Gemeinsamer Bundesausschuss

Resolution

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

of 12 May 2023

At its session on 12 May 2023, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

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

Last revised: 27.04.2023

Daridorexant

Resolution of: 12 May 2023
Entry into force on: 12 May 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 29 April 2022):

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 12 May 2023):

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; application for up to 4 weeks.

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

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

Appropriate comparator therapy:

Short-term drug therapy with short-acting benzodiazepines or non-benzodiazepine receptor agonists, followed by best-supportive-care.

Best supportive care is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life.

Extent and probability of the additional benefit of daridorexant compared to zolpidem:

An additional benefit is not proven.

Study results according to endpoints:[1]

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

[1] Data from the dossier assessment of the IQWiG (A22-123) and from the addendum (A23-22).

Summary of results for relevant clinical endpoints

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

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

Study 201: randomised controlled trial, daridorexant vs zolpidem

Mortality

endpoint; Study	Daridorexant		Zolpidem		Daridorexant vs Zolpidem
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
Overall mortality	61	0 (0)	60	0 (0)	-

Abbreviations used:
CI: confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; RR: relative risk

Morbidity

Endpoint; Study	Daridorexant			Zolpidem			Daridorexant vs zolpidem
	N[a]	Values at the start of the study MV (SD)	Change at end of treatment MV (SD)	N[a]	Values at the start of the study MV (SD)	Change at end of treatment MV (SD)	MD [95% CI]; p value[b]
Severity grade of insomnia							
Insomnia Severity Index (ISI)[c]	55	21.2 (2.7)	−8.5 (6.3)	56	21.2 (2.7)	−9.0 (5.0)	0.54 [−1.58; 2.67]; 0.613[d]
Self-reported sleep parameters							
Daytime wakefulness (SDQ-VAS VASDAY)[e]	57	32.8 (20.1)	16.0 (15.9)	59	32.4 (17.7)	17.3 (17.9)	−2.02 [−7.95; 3.9]; 0.501
Depth of sleep (SDQ-VAS VASDEPTH)[e]	57	30.2 (17.3)	20.1 (17.6)	59	31.8 (15.9)	20.5 (17.4)	−1.9 [−8.08; 4.28]; 0.545
Daily activity (SDQ-VAS VASFUNC)[e]	57	33.6 (20.5)	17.1 (16.6)	59	34.3 (17.0)	16.6 (17.3)	−0.62 [−6.54; 5.31]; 0.838
Sleep quality (SDQ-VAS VASQUAL)[e]	57	30.5 (17.9)	20.9 (17.7)	59	31.6 (15.8)	19.3 (15.6)	0.23 [−5.77; 6.23]; 0.939
Morning sleepiness (SDQ-VAS VASSLEEP)[e]	57	30.2 (19.7)	17.0 (17.6)	59	32.1 (16.9)	16.2 (15.8)	−0.87 [−6.51; 4.78]; 0.762
Polysomnography and self-reported sleep quantity parameters (presented additionally)							
Total duration of waking phases after sleep onset[g] (minutes)	58	95.1 (32.3)	−47.0 (34.0)	59	99.3 (39.1)	−37.1 (36.9)	−12.1 [−22.4; −1,8]; 0.021
Patient-reported total duration of waking phases after sleep onset[h] (minutes)	49	81.3 (48.7)	−35.5 (37.5)	48	78.6 (42.9)	−29.1 (27.3)	−3.4 [−13.5; 6.7]; 0.505
Sleep latency[g] (minutes)	58	70.2 (30.8)	−35.7 (37.6)	59	73.0 (35.0)	−45.8 (37.8)	7.9 [−0.04; 15.8]; 0.051
Patient-reported delayed onset of sleep[h] (minutes)	57	58.3 (30.8)	−23.7 (24.1)	59	51.6 (25.0)	−20.0 (19.3)	0.13 [−5.7; 6.0]; 0.964
Total sleep time[g] (minutes)	58	321.7 (46.0)	80.8 (53.4)	59	316.3 (55.3)	78.7 (54.0)	5.4 [−7.7; 18.6]; 0.416

