Gemeinsamer Bundesausschuss

Resolution

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

of 21 August 2025

At their session on 21 August 2025, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

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

Atogepant

Resolution of: 21 August 2025
Entry into force on: 21 August 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 11 August 2023):

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 August 2025):

See therapeutic indication according to marketing authorisation.

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

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

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

An additional benefit is not proven.

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

Extent and probability of the additional benefit of atogepant compared to erenumab or fremanezumab:

An additional benefit is not proven.

Study results according to endpoints:[1]

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 data available.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.

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

b) Adults 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)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment.
Morbidity	↔	No relevant differences for the benefit assessment.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↔	No relevant differences for the benefit assessment.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A25-38) unless otherwise indicated.

∅: No data available. n.a.: not assessable

Indirect comparison:
Atogepant (ADVANCE, ELEVATE, PROGRESS studies) vs erenumab (LIBERTY study) or fremanezumab (FOCUS study) via the bridge comparator placebo

Mortality

Endpoint	Atogepant or erenumab or fremanezumab		Placebo		Group difference
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Overall mortality[a, b]					
Atogepant vs placebo					
ELEVATE	125	0 (0)	128	0 (0)	–
ADVANCE	27	0 (0)	18	0 (0)	–
PROGRESS	64	0 (0)	56	0 (0)	–
Total					–
Erenumab or fremanezumab vs placebo					
LIBERTY	86	0 (0)	104	0 (0)	–
FOCUS	388	0 (0)	195	0 (0)	–
Total					–
Indirect comparison via bridge comparators					
Atogepant vs erenumab or fremanezumab					–

Morbidity

Endpoint	Atogepant or erenumab or fremanezumab		Placebo		Group difference
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Migraine days per month - reduction by ≥ 50% compared to baseline in month 3					
Atogepant vs placebo					
ELEVATE	123	67 (54.4)	127	39 (30.7)	1.77 [1.30; 2.41]; < 0.001
ADVANCE	26[c]	16 (61.5)[c]	17[c]	4 (23.5)[c]	2.62 [1.05; 6.49]; 0.0275[c]
PROGRESS	63[c]	26 (41.3)[c]	54[c]	14 (25.9)[c]	1.59

					[0.93; 2.73]; 0.1174[c]
Total					1.79 [1.38; 2.31]; <0.0001[c,d]
Erenumab or fremanezumab vs placebo					
LIBERTY	86	26 (30.2)	104	14 (13.5)	2.25 [1.25; 4.03]; 0.005
FOCUS	387	152 (39.3)	195	33 (17)	2.32 [1.66; 3.24]; < 0.001
Total					2.30 [1.72; 3.08]; <0.0001[c,d]
<u>Indirect comparison via bridge comparators</u>					
Atogepant vs erenumab or fremanezumab					0.78 [0.53; 1.14]; 0.1971[c]

Endpoint	Atogepant or erenumab or fremanezumab			Placebo			Group difference
	N	Values at the start of the study MV (SD)	Change in month 3 or week 12 MV (SE)	N	Values at the start of the study MV (SD)	Change in month 3 or week 12 MV (SE)	MD [95% CI]; p value SMD [95% CI]
Migraine days/month - change compared to baseline in month 3 (presented additionally)							
Atogepant vs placebo							
ELEVATE	123	8.9 (2.4)	-4.1 (0.4)	127	9.5 (2.3)	-2.3 (0.4)	-1.80 [-2.91; 0.69]; 0.002
ADVANCE	26	8.5 (2.5)	-4.2 (0.9)	17	7.9 (2.0)	-1.1 (1.1)	-3.11 [-5.91; -0.31]; 0.030
PROGRESS	63[c]	20.5 (5.8)[c]	-6.8 (0.9)[c]	54[c]	19.2 (5.2)[c]	-5.3 (1.0[c]	-1.48 [-4.11; 1.15]; 0.2692[c]
Total							-1.91 [-2.87; -0.95]; < 0.0001[c,d]
Erenumab or fremanezumab vs placebo							
LIBERTY	86	9.1 (2.3)	-1.6 (0.5)	104	9.1 (2.5)	-0.1 (0.4)	-1.51 [-2.73; -0.28]; 0.016
FOCUS	387	14.3 (5.4)	-4.1 (0.3)	195	14.2 (5.9)	-1.0 (0.5)	-3.10 [-4.26; -1.94]; < 0.001
Total							-2.35 [-3.19; -1.51]; < 0.0001[c,d]
Indirect comparison via bridge comparators							
Atogepant vs erenumab or fremanezumab							0.44 [-0.84; 1.71]; 0.5028[c]
Health status using EQ-5D VAS[e] (week 12)							
Atogepant vs placebo							
ELEVATE	n.d.[e]	77.1 (12.9)	7.0 (1.4)	n.d.[e]	75.9 (14.0)	5.0 (1.4)	1.97 [-1.80; 5.74]; 0.304
ADVANCE	n.d.[e]	79.0 (16.2)	3.2 (2.5)	n.d.[e]	83.8 (15.5)	3.31 (3.0)	-0.10 [-7.89; 7.70]; 0.980
PROGRESS	n.d.[e]	59.8 (23.0)	7.6 (3.2)	n.d.[e]	62.1 (15.9)	5.1 (3.6)	2.58

