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)
Daridorexant (reassessment following amendment of Annex III to the Pharmaceuticals Directive: insomnia)

of 15 August 2024

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 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 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 medicinal product Quviviq with the active ingredient daridorexant was approved on 29 April 2022 for the treatment of adults with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning. Quviviq was listed for the first time on 15 November 2022 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

According to the Pharmaceuticals Directive Annex III No. 32 (hypnotics/ hypnogenic agents or sedatives [sleep-inducing, sleep-initiating, sleep-promoting or tranquilisers] for the treatment of insomnia), daridorexant was reimbursable for a short-term therapy of up to four weeks at the time it was placed on the market. In the resolution on the benefit assessment of 12 May 2023, daridorexant was accordingly assessed with a maximum duration of use of four weeks.

At its session on 17 August 2023, the G-BA decided on an amendment to Annex III Number 32 of the Pharmaceuticals Directive. When the amendment came into force on 11 November

2023, the medicinal product Quviviq became reimbursable for the first time in the indication - treatment of adults with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning - (without limiting the duration of use) and thus, falls within the scope of Section 35a paragraph 1 SGB V by analogous application of the provision in Chapter 5 Section 1, paragraph 2, No. 4 of the G-BA's Rules of Procedure (VerfO). Accordingly, the pharmaceutical company was requested to submit a dossier. The information in Annex XII on daridorexant in the version of the resolution of 12 May 2023 is repealed with the present resolution.

The relevant date for the submission of a dossier was 1 March 2024 in analogous application of the regulation according to Chapter 5, Section 8, paragraph 1, No. 3 of the Rules of Procedure (VerfO) and taking into account the process sequence of the amendment to Annex III of the Pharmaceuticals Directive due to the first-time procedure in this case design.

On 28 February 2024, the pharmaceutical company submitted a dossier in due time for the active ingredient daridorexant for the therapeutic indication - treatment of adults with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 3 June 2024 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 daridorexant 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 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 daridorexant.

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 Daridorexant (Quviviq) in accordance with the product information

QUVIVIQ is indicated for the treatment of adult patients with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning.

Therapeutic indication of the resolution (resolution of 15 August 2024):

see the approved therapeutic indication

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

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adult patients with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning

Appropriate comparator therapy for daridorexant:

Best supportive care

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. For the treatment of insomnias, besides daridorexant, active ingredients from the different product classes of benzodiazepines (lormetazepam, flurazepam, triazolam, nitrazepam, temazepam, brotizolam, flunitrazepam, midazolam, lorazepam, oxazepam), antihistamines (diphenhydramine, doxylamine), sedative neuroleptics (melperone, pipamperone, promethazine), non-benzodiazepine receptor agonists (zopiclone, zolpidem, eszopiclone) as well as clomethiazole, L-tryptophan, chloral hydrate or melatonin are approved. The marketing authorisation of these active ingredients is usually limited to short-term use and sometimes to insomnias associated with a concomitant disease.

on 2. Non-organic insomnias constitute an indication for the use of psychotherapy according to Section 27 of the Psychotherapy Guideline.

on 3. There is a resolution from 12 May 2023 on the benefit assessment of daridorexant according to Section 35a SGB V , in which only a treatment period of up to 4 weeks was considered. By this resolution, the information in Annex XII on daridorexant in the version of the resolution of 12 May 2023 is repealed.

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 indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

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 indication according to Section 35a paragraph 7 SGB V (see “Information on Appropriate Comparator Therapy”).

Investigations on various active ingredients are considered in systematic reviews, but these cannot be considered as appropriate comparator therapy due to their marketing authorisation, usually only for short-term use or in the case of concomitant diseases. Overall, it can therefore be concluded that there is no conclusive evidence for the long-term treatment of sleep disorders. In addition, corresponding marketing authorisation restrictions on the above-mentioned active ingredients must be taken into account. The G-BA therefore came to the conclusion of determining Best Supportive Care (BSC) as an appropriate comparator therapy for the present therapeutic indication of long-term treatment of sleep disorders. Best supportive care (BSC) is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life.

In the course of long-term therapy, short-term medicinal therapy (max. 4 weeks) with short-acting benzodiazepines or non-benzodiazepine receptor agonists may also be indicated for patients.

There is also evidence for the efficacy of cognitive behavioural therapy for insomnia (CBT-I). The statements of the scientific-medical societies support the recommendations for carrying out a CBT-I. According to the Pharmaceuticals Directive,

before prescribing medicinal products, it should be checked whether non-medicinal therapies should be considered instead of prescribing medicinal products. In the present therapeutic indication, it is assumed that a CBT-I was performed prior to medicinal treatment and the patient did not respond adequately or a CBT-I could not be performed.

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 daridorexant is assessed as follows:

For adults with sleep disorders (insomnia) whose symptoms have persisted for at least 3 months and have a significant impact on daytime activity, the additional benefit is not proven.

Justification:

For the assessment of the additional benefit, the pharmaceutical company submitted evaluations of the 301 and 303 studies.

The 301 study was a double-blind randomised controlled trial comparing daridorexant to placebo in adults with chronic insomnia of at least moderate severity and inadequate sleep quantity.

A maximum one-month screening including a placebo run-in phase of up to 24 days was followed by a 12-week double-blind treatment phase that was in turn followed by a one-week placebo run-out phase and a 23-day follow-up.

During the treatment phase, 930 enrolled patients received either daridorexant 25 mg or 50 mg or placebo according to a 1:1:1 randomisation.

The 303 study is an extension study of the 301 study and comprises a 40-week double-blind treatment phase, followed by a placebo run-out phase and a 23-day follow-up. All patients who completed the double-blind study phase and the single-blind placebo run-out phase of the 301 study were able to participate in the 303 study.

