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) and
Annex XIIa – Combinations of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Finerenone (new therapeutic indication: chronic kidney disease in type 2 diabetes, stages 1 and 2 with albuminuria)

of 17 August 2023

At its session on 17 August 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. In Annex XII, the following information shall be added after No. 5 to the information on the benefit assessment of Finerenone in accordance with the resolution of 17 August 2023:

Finerenone

Resolution of: 17 August 2023
Entry into force on: 17 August 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 6 February 2023):

Kerendia is indicated for the treatment of chronic kidney disease (with albuminuria) associated with type 2 diabetes in adults.

Therapeutic indication of the resolution (resolution of 17 August 2023):

Kerendia is indicated for the treatment of chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes in adults.

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

Adults with chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes

Appropriate comparator therapy:

An optimised standard therapy for the treatment of chronic kidney disease and type 2 diabetes mellitus, taking into account the underlying disease(s) and common comorbidities (such as dyslipoproteinaemia, hypertension, anaemia, heart failure).

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

Hint for a non-quantifiable additional benefit

Study results according to endpoints:[1]

Adults with chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes

[1] Data from the dossier assessment of the IQWiG (A23-14) and from the addendum (A23-69), unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑	Advantage in overall mortality
Morbidity	↑	Advantages in case of renal failure and confirmed deterioration of CKD to stage 4 or 5
Health-related quality of life	↔	No relevant differences for the benefit assessment
Side effects	n.a.	There are no assessable data.
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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

FIDELIO-DKD and FIGARO-DKD studies: Finerenone vs placebo (each in addition to optimised standard therapy[2])

Mortality

Endpoint category Endpoint Study	Finerenone		Placebo		Finerenone vs placebo
	N	Median time to event in months [95% CI] Patients with event n (%)	N	Median time to event in months [95% CI] Patients with event n (%)	HR [95% CI]; p value[a]
Overall mortality					
FIDELIO-DKD	211	n.r. 17 (8.1)	221	n.r. 14 (6.3)	1.28 [0.63; 2.60]; 0.490
FIGARO-DKD	2,327	n.r. 166 (7.1)	2,304	n.r. 211 (9.2)	0.77 [0.63; 0.95] 0.013
Total[b]					0.80 [0.66; 0.98]; 0.029

[2] Patient-individual standard therapy according to local guidelines for the treatment of both kidney disease and other comorbidities such as cardiovascular disease or type 2 diabetes mellitus

Morbidity

Endpoint category Endpoint Study	Finerenone		Placebo		Finerenone vs placebo
	N	Median time to event in months [95% CI] Patients with event n (%)	N	Median time to event in months [95% CI] Patients with event n (%)	HR [95% CI]; p value[a]
Renal morbidity with eGFR decrease ≥ 57% (composite endpoint) *(presented additionally)*					
FIDELIO-DKD	*211*	*n.r.* *7 (3.3)*	*221*	*n.r.* *16 (7.2)*	*0.43 [0.18; 1.05]* *0.056*
FIGARO-DKD	*2,327*	*61.90 [n.c.]* *73 (3.1)*	*2,304*	*n.r.* *108 (4.7)*	*0.66 [0.49; 0.89]* *0.006*
Total[b]					*0.63 [0.48; 0.84];* *0.001*
Kidney failure[c, d]					
FIDELIO-DKD	211	n.r. 2 (0.9)	221	n.r. 8 (3.6)	0.25 [0.05; 1.20] 0.062
FIGARO-DKD	2,327	n.r. 22 (0.9)	2,304	n.r. 38 (1.6)	0.57 [0.34; 0.96] 0.032
Total[b]					0.52 [0.32; 0.85]; 0.008
Persistent decrease in eGFR to < 15 ml/min/1.73 m²					
FIDELIO-DKD	211	n.r. 1 (0.5)	221	n.r. 6 (2.7)	0.17 [0.02; 1.43] 0.064
FIGARO-DKD	2,327	n.r. 12 (0.5)	2,304	n.r. 21 (0.9)	0.56 [0.27; 1.13] 0.102
Total[b]					0.48 [0.25; 0.93]; 0.026
ESRD[c, e]					
FIDELIO-DKD	211	n.r. 1 (0.5)	221	n.r. 5 (2.3)	0.21 [0.02; 1.81] 0.118
FIGARO-DKD	2,327	n.r. 17 (0.7)	2,304	n.r. 34 (1.5)	0.49 [0.27; 0.87] 0.013
Total[b]					0.46 [0.26; 0.80]; 0.005
eGFR decrease ≥ 57%[c] *(presented additionally)*					
FIDELIO-DKD	*211*	*n.r.* *6 (2.8)*	*221*	*n.r.* *16 (7.2)*	*0.37 [0.14; 0.95]* *0.031*
FIGARO-DKD	*2,327*	*n.r.* *69 (3.0)*	*2,304*	*n.r.* *97 (4.2)*	*0.70 [0.51; 0.95]* *0.021*
Total[b]					*0.65 [0.48; 0.87];* *0.004*