							[-6.55; 11.71]; 0.575
Total							1.70 [-1.48; 4.88]; 0.295[d]
Erenumab or fremanezumab vs placebo							
LIBERTY	86	79.7 (16.8)	2.1 (2.1)	104	77.5 (19.9)	0.8 (1.8)	1.35 [-4.18; 6.88]; 0.630
FOCUS	388	69.6 (21.2)	5.45 (1.3)	195	70.1 (20.1)	1.2 (1.8)	4.22 [1.28; 7.17]; 0.005
Total							3.59 [0.99; 6.19]; 0.007[d]
Indirect comparison via bridge comparators							
Atogepant vs erenumab or fremanezumab							-1.89 [-5.99; 2.22]; 0.368

Health-related quality of life

Endpoint	**Atogepant or erenumab or fremanezumab**			**Placebo**			**Group difference**
	N	Values at the start of the study MV (SD)	Change in month 3 or week 12 MV (SE)	N	Values at the start of the study MV (SD)	Change in month 3 or week 12 MV (SE)	MD [95% CI]; p value
Health-related quality of life using MSQoL[f] (week 12)							
Role Function-Restrictive							
Atogepant vs placebo							
ELEVATE	n.d.[g]	41.5 (16.5)	32.3 (1.9)	n.d.[g]	42.8 (15.7)	15.0 (2.0)	17.27 [12.09; 22.45]; < 0.001
ADVANCE	n.d.[g]	50.4 (16.4)	31.1 (4.1)	n.d.[g]	43.2 (16.6)	15.2 (5.0)	15.89 [3.04; 28.74]; 0.016
PROGRESS	n.d.[g]	42.2 (18.5)	22.9 (2.9)	n.d.[g]	35.6 (18.5)	14.3 (3.2)	8.59 [0.37; 16.81]; 0.041
Total							14.92 [10.77; 19.06]; < 0.001[d]

Erenumab or fremanezumab vs placebo							
LIBERTY[h]	–	–	–	–	–	–	–
FOCUS	388	47.6 (17.4)	17.7 (1.4)	195	47.6 (19.0)	8.7 (1.9)	9.06 [5.77; 12.35]; < 0.001
Total							–
Indirect comparison via bridge comparators							
Atogepant vs erenumab or fremanezumab							5.86 [0.56; 11.15]; 0.030 **SMD[i]:** 0.18 [0.02; 0.35]
Role Function-Preventive							
Atogepant vs placebo							
ELEVATE	n.d.[g]	53.6 (21.9)	28.3 (1.8)	n.d.[g]	56.0 (21.1)	14.6 (1.9)	13.72 [8.83; 18.62]; < 0.001
ADVANCE	n.d.[g]	67.6 (17.4)	23.0 (3.5)	n.d.[g]	60.3 (23.9)	15.5 (4.2)	7.44 [-3.55; 18.43]; 0.182
PROGRESS	n.d.[g]	56.0 (22.9)	21.9 (2.7)	n.d.[g]	53.6 (24.4)	12.1 (3.1)	9.79 [1.94; 17.64]; 0.015
Total							11.97 [8.09; 15.86]; < 0.001[d]
Erenumab or fremanezumab vs placebo							
LIBERTY[h]	–	–	–	–	–	–	–
FOCUS	388	63.2 (20.4)	13.8 (1.3)	195	64.2 (21.0)	8.0 (1.7)	5.81 [2.82; 8.80]; < 0.001
Total							–
Indirect comparison via bridge comparators							
Atogepant vs erenumab or fremanezumab							6.16 [1.26; 11.07]; 0.014 **SMD[i]:** 0.21 [0.04; 0.38]
Emotional functioning							
Atogepant vs placebo							