The 303 extension study enrolled 137 patients from the daridorexant 50 mg arm and 57 patients from the placebo arm of the 301 study who continued treatment with daridorexant 50 mg or placebo received in the 301 study.

For the assessment of the additional benefit, the pharmaceutical company uses evaluations that consider the 301 and 303 studies as a continuous study with an additive treatment duration of 52 weeks and compare daridorexant with placebo.

This approach is inappropriate for methodological reasons. Due to the high percentage of dropouts at the end of the 12-week treatment phase of the 301 study, the intention-to-treat (ITT) principle was violated during the transition of study participants into the 303 study to such an extent that purely random discontinuations cannot be assumed:
Of 310 patients allocated to the daridorexant 50 mg arm of the 301 study, only 137 patients (44.2%) were transferred to the 303 extension study; only 57 of the 310 patients (18.4%) initially allocated to the placebo arm of the 301 study were included in the placebo arm of the

303 study. No information is available on the reasons why the majority of patients in the 301 study were not transferred to the 303 study.

Consequently, the combined evaluations of the 301 and 303 studies over an additive study duration of 52 weeks are not eligible for the assessment of an additional benefit of daridorexant.

Furthermore, a study duration of 12 weeks in the present therapeutic indication is considered insufficient for the benefit assessment, which is why the results of the 301 study alone are also not considered for the present assessment.

Overall, there are therefore no suitable data available for the benefit assessment of daridorexant in adults with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning.

The additional benefit of daridorexant over the appropriate comparator therapy for adults with sleep disorders (insomnia), whose symptoms have persisted for at least 3 months and have a significant impact on daytime activity, is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of the active ingredient daridorexant following the amendment of Annex III to the Pharmaceuticals Directive (exceptional case for daridorexant).

The therapeutic indication assessed here is as follows: QUVIVIQ is indicated for the treatment of adult patients with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning.

For adults with sleep disorders (insomnia) whose symptoms have persisted for at least 3 months and have a significant impact on daytime activity, best supportive care is determined to be the appropriate comparator therapy.

For the assessment of additional benefit, the pharmaceutical company presented evaluations that consider the 301 study and the 303 extension study as a continuous study with an additive treatment duration of 52 weeks and compare daridorexant with placebo.

Due to the high percentage of discontinuations before the transition to the 303 extension study, the intention-to-treat principle is not fulfilled in the evaluations presented. In addition, the comparator study duration of 12 weeks of the 301 study alone is considered insufficient in the present therapeutic indication.

In the overall assessment, no suitable data are therefore available for the benefit assessment of daridorexant. An additional benefit of daridorexant for adults with sleep disorders (insomnia), whose symptoms have persisted for at least 3 months and have a significant impact on daytime activity, 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 resolution is based on the information provided by the pharmaceutical company in the dossier.

These are based, among other things, on determining the number of patients with insomnia using data from a Barmer health report focussing on sleep disorders[2] and an extrapolation to the year 2024 using data from a DAK Gesundheit health report[3].

This approach results in uncertainties due to the lack of restriction to patients with a non-medicinal prior therapy and the definition criteria for insomnia on which the calculation of the prevalence is based. Overall, the information is therefore subject to uncertainty.

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 Quviviq (active ingredient: daridorexant) at the following publicly accessible link (last access: 1 July 2024):

https://www.ema.europa.eu/en/documents/product-information/quviviq-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: 15 July 2024).

Adult patients with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning

Treatment period:

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.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Daridorexant	Continuously, 1 x daily	365.0	1	365.0

2 Grobe TG, Steinmann S, Gerr J. Health Report 2019. Sleep disorders. Publication series on health analysis – Volume 17. BARMER; 2019

3 Marschall J, Hildebrandt S, Sydow H, Nolting H. Health Report 2017 - Analysis of data on incapacity for work. Update: Sleep disorders [online], 2017

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Best supportive care	Different from patient to patient			
Appropriate comparator therapy				
Best supportive care				
Best supportive care	Different from patient to patient			

Consumption:

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

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					
Daridorexant	50 mg	50 mg	1 x 50 mg	365.0	365.0 x 50 mg
Best supportive care		Different from patient to patient			
Appropriate comparator therapy					
Best supportive care					
Best supportive care		Different from patient to patient			

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 fixed reimbursement rates 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					
Daridorexant 50 mg	30 FCT	€ 97.93	€ 2.00	€ 4.80	€ 91.13
Abbreviations: FCT = film-coated tablets					

LAUER-TAXE® last revised: 15 July 2024

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 need 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 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 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.

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 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:

Adult patients with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning

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 daridorexant (Quviviq); Quviviq 25mg/50mg film-coated tablets; last revised: April 2024

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 October 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 28 February 2024, the pharmaceutical company submitted a dossier for the benefit assessment of daridorexant to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 3 VerfO.

By letter dated 1 March 2024 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 daridorexant.

The dossier assessment by the IQWiG was submitted to the G-BA on 27 May 2024, and the written statement procedure was initiated with publication on the G-BA website on 3 June 2024. The deadline for submitting statements was 24 June 2024.

The oral hearing was held on 8 July 2024.

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 6 August 2024, and the proposed draft resolution was approved.

At its session on 15 August 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	24 October 2023	Determination of the appropriate comparator therapy
Working group Section 35a	3 July 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	8 July 2024	Conduct of the oral hearing
Working group Section 35a	17 July 2024 31 July 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	6 August 2024	Concluding discussion of the draft resolution
Plenum	15 August 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 15 August 2024

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

Prof. Hecken