Rimegepant (migraine prophylaxis)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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[1] Translation of Sections I 1 to I 4 of the dossier assessment *Rimegepant (Migräneprophylaxe) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Keywords

Rimegepant, Migraine Disorders, Benefit Assessment

Medical and scientific advice

- No advisor on medical and scientific questions was available for the present dossier assessment.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by two persons.

IQWiG thanks the respondents for participating in the written exchange about how they experienced the disease and its treatment and about the treatment goals. The respondents were not involved in the actual preparation of the dossier assessment.

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Part I: Benefit assessment

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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug rimegepant. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the 'company'). The dossier was sent to IQWiG on 02 June 2025.

Research question

The aim of the present report is to assess the added benefit of rimegepant in comparison with the appropriate comparator therapy (ACT) for the preventive treatment of episodic migraine in adults with at least 4 migraine attacks per month.

The research questions presented in Table 2 were defined in accordance with the ACT specified by the G-BA.

Table 2: Research question for the benefit assessment of rimegepant

Research question	Therapeutic indication	ACT[a]
1	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine and for whom conventional migraine prophylaxis is an option	Amitriptyline or erenumab or flunarizine (if treatment with beta-blockers is contraindicated or has not been sufficiently effective) or metoprolol or propranolol
2	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine who do not respond to, are unsuitable for, or do not tolerate any of the following drug treatments/drug classes[b]: metoprolol, propranolol, flunarizine, amitriptyline	Eptinezumab or erenumab or fremanezumab or galcanezumab

a. Presented is the respective ACT specified by the G-BA.
b. In research question 2, treatment with biologic agents may be an option if patients previously did not respond to or did not tolerate at least 2 drug therapies (drug classes from research question 1). In cases where the drugs are not suitable for patients from research question 1, this must be documented and justified.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

For easier presentation and better readability, this benefit assessment uses the following wordings for the research questions in the running text:

- Research question 1: adults for whom conventional migraine prophylaxis is an option
- Research question 2: adults for whom conventional migraine prophylaxis is not an option

The ACT was adjusted immediately before the start of the procedure on 27 May 2025. When determining the ACT, the company refers to that used for the assessment of eptinezumab for migraine prophylaxis. For research question 1, this includes the drugs topiramate and clostridium botulinum toxin type A in addition to the drugs listed in Table 2. For this research question, the company additionally supplemented the drug atogepant as a further appropriate treatment option in addition to the ACT that was used at the time for the assessment of eptinezumab. For research question 2, the ACT specified by the company corresponds to that of the G-BA. The deviations from the ACT for research question 1 have no consequences for this assessment, as the company does not present any data for the benefit assessment, either for the additional treatment options it listed or for those specified by the G-BA (see below). The benefit assessment is conducted in comparison with the ACT specified by the G-BA. Since no suitable data are available for either of the 2 research questions designated by the G-BA, the assessment below is performed in a joint section of the report.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 12 weeks were used to derive the added benefit.

Results

Concurring with the company, the check of completeness of the study pool identified no relevant study for research question 1. For research question 2, the company identified the CHALLENGE-MIG study and presented results for the total population of the study. However, the company describes that it is not possible to process the results in accordance with the requirements of the benefit assessment pursuant to the G-BA's rules of procedure, as it is not the sponsor of the study and only has access to publicly available information. For this reason, the company does not derive any added benefit for research question 2 either.

The CHALLENGE-MIG study potentially comprises a relevant subpopulation for research question 2. However, the results for the total population are not suitable for research question 2 of this benefit assessment. This is explained below.

The CHALLENGE-MIG study is a completed double-blind phase 4 study comparing rimegepant with galcanezumab. It included patients aged 18 to 75 years with migraine with or without aura . A total of 293 patients were randomly assigned to the rimegepant arm and 287 to the galcanezumab arm.

Research question 2 of this benefit assessment covers adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine and who do not respond to, are unsuitable for, or do not tolerate any of the drug classes from research question 1. In response to research question 2, the G-BA also points out that treatment with biologic agents in the context of a clinical trial may be considered for patients if they have not

responded to or have not tolerated at least two drug therapies (drug classes from research question 1). In cases where the drugs are not suitable for patients from research question 1, this must be documented and justified.

