the benefit assessment can be derived.

The overall assessment does not show any relevant differences for the benefit assessment between atogepant and erenumab or fremanezumab. An additional benefit 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 resolution is based on the information presented by the pharmaceutical company in the dossier.

This is based, among other things, on the estimate of the number of migraine patients among those with statutory health insurance based on routine data analyses by the Institute for Applied Health Research (InGef) and the Techniker Krankenkasse. In further steps, an analysis of SHI routine data based on the German Analysis Database for Evaluation and Healthcare Research (DADB) is used to determine the percentage of patients who have at least 4 migraine days per month and the number of patients with different prescription patterns with regard to conventional migraine prophylactics or CGRP (receptor) antibodies for the purpose of demarcation of patient populations a and b.

Overall, the information provided by the pharmaceutical company is subject to uncertainties. These result, among other things, from a potentially deviating prevalence of migraine and uncertainties regarding the percentages used for patients with at least 4 migraine days per month as well as limitations regarding one of the prescription patterns used to determine the percentages for the patient population b.

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 Aquipta (active ingredient: atogepant) at the following publicly accessible link (last access: 1 July 2025):

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

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: 1 August 2025).

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

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 varies 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 flunarizine, costs are shown for 6 months, as the product information limits the use of flunarizine for prophylaxis of migraine to a maximum of 6 months regardless of response. This does not prevent the resumption of flunarizine therapy at a later date.
The starting dose of 10 mg daily for those under 65 and 5 mg for those over 65 years of age should not be given for longer than is necessary for symptom relief (usually no longer than two months). Subsequently, the daily dose should be reduced to a maintenance dose by taking flunarizine either only every other day or for 5 consecutive days followed by two treatment-free days.
A range is shown for the treatment costs of flunarizine, taking into account the information provided. The lower limit of the range results from the lowest starting dose (5 mg once a day), combined with a maintenance dose every other day. The upper limit of the range is calculated

from the highest starting dose (10 mg once a day), taking into account the administration of the maintenance dose on 5 days, followed by two treatment-free days.
Only a treatment duration of 6 months is used for the calculation (therefore possible discarding because of using whole packs is taken into account in consumption). Notwithstanding this, the costs may be higher if treatment with flunarizine is started again at a later date.

a) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Atogepant	Continuously 1 x daily	365.0	1.0	365.0
Appropriate comparator therapy				
Amitriptyline or Clostridium botulinum toxin type A (only suitable for chronic migraine) or erenumab or flunarizine (only suitable if treatment with beta-receptor blockers is contraindicated or has not shown sufficient effect) or metoprolol or propranolol				
Amitriptyline	Continuously, 1 x daily	365	1.0	365.0
Clostridium botulinum toxin type A	Continuously, 1 x every 84 days	4.3	1.0	4.3
Erenumab	Continuously, 1 x every 28 days	13.0	1.0	13.0
Flunarizine	Up to 6 months	121.6 – 147.7	1.0	121.6 – 147.7
Metoprolol	Continuously, 1 - 2 x daily	365.0	1.0	365.0
Propranolol	Continuously, 2 - 3 x daily	365.0	1.0	365.0

Consumption:

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					
Atogepant	60 mg	60 mg	1 x 60 mg	365.0	365 x 60 mg
Appropriate comparator therapy					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Amitriptyline or Clostridium botulinum toxin type A (only suitable for chronic migraine) or erenumab or flunarizine (only suitable if treatment with beta-receptor blockers is contraindicated or has not shown sufficient effect) or metoprolol or propranolol					
Amitriptyline	25 mg – 75 mg	25 mg – 75 mg	1 x 25 mg – 1 x 75 mg	365.0	365 x 25 mg – 365 x 75 mg
Clostridium botulinum toxin type A	155 – 195 Units	155 - 195 units	1 x 200 Units	4.3	4.3 x 200 Units
Erenumab	70 mg – 140 mg	70 mg – 140 mg	1 x 70 mg – 1 x 140 mg	13.0	13 x 70 mg – 13 x 140 mg
Flunarizine	5 mg – 10 mg	5 mg – 10 mg	1 x 5 mg – 1 x 10 mg	121.6 – 147.7	121.6 x 5 mg – 147.7 x 10 mg
Metoprolol	100 mg – 200 mg	100 mg – 200 mg	1 x 100 mg – 1 x 200 mg	365.0	365 x 100 mg – 365 x 200 mg
Propranolol	40 mg	80 mg – 120 mg	2 x 40 mg – 3 x 40 mg	365.0	730 x 40 mg – 1095 x 40 mg

b) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol)

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Atogepant	Continuously, 1 x daily	365.0	1.0	365.0
Appropriate comparator therapy				
Eptinezumab or erenumab or fremanezumab or galcanezumab				
Eptinezumab	Continuously, 1 x every 84 days	4.3	1.0	4.3

