Vericiguat (chronic heart failure)

Resolution of: 3 March 2022
Entry into force on: 3 March 2022
Federal Gazette, BAnz AT 14 04 2022 B9

Valid until: unlimited

Therapeutic indication (according to the marketing authorisation of 16 July 2021):

Verquvo is indicated for the treatment of symptomatic chronic heart failure in adult patients with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy.

Therapeutic indication of the resolution (resolution of 3 March 2022):

see therapeutic indication according to marketing authorisation.

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

Adults with symptomatic, chronic heart failure with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy

Appropriate comparator therapy:

An optimised standard therapy for the treatment of symptomatic chronic heart failure and underlying conditions such as hypertonia, arrhythmias, coronary heart disease, diabetes mellitus, hypercholesterolaemia and concomitant symptoms

Extent and probability of the additional benefit of vericiguat compared to optimised standard therapy for symptomatic, chronic heart failure:

Hint for a minor additional benefit

Study results according to endpoints:[1]

Adults with symptomatic chronic heart failure with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy

[1] Data from the dossier assessment of the IQWiG (A21-120) and from the addendum (A22-08), unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment.
Morbidity	↑	Advantage in total hospitalisation
Health-related quality of life	↑	Improvement by ≥ 5 points in the KCCQ-OSS; no statistically significant difference for an improvement by ≥ 15 points (corresponds to 15%)
Side effects	↔	No relevant difference for the benefit assessment for the overall rate of SAEs and discontinuation due to AEs; in detail, one advantage and disadvantage for each of the specific AEs

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

VICOTRIA study: vericiguat vs placebo (each in addition to optimised standard therapy[2])

Mortality

Endpoint	Vericiguat + optimised standard therapy		Placebo + optimised standard therapy		Intervention vs control
	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] Absolute difference (AD)
Overall mortality	2,158	n.a. 443 (20.5)	2,158	n.a. 464 (21.5)	0.94 [0.83; 1.07]; 0.363
Cardiovascular death (presented additionally)	2,158	n.a. 358 (16.6)	2,158	n.a. 384 (17.8)	0.92 [0.80; 1.06]; 0.256

[2] In terms of patient-individual therapy of heart failure through the use of ACE inhibitors, angiotensin II receptor blockers (ARBs), sacubitril/valsartan, beta-blockers, mineralocorticoid receptor antagonists (MRAs), diuretics, including the treatment of other cardiovascular risk factors and comorbidities

Morbidity

Endpoint	Vericiguat + optimised standard therapy		Placebo + optimised standard therapy		Intervention vs control
	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] *Absolute difference (AD)*
Total hospitalisation	2,158	13.5 [12.2; 14.9] 1,092 (50.6)	2,158	11.2 [10.2; 12.7] 1,158 (53.7)	0.91 [0.83; 0.98]; 0.019 *AD = 3.1%*
Hospitalisation due to heart failure[h] (presented additionally)	*2,158*	*n.a.* *602 (27.9)*	*2,158*	*n.a.* *659 (30.5)*	*0.88 [0.79; 0.99]; 0.029* *AD = 2.6%*
Myocardial infarction	2,158	n.a. 39 (1.8)	2,158	n.a. 37 (1.7)	1.04 [0.66; 1.63]; 0.863
Stroke	2,158	n.a. 32 (1.5)	2,158	n.a. 31 (1.4)	1.02 [0.62; 1.68]; 0.930
Endpoint	**Vericiguat + optimised standard therapy**		**Placebo + optimised standard therapy**		**Intervention vs control**
	N[b]	Patients with event n (%)	N[b]	Patients with event n (%)	RR [95% CI] p value[c] *Absolute difference (AD)*
Health status					
EQ-5D VAS improvement ≥ 15 points[d]	1,753	483 (27.6)	1,739	460 (26.5)	1.04 [0.93; 1.16]; 0.457