ELEVATE	n.d.[g]	57.1 (26.5)	25.4 (2.0)	n.d.[g]	58.1 (24.7)	13.1 (2.0)	12.35 [7.04; 17.66]; < 0.001
ADVANCE	n.d.[g]	54.8 (27.0)	29.7 (4.6)	n.d.[g]	57.1 (20.8)	15.8 (5.6)	13.88 [-0.59; 28.35]; 0.060
PROGRESS	n.d.[g]	50.3 (27.3)	22.9 (2.9)	n.d.[g]	48.2 (27.9)	13.6 (3.3)	9.28 [0.92; 17.65]; 0.030
Total							11.68 [7.40; 15.96]; < 0.001[d]
Erenumab or fremanezumab vs placebo							
LIBERTY[h]	–	–	–	–	–	–	–
FOCUS	388	60.6 (23.9)	15.2 (1.5)	195	60.6 (25.3)	6.1 (2.1)	9.14 [5.52; 12.77]; < 0.001
Total							–
Indirect comparison via bridge comparators							
Atogepant vs erenumab or fremanezumab							2.54 [-3.07; 8.15]; 0.375
General impairment due to headache using HIT-6[j] (week 12)							
Atogepant vs placebo							
ELEVATE	n.d.[g]	64.6 (4.3)	-10.8 (0.8)	n.d.[g]	64.8 (4.1)	-4.8 (0.8)	-5.99 [-8.02; -3.96]; < 0.001
ADVANCE	n.d.[g]	63.1 (4.8)	-9.1 (1.3)	n.d.[g]	64.6 (3.9)	-3.3 (1.6)	-5.83 [-10.01; -1.64]; 0.007
PROGRESS	n.d.[g]	64.5 (4.7)	-7.8 (1.0)	n.d.[g]	66.3 (3.5)	-4.1 (1.1)	-3.67 [-6.50; -0.83]; 0.012
Total							-5.29 [-6.82; -3.75]; < 0.001[d]
Erenumab or fremanezumab vs placebo							
LIBERTY	86	62.5 (3.9)	-6.1 (0.7)	104	62.2 (5.2)	-2.5 (0.5)	-3.60 [-5.30; -1.90]; < 0.001
FOCUS	388	64.2 (4.4)	-6.05 (0.5)	195	64.0 (5.2)	-2.3 (0.7)	-3.37 [-4.45; -2.30] < 0.001

Total	-3.44 [-4.34; -2.53]; < 0.001[d]
Indirect comparison via bridge comparators	
Atogepant vs erenumab or fremanezumab	-1.85 [-3.64; -0.07]; 0.042 **SMD[i]:** -0.17 [-0.33; -0.01]

Side effects[b]

Endpoint	**Atogepant or erenumab or fremanezumab**		**Placebo**		**Group difference**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Total adverse events (presented additionally)					
Atogepant vs placebo					
ELEVATE	125	68 (54.4)	128	70 (54.7)	–
ADVANCE	27	12 (44.4)	18	13 (72.2)	–
PROGRESS	64	39 (60.9)	56	31 (55.4)	–
Total					–
Erenumab or fremanezumab vs placebo					
LIBERTY	86	52 (60.5)	104	61 (58.7)	–
FOCUS	388	208 (53.6)	195	101 (51.8)	–
Total					–
Serious adverse events (SAEs)					
Atogepant vs placebo					
ELEVATE	125	4 (3.2)	128	0 (0)	9.21 [0.50; 169.38]; 0.044
ADVANCE	27	0 (0)	18	0 (0)	–
PROGRESS	64	1 (1.6)	56	0 (0)	2.63 [0.11; 63.31]; 0.515
ELEVATE/PROGRESS, total					5.20 [0.61; 44.56]; 0.132[d]
Erenumab or fremanezumab vs placebo					
LIBERTY	86	2 (2.3)	104	1 (1.0)	2.42 [0.22; 26.22]; 0.592