Endpoint category Endpoint Study	Finerenone		Placebo		Finerenone vs placebo
	N	Median time to event in months [95% CI] Patients with event n (%)	N	Median time to event in months [95% CI] Patients with event n (%)	HR [95% CI]; p value[a]
Renal death[c] *(presented additionally)*					
FIDELIO-DKD	*211*	*n.r.* *0 (0)*	*221*	*n.r.* *0 (0)*	*n.c.*
FIGARO-DKD	*2,327*	*n.r.* *0 (0)*	*2,304*	*n.r.* *1 (< 0.1)*	*0.00 [0.00; n.d.];* *0.365*
Total[b]					-
Confirmed deterioration of CKD to stage 4 or 5[o]					
FIDELIO-DKD	*211*	*n.r.* *11 (5.2)*	*221*	*n.r.* *18 (8.1)*	*0.62 [0.29; 1.31]* *0.204*
FIGARO-DKD	*2,327*	*n.r.* *56 (2.4)*	*2,304*	*n.r.* *79 (3.4)*	*0.69 [0.49; 0.97];* *0.031*
Total[b]					*0.67 [0.49; 0.91];* *0.011*
Cardiovascular morbidity (composite endpoint[g]) (presented additionally)					
FIDELIO-DKD	*211*	*n.r.* 34 (16.1)	*221*	*n.r.* 33 (14.9)	1.08 [0.67; 1.75] 0.740
FIGARO-DKD	*2,327*	*n.r.* 263 (11.3)	*2,304*	*n.r.* 291 (12.6)	0.89 [0.75; 1.05] 0.169
Totalb					0.91 [0.78; 1.06]; 0.238
Cardiovascular death[c]					
FIDELIO-DKD	*211*	*n.r.* *13 (6.2)*	*221*	*n.r.* *12 (5.4)*	1.15 [0.52; 2.52] 0.729
FIGARO-DKD	*2,327*	*n.r.* 105 (4.5)	*2,304*	*n.r.* 124 (5.4)	0.83 [0.64; 1.08]; 0.166
Total[b]					0.86 [0.67; 1.10]; 0.225
Non-fatal myocardial infarction[c]					
FIDELIO-DKD	*211*	*n.r.* *8 (3.8)*	*221*	*n.r.* *9 (4.1)*	*0.93 [0.36; 2.41]* *0.876*
FIGARO-DKD	*2,327*	*n.r.* *55 (2.4)*	*2,304*	*n.r.* *49 (2.1)*	*1.11 [0.75; 1.63]* *0.599*
Total[b]					1.10 [0.77; 1.57]; 0.608
Non-fatal stroke[c]					
FIDELIO-DKD	*211*	*n.r.* *8 (3.8)*	*221*	*n.r.* *11 (5.0)*	*0.77 [0.31; 1.91]* *0.572*

Endpoint category Endpoint Study	Finerenone		Placebo		Finerenone vs placebo
	N	Median time to event in months [95% CI] Patients with event n (%)	N	Median time to event in months [95% CI] Patients with event n (%)	HR [95% CI]; p value[a]
FIGARO-DKD	*2,327*	*n.r.* *76 (3.3)*	*2,304*	*n.r.* *65 (2.8)*	*1.15 [0.83; 1.61]* *0.400*
Total[b]					1.11 [0.81; 1.51]; 0.514
Severe heart failure events (operationalised as hospitalisation due to heart failure)c					
FIDELIO-DKD	*211*	*n.r.* *9 (4.3)*	*221*	*n.r.* *13 (5.9)*	*0.72 [0.31; 1.68]* *0.442*
FIGARO-DKD	*2,327*	*n.r.* *59 (2.5)*	*2,304*	*n.r.* *91 (3.9)*	*0.64 [0.46; 0.89];* *0.008*
Total[b]					0.65 [0.48; 0.88]; 0.005
Serious cardiovascular events (presented additionally)[g]					
FIDELIO-DKD	*211*	*n.d.[h]*	*221*	*n.d.[h]*	*n.d.*
FIGARO-DKD	*2,327*	*n.d.[h]*	*2,304*	*n.d.[h]*	*n.d.*
Total[d]					*0.99 [0.86; 1.13];* *0.839*
Total hospitalisation					
FIDELIO-DKD	*211*	*47.43 [n. c.]* *87 (41.2)*	*221*	*45.83 [n. c.]* *94 (42.5)*	*0.94 [0.70; 1.26]* *0.662*
FIGARO-DKD	*2,327*	*n.r.* *903 (38.8)*	*2,304*	*57.10 [n. c.]* *918 (39.8)*	*0.97 [0.88; 1.06]* *0.506*
Total[b]					*0.97 [0.78; 1.20];* *0.758*

