Gemeinsamer Bundesausschuss

Justification

of 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)
Lasmiditan (migraine acute treatment)

of 5 October 2023

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of 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 trials the pharmaceutical company has 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.

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 lasmiditan (Rayvow) on 1 March 2022 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. In the present case, the G-BA, by resolution of 5 January 2023, only suspended the obligation to submit the dossier pursuant to Chapter 5 Section 11 VerfO until 17 April 2023, provided that the medicinal product is placed on the market within the suspension period. The temporary suspension of the obligation to submit the dossier pursuant to Chapter 5 Section 11 VerfO shall not affect the legal effects linked to the relevant points date pursuant to Chapter 5 Section 8, paragraph 1, sentence 1, no. 1VerfO. 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 17 April 2023.

The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on the G-BA website (www.g-ba.de) on 17 July 2023, 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 lasmiditan compared to 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 has 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 lasmiditan.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has 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 Lasmiditan (Rayvow) in accordance with the product information

Rayvow is indicated for the acute treatment of the headache phase of migraine attacks, with or without aura in adults.

Therapeutic indication of the resolution (resolution of 05.10.2023):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

Adults with migraine with or without aura who need acute treatment

Appropriate comparator therapy for lasmiditan:

- A patient-individual therapy taking into account pretreatment, the severity of the attack as well as existing concomitant diseases, selecting selective serotonin 5HT1 receptor agonists (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) and non-steroidal antirheumatic drugs (acetylsalicylic acid, diclofenac, ibuprofen)

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA:

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.

1 General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO:

on 1. In addition to lasmiditan, the triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan), some nonsteroidal anti-inflammatory drugs (NSAIDs): acetylsalicylic acid, diclofenac and ibuprofen) as well as paracetamol, phenazone and ergotamine have a marketing authorisation for the treatment of acute migraine attacks. Caffeine is used in paracetamol combination preparations. Metoclopramide (as a monopreparation) is approved for nausea and vomiting in acute migraine attacks and is therefore not considered as an appropriate comparator therapy. In addition, rimegepant is approved in the EU but not available on the German market.

on 2. Non-medicinal treatment is not indicated for the acute treatment of migraine.

on 3. For the acute treatment of migraine, there are no resolutions from the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V.

According to Annex III of the Pharmaceuticals Directive, combinations of active ingredients for migraine are excluded from prescription (Annex III to the Pharmaceuticals Directive: Overview of prescription limitations and exclusions in the provision of medicinal products under the Pharmaceuticals Directive and on the basis of other regulations (Section 34, paragraph 1, sentence 6 and paragraph 3 SGB V), No. 36).

In addition, there is a resolution of the G-BA on the active ingredient lasmiditan on the exemption from the definition of reference price groups "Selective serotonin 5HT1 agonists, group 1" in stage 2 dated 17 November 2022.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present therapeutic indication.

It should be noted that the robust evidence on treatment options in the present therapeutic indication in the absence of direct comparator studies is limited overall. Therefore, of the medicinal therapy options approved in Germany, no active ingredient can be explicitly emphasised as a therapeutic standard in the acute treatment of migraine.

For the appropriate comparator therapy, the combination of sumatriptan plus naproxen mentioned in guidelines and reviews cannot be taken into account, as there

is no marketing authorisation for naproxen in the therapeutic indication. There is insufficient evidence for paracetamol, phenazone and ergotamine.

The efficacy, in particular, of the active ingredients from the NSAID and triptan product classes in the acute treatment of migraine attacks has been adequately confirmed by placebo-controlled studies. Both product classes have been established in the care of migraine patients for many years and have proven effective in the acute treatment of migraine attacks. Despite limited direct comparator evidence between NSAIDs and triptans, divergent therapy recommendations have emerged for both product classes, taking into account many years of clinical experience. Also taking into account the recently updated AWMF (Association of the Scientific-Medical Societies) guideline "Therapy of migraine attacks and prophylaxis of migraine" of 18 October 2022, a recommendation can be derived for NSAIDs, in particular, for mild to moderate migraine attacks and a recommendation for triptans, in particular, for severe migraine attacks as well as in case of non-response to NSAIDs and other analgesics.

Based on the evidence and the recommendations, it cannot be assumed that NSAIDs and triptans are equally appropriate for all patients in the present therapeutic indication. Rather, criteria such as the severity of the attack, pretreatment and any concomitant diseases must be taken into account for therapy selection.

Overall, the G-BA therefore considers it appropriate in the present therapeutic indication to use a patient-individual therapy as the appropriate comparator therapy for lasmiditan, taking into account the pretreatment, the severity of the attack as well as existing concomitant diseases, selecting selective serotonin 5HT1 receptor agonists (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) and nonsteroidal antirheumatic drugs (acetylsalicylic acid, diclofenac, ibuprofen).