Endpoint; Study	Daridorexant			Zolpidem			Daridorexant vs zolpidem
	N[a]	Values at the start of the study MV (SD)	Change at end of treatment MV (SD)	N[a]	Values at the start of the study MV (SD)	Change at end of treatment MV (SD)	MD [95% CI]; p value[b]
Patient-reported total sleep time[h] (minutes)	57	316.1 (49.3)	77.4 (58.7)	59	321.9 (53.0)	53.2 (35.5)	21.5 [5.7; 37.3]; 0.008

a) Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at start of study can be based on other patient numbers.
b) Effect, CI and p value: Mixed model with repeated measures (MMRM) adjusted for baseline, sex and interaction of time and treatment.
c) Values at baseline refer to visit 1 at the beginning of the screening phase. Lower (decreasing) values mean better symptomatology; negative effects (intervention minus control) mean an advantage for the intervention (scale range 0 to 28).
d) The calculation is based on an unpaired t-test.
e) Patient-reported sleep parameters using the SDQ; values at baseline refer to the MV of the entries between the screening phase (visit 2) and randomisation (visit 3) over 7 consecutive days; collected until the end of the double-blind treatment phase (week 4); weekly MV of the week is calculated if data are available on ≥ 3 days.
f) Higher (increasing) values mean better symptomatology; positive effects (intervention minus control) mean an advantage for the intervention (scale range 0 to 100).
g) MV of 2 consecutive nights each; values at baseline refer to PSG measurement during the screening phase between day 14 and day 6 before randomisation (visit 2); last PSG measurement was at week 4 (day 28 and day 29).
h) Patient-reported sleep parameters using the SDQ; values at baseline refer to the MV of the entries between the screening phase (visit 2) and randomisation (visit 3) over 7 consecutive days; collected until the end of the double-blind treatment phase (week 4); weekly MV of the week is calculated if data are available on ≥ 3 days.

Abbreviations used:
ISI: Insomnia Severity Index; CI: confidence interval; MD: mean difference; MMRM: mixed model for repeated measures; MV: mean value; N: number of patients evaluated; PSG: polysomnography; SD: standard deviation; SDQ: sleep diary; VAS: visual analogue scale

Health-related quality of life

No data available.

Side effects

endpoint; Study	Daridorexant		Zolpidem		Daridorexant vs Zolpidem
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value
AE (presented additionally)	61	21 (34.4)	60	24 (40.0)	
SAE	61	1 (1.6)	60	0 (0)	– 0.529[a]
Therapy discontinuation due to AEs	61	1 (1.6)	60	1 (1.7)	0.98 [0.06; 15.37]; 0.991

a) IQWiG calculation, unconditional exact test (CSZ method).

Abbreviations used:
CI: confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; RR: relative risk; SAE: serious adverse event; AE: adverse event

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

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

approx. 1,900 – 79,000 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Quviviq (active ingredient: daridorexant) at the following publicly accessible link (last access: 30 March 2023):

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

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Daridorexant	€ 286.34
Appropriate comparator therapy:	
Benzodiazepines	
Lormetazepam	€ 24.46
Triazolam	€ 10.97 - € 12.23
Temazepam	€ 21.90 - € 23.20
Brotizolam	€ 12.23
Flunitrazepam	€ 12.23 - € 24.46
Midazolam	€ 37.64 - € 58.85
Lorazepam	€ 10.73 - € 23.74
Oxazepam	€ 20.21 - € 21.79
Non-benzodiazepine receptor agonists	
Zolpidem	€ 24.42
Zopiclone	€ 24.06
Eszopiclone	€ 13.03 - € 16.19
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 2023)

Costs for additionally required SHI services: not applicable

5. 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 Daridorexant

Medicinal products with the new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients that, according to their approval, can be used in a combination therapy with daridorexant for the treatment of insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning (application for up to 4 weeks):

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

A designation of the concomitant active ingredients shall be made in a further resolution. The adoption of the resolution will be preceded by a written and oral written statement procedure pursuant to Chapter 5, Section 19 of the Regulation, in the course of which the pharmaceutical companies concerned will be given the opportunity to comment on the planned designation.

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

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 12 May 2023.

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

Berlin, 12 May 2023

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

Prof. Hecken