Study Endpoint category Endpoint	Finerenone			Placebo			Finerenone vs placebo
	N[i]	Values at start of study MV (SD)	Mean change in the course of the study MV[j] [95% CI]	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	MD [95% CI]; p value[j]
Health status (EQ-5D VAS)[k]							
FIDELIO-DKD	194	74.6 (16.2)	0.12 [-2.22; 2.45]	205	75.0 (16.5)	0.04 [-2.10; 2.19]	0.07 [-2.28; 2.43] 0.952
FIGARO-DKD	2,151	73.1 (16.9)	0.43 [-0.26; 1.12]	2,133	74.4 (16.5)	0.41 [-0.30; 1.12]	0.02 [-0.72; 0.77] 0.956
Total[m]							0.10 [-0.57; 0.77]; 0.766

Health-related quality of life

Study Endpoint category Endpoint	Finerenone			Placebo			Finerenone vs placebo
	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	MD [95% CI]; p value[j]
KDQOL-36[l]							
PCS							
FIDELIO-DKD	193	43.4 (9.9)	-0.44 [-1.68; 0.81]	202	43.6 (9.9)	-2.24 [-3.59; -0.89]	1.80 [0.37; 3.24] 0.014
FIGARO-DKD	2,137	43.4 (9.8)	-1.25 [-1.66; -0.84]	2,122	43.7 (9.8)	-1.24 [-1.66; -0.82]	-0.01 [-0.45; 0.43]; 0.964
Total[m]							0.13 [-0.26; 0.52]; 0.509
MCS							
FIDELIO-DKD	193	51.3 (9.4)	-0.28 [-1.67; 1.12]	202	52.8 (9.3)	-1.37 [-2.72; -0.01]	1.09 [-0.36; 2.55]; 0.141
FIGARO-DKD	2,137	50.8 (10.0)	-0.37 [-0.81; 0.06]	2,122	51.0 (9.8)	-0.32 [-0.76; 0.13]	-0.06 [-0.53; 0.41]; 0.804
Total[m]							0.04 [-0.38; 0.46]; 0.855
Disease burden of kidney disease							
FIDELIO-DKD	194	75.2 (25.9)	4.24 [1.11; 7.37]	205	76.2 (25.1)	2.88 [-0.49; 6.24]	1.37 [-2.05; 4.78]; 0.432
FIGARO-DKD	2,148	75.4 (26.2)	1.47 [0.38; 2.55]	2,128	76.1 (25.1)	0.95 [-0.15; 2.05]	0.51 [-0.63; 1.66]; 0.381
Total[m]							0.60 [-0.49; 1.68]; 0.281[n]

Study Endpoint category Endpoint	Finerenone			Placebo			Finerenone vs placebo
	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	MD [95% CI]; p value[j]
Symptoms and problems of kidney disease							
FIDELIO-DKD	194	82.6 (15.4)	-0.19 [-1.82; 1.45]	205	84.5 (13.6)	-2.25 [-3.97; -0.53]	2.06 [0.24; 3.88]; 0.027
FIGARO-DKD	2,151	83.1 (15.6)	-1.01 [-1.61; -0.42]	2,133	83.9 (15.0)	-1.04 [-1.63; -0.44]	0.02 [-0.61; 0.65]; 0.944
Total[m]							0.16 [-0.41; 0.73]; 0.586
Effects of kidney disease on daily life							
FIDELIO-DKD	194	87.5 (14.5)	0.62 [-1.11; 2.34]	205	88.7 (14.3)	-1.72 [-3.62; 0.18]	2.34 [0.36; 4.31]; 0.021
FIGARO-DKD	2,143	87.2 (15.9)	0.46 [-0.18; 1.10]	2,128	87.4 (15.4)	-0.05 [-0.72; 0.61]	0.52 [-0.17; 1.20]; 0.139
Total[m]							0.34 [-0.28; 0.96]; 0.288

a. HR [95% CI] for the individual studies from Cox regression model, stratified by region, and for the FIGARO-DKD study, additionally by UACR at the time of screening and cardiovascular history; p value: Log-rank test stratified by the same factors

b. Calculation from IPD meta-analysis with study factor as fixed effect (for model, see footnote "a"); stratified by region, UACR at time of screening and cardiovascular history

c. The presentation of the individual components does not include the qualifying events, but all events that occurred during the study.

d. Renal failure was defined as the occurrence of ESRD or an eGFR < 15 ml/min/1.73 m², confirmed by a 2nd measurement ≥ 4 weeks after the 1st measurement.

e. An ESRD was defined according to Module 4 B as:

- Kidney transplant
- Peritoneal or haemodialysis required for at least 30 days and for which it is not apparent that treatment can be stopped after 90 days.
- Acute kidney damage leading to dialysis or death and occurring during dialysis treatment
- Renal replacement therapy indicated for symptomatic uraemia (eGFR of < 15 ml/min/1.73m2 for at least 30 days) or asymptomatic uraemia (eGFR of < 8 ml/min/1.73m2) but not available or accessible, rejected or considered futile; ESRD is then diagnosed even without initiation of renal replacement therapy.

f. A death was classified as renal if the patient dies and has not received clinically indicated renal replacement therapy and there is no other probable cause of death.

g. Composite endpoint consisting of hospitalisation due to heart failure, other cardiovascular hospitalisation (unstable angina pectoris, arrhythmias, peripheral artery occlusive disease) or adjudicated cardiovascular event associated with hospitalisation (cardiovascular death, new onset of atrial fibrillation or flutter, non-fatal myocardial infarction, non-fatal stroke, transient ischaemic attack)

h. In the IPD meta-analysis, 428 (16.9%) patients in the intervention arm and 430 (17.0%) patients in the comparator arm had an event.

i. 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.

j. Changes and mean difference of the individual studies: MMRM with the covariates treatment group, region, eGFR at the time of screening, time, interaction between treatment and time, baseline value and interaction between baseline value and time, and for the FIDELIO-DKD study, additionally the covariate UACR at the time of screening or for the FIGARO-DKD study, additionally the covariate history of cardiovascular disease

Study Endpoint category Endpoint	Finerenone			Placebo			Finerenone vs placebo
	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	N[i]	Values at start of study MV (SD)	Mean change in the course of study MV[j] [95% CI]	MD [95% CI]; p value[j]
k. Higher (increasing) values mean better symptomatology; positive effects (intervention minus control) mean an advantage for the intervention (scale range 0 to 100). l. Higher (increasing) values mean better symptomatology/ health-related quality of life; positive effects (intervention minus control) mean an advantage for the intervention (scale range: PCS 13 to 69 points; MCS 10 to 70 points; kidney disease burden, symptoms and problems of kidney disease, and impact of kidney disease on daily life each 0 to 100 points). m. Calculation from IPD meta-analysis: MMRM with covariates study, treatment group, region, eGFR at time of screening, UACR at time of screening, history of cardiovascular disease, time, interaction between treatment and time, baseline value and interaction between baseline value and time. n. Own calculation from aggregated data. Results from IPD meta-analysis are not available. o. Decrease in eGFR by ≥ 25% to < 30 ml/min/1.73 m^2 or to < 15 ml/min/1.73m^2 compared to baseline, which had to be confirmed in a 2nd measurement, ≥ 4 weeks after the 1st measurement							
Abbreviations used: eGFR: estimated glomular filtration rate; ESRD: end-stage renal disease; HR: hazard ratio; IPD: individual patient data; KDQOL: Kidney Disease Quality of Life; CI: confidence interval; MCS: mental component summary score; MD: mean difference; MMRM: mixed model for repeated measures; MV: mean value; n: number of patients with (at least 1) event; N: Number of patients evaluated; n.c.: not calculable; n.r. = not reached; PCS: physical component summary score; RCT: randomised controlled trial; SD: standard deviation; SMD: standardised mean difference; UACR: urine albumin-creatinine ratio; VAS: visual analogue scale							

Side effects

No suitable data available.

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

Adults with chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes

approx. 436,400 – 493,750 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 Kerendia (active ingredient: finerenone) at the following publicly accessible link (last access: 27 April 2023):

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

No patients with symptomatic chronic heart failure with reduced left ventricular ejection fraction (HFrEF; NYHA stages II to IV) were studied.

4. Treatment costs

Annual treatment costs:

Adults with chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Finerenone	€ 1,195.71
+ optimised standard therapy	Different from patient to patient
Appropriate comparator therapy:	
Optimised standard therapy	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 July 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 the assessed medicinal product

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

Adults with chronic kidney disease (stages 3 and 4 with albuminuria) associated with type 2 diabetes

The following medicinal products with new active ingredients that can be used in a combination therapy with finerenone in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

- Dapagliflozin (Forxiga)

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. In Annex XIIa of the Pharmaceuticals Directive, the following information shall be added in alphabetical order:

"Active ingredient of the assessed medicinal product

Finerenone

Resolution according to Section 35a paragraph 3 SGB V from

17 August 2023

Therapeutic indication of the resolution

Kerendia is indicated for the treatment of chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes in adults.

Patient group

Adults with chronic kidney disease (stages 1 and 2 with albuminuria) associated with type 2 diabetes

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names)

Dapagliflozin (Forxiga)

Period of validity of the designation (since... or from... to)

Since 17 August 2023"

III. The resolution will enter into force on the day of its publication on the website of the G-BA on 17 August 2023.

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

Berlin, 17 August 2023

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

Prof. Hecken