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Erenumab	Continuously, 1 x every 28 days	13.0	1.0	13.0
Fremanezumab	Continuously, 1 x every 30.4 days or Continuously, 1 x every 91.2 days	12.0 or 4.0	1.0	12.0 or 4.0
Galcanezumab	Continuously, 1 x every 30.4 days	12.0	1.0	12.0

Consumption:

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					
Atogepant	60 mg	60 mg	1 x 60 mg	365.0	365 x 60 mg
Appropriate comparator therapy					
Eptinezumab or erenumab or fremanezumab or galcanezumab					
Eptinezumab	100 mg – 300 mg	100 mg – 300 mg	1 x 100 mg – 3 x 100 mg	4.3	4.3 x 100 mg – 12.9 x 100 mg
Erenumab	70 mg – 140 mg	70 mg – 140 mg	1 x 70 mg – 1 x 140 mg	13.0	13 x 70 mg – 13 x 140 mg
Fremanezumab	225 mg	225 mg	1 x 225 mg	12.0	12 x 225 mg
	or				
	675 mg	675 mg	3 x 225 mg	4.0	12 x 225 mg
Galcanezumab	120 mg	120 mg	1 x 120 mg	12.0	12 x 120 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:

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					
Atogepant 60 mg	98 TAB	€ 982.50	€ 1.77	€ 53.77	€ 926.96

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
Appropriate comparator therapy					
Amitriptyline 25 mg[2]	100 FCT	€ 18.60	€ 1.77	€ 0.58	€ 16.25
Amitriptyline 75 mg[2]	100 TAB	€ 29.74	€ 1.77	€ 1.46	€ 26.51
Clostridium botulinum toxin type A 200 units	1 PSI	€ 984.40	€ 1.77	€ 53.88	€ 928.75
Eptinezumab 100 mg	1 CIS	€ 768.39	€ 1.77	€ 41.92	€ 724.70
Erenumab 70 mg	3 SFI	€ 773.69	€ 1.77	€ 0.00	€ 771.92
Erenumab 140 mg	3 SFI	€ 773.69	€ 1.77	€ 0.00	€ 771.92
Flunarizine 5 mg[2]	100 HC	€ 32.82	€ 1.77	€ 1.70	€ 29.35
Flunarizine 5 mg[2]	50 HC	€ 22.69	€ 1.77	€ 0.90	€ 20.02
Flunarizine 10 mg[2]	100 HC	€ 52.66	€ 1.77	€ 3.27	€ 47.62
Flunarizine 10 mg[2]	50 HC	€ 33.40	€ 1.77	€ 1.75	€ 29.88
Fremanezumab 225 mg	3 PEN	€ 1,312.28	€ 1.77	€ 0.00	€ 1,310.51
Galcanezumab 120 mg	3 SFI	€ 1,465.38	€ 1.77	€ 80.51	€ 1,383.10
Metoprolol 100 mg[2]	100 TAB	€ 14.10	€ 1.77	€ 0.22	€ 12.11
Metoprolol 200 mg[2]	100 SRT	€ 19.50	€ 1.77	€ 0.65	€ 17.08
Propranolol 40 mg[2]	100 FCT	€ 19.49	€ 1.77	€ 0.65	€ 17.07
Abbreviations: FCT = film-coated tablets; HC = hard capsules; CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; PEN = solution for injection in a pre-filled pen; PSI = powder for solution for injection; SRT = sustained release tablet; TAB = tablet					

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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.

Because there are no 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, no costs for additionally required SHI services had to be taken into account.

[2] Fixed reimbursement rate

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 who have at least 4 migraine days per month with an indication for prophylaxis of migraine and are eligible for conventional migraine prophylactics

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 atogepant (Aquipta); AQUIPTA® 10 mg/60 mg tablets; last revised: May 2025

b) Adults who have at least 4 migraine days per month with an indication for prophylaxis of migraine and do not respond, are ineligible or intolerant to any of the medicinal therapies/ product classes (amitriptyline, Clostridium botulinum toxin type A, flunarizine, metoprolol, propranolol)

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 atogepant (Aquipta); AQUIPTA® 10 mg/60 mg tablets; last revised: May 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 Aquipta 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 the authorisation dossier for the assessment of the clinical efficacy and safety of the medicinal product in the therapeutic indication to be assessed.

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 (4.2%) of the total number of study participants.

As part of the written statement procedure, the pharmaceutical company updated the information on the number of study participants in authorisation-relevant studies on which the calculation is based. The updated calculation is considered plausible.

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 9 April 2024, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

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

By letter dated 1 March 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 atogepant.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 2 June 2025. The deadline for submitting statements was 23 June 2025.

The oral hearing was held on 7 July 2025.

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 session of the Subcommittee on 12 August 2025, and the proposed draft resolution was approved.

At their session on 21 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	9 April 2024	Determination of the appropriate comparator therapy
Working group Section 35a	2 July 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on	7 July 2025	Conduct of the oral hearing

Medicinal Products		
Working group Section 35a	15 July 2025 5 August 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	12 August 2025	Concluding discussion of the draft resolution
Plenum	21 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 21 August 2025

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

Prof. Hecken