Within the framework of the written and oral statement procedure, it was discussed to what extent patients with cardiovascular-related triptan contraindications or triptan failure should be addressed as a separate patient group within the framework of the benefit assessment. Based on the information provided in the written statement procedure, it can be assumed that this is only a small percentage of patients in the present therapeutic indication (estimates are in the single-digit percentage range). Against this background, no separate patient population with cardiovascular-related triptan contraindication or triptan failure is defined.

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 lasmiditan is assessed as follows:

For adults with migraine with or without aura who require acute treatment, the additional benefit of lasmiditan is not proven.

Justification:

The pharmaceutical company does not present data for the assessment of the additional benefit of lasmiditan compared to the appropriate comparator therapy for adults with migraine with or without aura who require acute treatment.

The LAHJ (SAMURAI), LAHK (SPARTAN) and LAIJ (CENTURION) studies presented in the dossier are randomised controlled trials comparing lasmiditan versus placebo in the acute treatment of the headache phase of migraine attacks with or without aura. In accordance with the pharmaceutical company's approach in the dossier, these studies are not considered for the present benefit assessment due to the lack of comparison with the appropriate comparator therapy.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Rayvow with the active ingredient lasmiditan.

Lasmiditan is used for the acute treatment of the headache phase of migraine attacks in adults with migraine with or without aura.

The G-BA determined a patient-individual therapy as an appropriate comparator therapy, taking into account pretreatment, the severity of the attack as well as existing concomitant diseases, selecting selective serotonin 5HT1 receptor agonists (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) and nonsteroidal antirheumatic drugs (acetylsalicylic acid, diclofenac, ibuprofen).

For the assessment of additional benefit, the pharmaceutical company submits the LAHJ (SAMURAI), LAHK (SPARTAN) and LAIJ (CENTURION) RCTs, in which lasmiditan was compared with placebo in each case. In accordance with the pharmaceutical company's approach in the dossier, these studies are not considered for the present benefit assessment due to the lack of comparison with the appropriate comparator therapy.

An additional benefit of lasmiditan compared to the appropriate comparator therapy is therefore not proven.

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

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

The number of patients submitted by the pharmaceutical company with the dossier is an underestimate, as the prevalence of migraine used to derive the number of patients is based exclusively on SHI data. In principle, patients with migraine with or without aura who have so far taken pharmacy-only, non-prescription medicinal products for the acute treatment of migraine attacks and who are not (yet) undergoing medical treatment for their migraine are also eligible for treatment with lasmiditan. Therefore, not all patients in the SHI target population are adequately covered.

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 Rayvow (active ingredient: lasmiditan) at the following publicly accessible link (last access: 20 April 2023):

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

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 September 2023).

The appropriate comparator therapy comprises pharmacy-only, non-prescription medicinal products. These are excluded from care according to Section 31 SGB V. An exceptional circumstance according to Section 34, paragraph 1, sentence 2 SGB V does not exist. Thus, the prescription of these medicinal products is not allowed at the expense of the statutory health insurance. Therefore, the cost illustration for these preparations is omitted in the resolution according to Section 35a paragraph 3 SGB V.

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.

The annual treatment costs vary from patient to patient depending on the frequency of attacks. For the purpose of comparability, the costs are calculated for an exemplary range of 1 to 60 migraine attacks per year.

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				
Lasmiditan	1-2 x per migraine attack	1 – 60	1	1 – 60
Appropriate comparator therapy				
A patient-individual therapy, selecting selective serotonin 5HT1 receptor agonists (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) and non-steroidal antirheumatic drugs (acetylsalicylic acid, diclofenac, ibuprofen)				
Almotriptan	1-2 x per migraine attack	1 – 60	1	1 – 60
Eletriptan	1-2 x per migraine attack	1 – 60	1	1 – 60
Frovatriptan	1-2 x per migraine attack	1 – 60	1	1 – 60
Naratriptan	1-2 x per migraine attack	1 – 60	1	1 – 60
Rizatriptan	1-2 x per migraine attack	1 – 60	1	1 – 60

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Sumatriptan	1-2 x per migraine attack	1 – 60	1	1 – 60
Zolmitriptan	1-2 x per migraine attack	1 – 60	1	1 – 60