The CHALLENGE-MIG study included patients irrespective of their prior preventive therapies. Overall, prior to study enrolment, 92 (15.9%) of the 580 enrolled patients had received previous migraine prophylaxis, 64 (11%) of the enrolled patients (rimegepant: n = 39; galcanezumab: n = 25) showed treatment failure with at least one previous preventive therapy. As described, according to the G-BA, patients can be assigned to research question 2 if they have previously not responded to or have not tolerated at least two drug therapies (drug classes from research question 1). However, it is unclear whether and, if so, how many of the patients in the CHALLENGE-MIG study met the requirements regarding prior preventive therapies for research question 2, or whether there were contraindications for one or more of the drugs considered to be an option as an ACT for research question 1. The results of the total population of the CHALLENGE-MIG study are therefore not suitable for assessing the added benefit of rimegepant versus the G-BA's ACT for the preventive treatment of episodic migraine in adults with at least 4 migraine attacks per month.

Results on added benefit

The company did not present any data on the preventive treatment of episodic migraine in adults with at least four migraine attacks per month for whom conventional migraine prophylaxis is an option (research question 1). Suitable data for adults for whom conventional migraine prophylaxis is not an option (research question 2) are not available. There is no hint of an added benefit of rimegepant in comparison with the ACT for either research question; an added benefit is therefore not proven for either of them.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 shows a summary of probability and extent of the added benefit of rimegepant.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Rimegepant – probability and extent of added benefit

Research question	**Therapeutic indication**	**ACT[a]**	**Probability and extent of added benefit**
1	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine and for whom conventional migraine prophylaxis is an option	Amitriptyline or erenumab or flunarizine (if treatment with beta-blockers is contraindicated or has not been sufficiently effective) or metoprolol or propranolol	Added benefit not proven
2	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine who do not respond to, are unsuitable for, or do not tolerate any of the following drug treatments/drug classes[b]: metoprolol, propranolol, flunarizine, amitriptyline	Eptinezumab or erenumab or fremanezumab or galcanezumab	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. In research question 2, treatment with biologic agents may be an option if patients previously did not respond to or did not tolerate at least 2 drug therapies (drug classes from research question 1). In cases where the drugs are not suitable for patients from research question 1, this must be documented and justified.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

I 2 Research question

The aim of the present report is to assess the added benefit of rimegepant in comparison with the ACT for the preventive treatment of episodic migraine in adults with at least 4 migraine attacks per month.

The research questions presented in Table 4 were defined in accordance with the ACT specified by the G-BA.

Table 4: Research question for the benefit assessment of rimegepant

Research question	Therapeutic indication	ACT[a]
1	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine and for whom conventional migraine prophylaxis is an option	Amitriptyline or erenumab or flunarizine (if treatment with beta-blockers is contraindicated or has not been sufficiently effective) or metoprolol or propranolol
2	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine who do not respond to, are unsuitable for, or do not tolerate any of the following drug treatments/drug classes[b]: metoprolol, propranolol, flunarizine, amitriptyline	Eptinezumab or erenumab or fremanezumab or galcanezumab

a. Presented is the respective ACT specified by the G-BA.
b. In research question 2, treatment with biologic agents may be an option if patients previously did not respond to or did not tolerate at least 2 drug therapies (drug classes from research question 1). In cases where the drugs are not suitable for patients from research question 1, this must be documented and justified.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

For easier presentation and better readability, this benefit assessment uses the following wordings for the research questions in the running text:

- Research question 1: adult patients who are candidates for conventional migraine prophylaxis
- Research question 2: adult patients who are not candidates for conventional migraine prophylaxis

The ACT was adjusted immediately before the start of the procedure on 27 May 2025. When determining the ACT, the company refers to that used for the assessment of eptinezumab for migraine prophylaxis [3]. For research question 1, this includes the drugs topiramate and clostridium botulinum toxin type A in addition to the drugs listed in Table 4. For this research question, the company additionally supplemented the drug atogepant as a further appropriate treatment option in addition to the ACT that was used at the time for the

assessment of eptinezumab. For research question 2, the ACT specified by the company corresponds to that of the G-BA. The deviations from the ACT for research question 1 have no consequences for this assessment, as the company does not present any data for the benefit assessment, either for the additional treatment options it listed or for those specified by the G-BA (see below). The benefit assessment is conducted in comparison with the ACT specified by the G-BA. Since no suitable data are available for either of the 2 research questions designated by the G-BA, the assessment below is performed in a joint section of the report.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs with a minimum duration of 12 weeks were used to derive the added benefit. This concurred with the company's inclusion criteria.