FOCUS	388	4 (1.0)	195	3 (1.5)	0.67 [0.15; 2.96]; 0.625
Total					0.96 [0.27; 3.40]; 0.950[d]
Indirect comparison via bridge comparator					
Atogepant vs erenumab or fremanezumab					5.42 [0.45; 65.54]; 0.184
Therapy discontinuation due to adverse events					
Atogepant vs placebo					
ELEVATE	125	2 (1.6)	128	1 (0.8)	2.05 [0.19; 22.30]; 0.601
ADVANCE	27	1 (3.7)	18	1 (5.6)	0.67 [0.04; 9.99]; 0.808
PROGRESS	64	2 (3.1)	56	2 (3.6)	0.88 [0.13; 6.01]; 0.975
Total					1.07 [0.29; 3.98]; 0.920[d]
Erenumab or fremanezumab vs placebo					
LIBERTY	86	0 (0)	104	2 (1.9)	0.24 [0.01; 4.96]; 0.228
FOCUS	388	3 (0.8)	195	2 (1.0)	0.75 [0.13; 4.47]; 0.829
Total					0.57 [0.12; 2.64]; 0.470[d]
Indirect comparison via bridge comparators					
Atogepant vs erenumab or fremanezumab					1.89 [0.25; 14.24]; 0.538

a. The results on overall mortality are based on the data on fatal AEs.
b. Includes events that occurred within the 12-week double-blind treatment phase; for ELEVATE/ ADVANCE/ PROGRESS, events that occurred within the 4-week follow-up phase are also included
c. Data subsequently submitted by the pharmaceutical company in the written statement procedure.
d. Meta-analysis, fixed-effect model (inverse variance method)
e. It is unclear how many patients were actually included in the evaluation; it is assumed that those patients for whom the baseline value and at least 1 post-baseline value were available were included. Number of patients who were at least included in the evaluation, as the baseline value and the value for week 12 are available for them (atogepant vs placebo): 69 vs 73 in ELEVATE, 23 vs 16 in ADVANCE, 27 vs 21 in PROGRESS
f. Higher values mean a better health status (scale range: 0 to 100) or a better health-related quality of life (scale range: Role Function-Restrictive 7 to 42, Role Function-Preventive 4 to 24, emotional functioning 3 to 18); in the direct comparison, a positive group difference corresponds to an advantage of atogepant or erenumab or fremanezumab. In the indirect comparison, a positive effect corresponds to an advantage of atogepant.
g. It is unclear how many patients were actually included in the evaluation; it is assumed that those patients for whom the baseline value and at least 1 post-baseline value were available were included. Number of patients who were at least included in the evaluation, as the baseline value and the value for week 12 are available for them (atogepant vs placebo): 116 vs 123 in ELEVATE, 23 vs 16 in ADVANCE, 60 vs 47 in PROGRESS

h. Endpoint not assessed
i. If the CI for the SMD is completely outside the irrelevant range [-0.2; 0.2], this is interpreted as a relevant effect. In other cases, the presence of a relevant effect cannot be derived.
j. Lower values mean less general impairment due to headache (scale range: 36 to 78); in the direct comparison, a negative group difference corresponds to an advantage of atogepant or erenumab or fremanezumab. In the indirect comparison, a negative effect corresponds to an advantage of atogepant.

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; EQ-5D = European Quality of Life 5 Dimensions; HIT-6 = Headache Impact Test-6; n.d. = no data available; CI = confidence interval; MSQoL = Migraine-Specific Quality of Life; N = number of patients evaluated; n = number of patients with (at least one) event; RR = relative risk; SMD = standardised mean difference; AE = adverse event; SAE = serious adverse event; VAS = visual analogue scale; vs = versus

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

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

Approx. 1,352,300 – 1,686,700 patients

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)

Approx. 34,600 – 39,500 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for 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

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Atogepant	€ 3,452.45
Appropriate comparator therapy:	
Amitriptyline	€ 59.31 – € 96.76
Clostridium botulinum toxin type A	€ 3,993.63
Erenumab	€ 3,344.99
Flunarizine	€ 49.37 – € 77.50
Metoprolol	€ 44.20 – € 62.34
Propranolol	€ 124.61 – € 186.92

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2025)

Costs for additionally required SHI services: not applicable

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)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Atogepant	€ 3,452.45
Appropriate comparator therapy:	
Eptinezumab	€ 3,116.21
Erenumab	€ 3,344.99
Fremanezumab	€ 5,242.04
Galcanezumab	€ 5,532.40

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2025)

Costs for additionally required SHI services: not applicable

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

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

a) Adults with 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.

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.

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

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

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

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is ≥ 5 per cent of the total number of study participants.

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

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 21 August 2025.

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

Berlin, 21 August 2025

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

Prof. Hecken