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					
Lasmiditan	100 mg	100 – 200 mg	1 x 100 mg – 2 x 100 mg	1 – 60	1 x 100 mg – 120 x 100 mg
Appropriate comparator therapy					
A patient-individual therapy, selecting selective serotonin 5HT1 receptor agonists (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan) and non-steroidal antirheumatic drugs (acetylsalicylic acid, diclofenac, ibuprofen)					
Almotriptan	12.5 mg	12.5 – 25 mg	1 x 12.5 mg – 2 x 12.5 mg	1 – 60	1 x 12.5 mg – 120 x 12.5 mg
Eletriptan	40 mg	40 – 80 mg	1 x 40 mg – 2 x 40 mg	1 – 60	1 x 40 mg – 120 x 40 mg
Frovatriptan	2.5 mg	2.5 – 5 mg	1 x 2.5 mg – 2 x 2.5 mg	1 – 60	1 x 2.5 mg – 120 x 2.5 mg
Naratriptan	2.5 mg	2.5 – 5 mg	1 x 2.5 mg – 2 x 2.5 mg	1 – 60	1 x 2.5 mg – 120 x 2.5 mg
Rizatriptan	10 mg	10 – 20 mg	1 x 10 mg – 2 x 10 mg	1 – 60	1 x 10 mg – 120 x 10 mg
Sumatriptan	50 mg – 100 mg	50 – 200 mg	1 x 50 mg – 2 x 100 mg	1 – 60	1 x 50 mg – 120 x 100 mg
Zolmitriptan	2.5 mg – 5 mg	2.5 – 10 mg	1 x 2.5 mg – 2 x 5 mg	1 – 60	1 x 2.5 mg – 120 x 5 mg

Costs:

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					
Lasmiditan 100 mg	2 FCT	€ 47.98	€ 2.00	€ 3.48	€ 42.50
Lasmiditan 100 mg	6 FCT	€ 121.32	€ 2.00	€ 10.44	€ 108.87
Appropriate comparator therapy					
Almotriptan 12.5 mg[2]	14 FCT	€ 33.68	€ 2.00	€ 1.77	€ 29.91
Eletriptan 40 mg[2]	6 FCT	€ 21.79	€ 2.00	€ 0.83	€ 18.96
Eletriptan 40 mg[2]	12 FCT	€ 31.02	€ 2.00	€ 1.56	€ 27.46
Frovatriptan 2.5 mg[2]	3 FCT	€ 16.80	€ 2.00	€ 0.43	€ 14.37
Frovatriptan 2.5 mg[2]	12 FCT	€ 30.74	€ 2.00	€ 1.54	€ 27.20
Naratriptan 2.5 mg[2]	2 FCT	€ 15.09	€ 2.00	€ 0.30	€ 12.79
Naratriptan 2.5 mg[2]	12 FCT	€ 30.74	€ 2.00	€ 1.54	€ 27.20
Rizatriptan 10 mg[2]	3 TAB	€ 16.89	€ 2.00	€ 0.44	€ 14.45
Rizatriptan 10 mg[2]	18 TAB	€ 39.87	€ 2.00	€ 2.26	€ 35.61
Sumatriptan 50 mg[2]	2 TAB	€ 14.82	€ 2.00	€ 0.28	€ 12.54
Sumatriptan 100 mg[2]	12 FCT	€ 31.31	€ 2.00	€ 1.58	€ 27.73
Zolmitriptan 2.5 mg[2]	2 ODT	€ 14.90	€ 2.00	€ 0.28	€ 12.62
Zolmitriptan 5 mg[2]	12 ODT	€ 31.56	€ 2.00	€ 1.60	€ 27.96
Abbreviations: FCT = film-coated tablets, TAB = tablets, ODT = orally disintegrating tablets					

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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.

[2] Fixed reimbursement rate

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.

2.5 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 designates 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 authorised 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 has 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 has 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.

In the case of information on "determined" or "undetermined" combinations, the assessed medicinal product can be used in a combination therapy according to this information on the basis of the marketing authorisation under Medicinal Products Act. For the designation, the G-BA, within the scope of its legislative discretion, uses the constellation of a "determined" or an "undetermined" combination as a justifiable interpretation variant.

If a designation as a so-called determined or as a so-called indetermined combination is omitted due to the lack of information on a combination therapy in the product information of the assessed medicinal product, the non-designation in the resolution according to Section 35a, paragraph 3, sentence 1 SGB V does not affect the possibility that the assessed medicinal product can be used in an open-label combination under marketing authorisation regulations.

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 information 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 has 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 SGBV.

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:

Adults with migraine with or without aura who need acute treatment

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 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 its session on 24 January 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 17 April 2023, the pharmaceutical company submitted a dossier for the benefit assessment of lasmiditan to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 17 April 2023 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 lasmiditan.

The dossier assessment by the IQWiG was submitted to the G-BA on 22 June 2023, and the written statement procedure was initiated with publication on the G-BA website on 17 July 2023. The deadline for submitting statements was 7 August 2023.

The oral hearing was held on 28 August 2023.

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 26 September 2023, and the proposed resolution was approved.

At its session on 5 October 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	24 January 2023	Determination of the appropriate comparator therapy
Working group Section 35a	15 August 2023	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	26 September 2023	Conduct of the oral hearing
Working group Section 35a	5 September 2023 19 September 2023	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal products	26 September 2023	Concluding discussion of the draft resolution
Plenum	5 October 2023	Adoption of the resolution on the amendment of the AM-RL

Berlin, 5 October 2023

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

Prof. Hecken