I 3 Information retrieval and study pool

The study pool for the assessment was compiled on the basis of the following information:

Sources used by the company in the dossier:

- Study list on rimegepant (status: 11 April 2025)
- Bibliographical literature search on rimegepant (last search on 24 March 2025)
- Search in trial registries/trial results databases for studies on rimegepant (last search on 24 March 2025)
- Search on the G-BA website for rimegepant (last search on 24 March 2025)

To check the completeness of the study pool:

- Search in trial registries for studies on rimegepant (last search on 12 June 2025); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check of completeness of the study pool identified no relevant study for research question 1. For research question 2, the company identified the CHALLENGE-MIG study [4] and presents its findings. However, the company describes that it is not possible to process the results in accordance with the requirements of the benefit assessment pursuant to the G-BA's rules of procedure [5], as it is not the sponsor of the study and only has access to publicly available information. For this reason, the company does not derive any added benefit for research question 2 either. In Module 4 Section 4.4, the company additionally presents supplementary results from the BHV3000-305 approval study [6] in Module 4 Section 4.4. This RCT compares preventive treatment with rimegepant versus placebo in adults with migraine (with or without aura). Concurring with the company, the study BHV3000-305 is assessed as unsuitable for the benefit assessment of rimegepant in the present therapeutic indication due to the lack of comparison with the ACT.

The CHALLENGE-MIG study potentially comprises a relevant subpopulation for research question 2. However, the results for the total population are not suitable for research question 2 of this benefit assessment. This is explained below.

CHALLENGE-MIG

The CHALLENGE-MIG study is a completed double-blind phase 4 study comparing rimegepant with galcanezumab. The study included patients aged 18 to 75 years with migraine with or without aura (defined according to the International Classification of Headache Disorders, third edition [ICHD-3] [7]). All patients had to have experienced migraine for at least 1 year, and the migraine had to have first appeared before the age of 50. In addition, patients had to have experienced an average of 4 to 14 days of migraine headaches and at least 2 migraine

attacks per month in the 3 months prior to the first study visit and in the prospective baseline phase. A total of 293 patients were randomly assigned to the rimegepant arm and 287 to the galcanezumab arm. The company presented the results of the total population.

Fulfilment of criteria for preventive pre-therapies unclear

Research question 2 of this benefit assessment covers adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine who do not respond to, are unsuitable for, or do not tolerate any of the following drug therapies/drug classes: metoprolol, propranolol, flunarizine, amitriptyline. In response to research question 2, the G-BA also points out that treatment with biologic agents in the context of a clinical trial may be considered for patients if they have not responded to or have not tolerated at least two drug therapies (drug classes from research question 1). In cases where the drugs are not suitable for patients from research question 1, this must be documented and justified.

The CHALLENGE-MIG study included patients irrespective of their prior preventive therapies. As described, according to the G-BA, patients can be assigned to research question 2 if they have previously not responded to or have not tolerated at least two drug therapies (drug classes from research question 1). It is unclear how many of the patients with treatment failure from the CHALLENGE-MIG study met these criteria. The 11% who did not respond also include patients who received drugs that were not part of the ACT for research question 1 (see Table 4). For example, 30 patients received topiramate as pretreatment. Information on the number of failed treatment attempts is missing. There is also no information available as to whether there were any contraindications for one or more of the drugs considered appropriate as an ACT for research question 1. It is therefore unclear whether and, if so, how many of the patients in the CHALLENGE-MIG study met the requirements regarding prior preventive therapies for research question 2. The results of the total population of the CHALLENGE-MIG study are therefore not suitable for assessing the added benefit of rimegepant versus the G-BA's ACT for the preventive treatment of episodic migraine in adults with at least 4 migraine attacks per month. Based on publicly available data, it is therefore not possible to process the data in accordance with research question 2.

I 4 Results on added benefit

The company did not present any data on the preventive treatment of episodic migraine in adults with at least four migraine attacks per month for whom conventional migraine prophylaxis is an option (research question 1). Suitable data for adults for whom conventional migraine prophylaxis is not an option (research question 2) are not available. There is no hint of an added benefit of rimegepant in comparison with the ACT for either research question; an added benefit is therefore not proven for either of them.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of rimegepant in comparison with the ACT is summarized in Table 5.

Table 5: Rimegepant – probability and extent of added benefit

Research question	Therapeutic indication	ACT[a]	Probability and extent of added benefit
1	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine and for whom conventional migraine prophylaxis is an option	Amitriptyline or erenumab or flunarizine (if treatment with beta-blockers is contraindicated or has not been sufficiently effective) or metoprolol or propranolol	Added benefit not proven
2	Adults with at least 4 migraine attacks per month with an indication for preventive treatment of episodic migraine who do not respond to, are unsuitable for, or do not tolerate any of the following drug treatments/drug classes[b]: metoprolol, propranolol, flunarizine, amitriptyline	Eptinezumab or erenumab or fremanezumab or galcanezumab	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. In research question 2, treatment with biologic agents may be an option if patients previously did not respond to or did not tolerate at least 2 drug therapies (drug classes from research question 1). In cases where the drugs are not suitable for patients from research question 1, this must be documented and justified.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The assessment described above concurs with that by the company.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

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