Health-related quality of life

Endpoint	Vericiguat + optimised standard therapy		Placebo + optimised standard therapy		Intervention vs control
	N[b]	Patients with event n (%)	N[b]	Patients with event n (%)	RR [95% CI] p value[c] *Absolute difference (AD)*
KCCQ-OSS improvement ≥ 15 points[d]	1,655	558 (33.7)	1,628	536 (34.6)	0.98 [0.89; 1.07]; 0.606
Domains (presented additionally)					
Physical limitations	*1,726*	*588 (34.1)*	*1,718*	*576 (33.5)*	*1.02 [0.93; 1.12]*
Symptoms (KCCQ-TSS)	*1,760*	*581 (33.0)*	*1,751*	*613 (35.0)*	*0.94 [0.86; 1.03]*
Social limitations	*1,669*	*656 (39.3)*	*1,642*	*610 (37.1)*	*1.06 [0.97; 1.15]*
Psychological limitations	*1,760*	*755 (42.9)*	*1,751*	*738 (42.1)*	*1.02 [1.94; 1.10]*
KCCQ-OSS improvement ≥ 5 points[d]	1,655	953 (57.6)	1,628	865 (53.1)	1.08 [1.02; 1.15]; 0.010 *AD = 4.5%*
Domains (presented additionally)					
Physical limitations	*1,726*	*867 (50.2)*	*1,718*	*869 (50.6)*	*0.99 [0.93; 1.06]*
Symptoms (KCCQ-TSS)	*1,760*	*939 (53.4)*	*1,751*	*926 (52.9)*	*1.01 [0.95; 1.07]*
Social limitations	*1,669*	*928 (55.6)*	*1,642*	*882 (53.7)*	*1.04 [0.97; 1.10]*
Psychological limitations	*1,760*	*1,020 (58.0)*	*1,751*	*977 (55.8)*	*1.04 [0.98; 1.10]*

Side effects

Endpoint	Vericiguat + optimised standard therapy		Placebo + optimised standard therapy		Intervention vs control
	N[b]	Patients with event n (%)	N[b]	Patients with event n (%)	RR [95% CI]; p value[c] *Absolute difference (AD)*
Overall rates					
AE (presented additionally)[e]	*2,152*	*1,726 (80.2)*	*2,151*	*1,741 (80.9)*	–
SAE[e]	2,152	702 (32.6)	2,151	743 (34.5)	0.94 [0.87; 1.03]; 0.182[f]
Discontinuation due to AEs[e]	2,152	139 (6.5)	2,151	134 (6.2)	1.04 [0.82; 1.30]; 0.758[f]
Specific adverse events					
Hypotension (PT, SAE)[e]	2,152	31 (1.4)	2,151	38 (1.8)	0.82 [0.51; 1.31]; 0.530[g]
Blood and lymphatic system disorders (SOC, SAE)	2,152	39 (1.8)	2,151	20 (0.9)	1.92 [1.15; 3.21]; 0.013[g] *AD = 0.9%*
Atrial fibrillation (PT, SAE)[e]	2,152	9 (0.4)	2,151	26 (1.2)	0.38 [0.19; 0.73]; 0.004[g] *AD = 0.8%*

a. Unless otherwise stated, HR [95% CI], based on Cox regression model with treatment as covariate, stratified by region and ancestry; p value based on two-sided log-rank test, stratified by region and ancestry

b. Endpoints of the categories morbidity and health-related quality of life: missing values were replaced by means of LOCF

c. Unless otherwise stated: RR [95% CI] according to Mantel-Haenszel method, stratified by region and ancestry, p value of RR based on two-sided Wald test

d. Percentage of patients with an increase of ≥ 15 points and 5 points respectively compared to the baseline at week 32 with a scale range of 0 to 100. Higher (increasing) values mean an improvement of health-related quality of life / symptomatology.

e. No indication whether disease-related events are included in the overall rate, no distinction possible between side effects of the intervention and symptomatology of the underlying disease

f. RR [95% CI] based on log-binomial regression model with Wald CI, p value based on two-sided Wald test

g. RR [95% CI] based on log-binomial regression model with Wald CI. If the event rate in ≥ 1 group is ≤ 1%: Peto OR as estimator for the relative risk; p value: own calculation, unconditional exact test (CSZ method according to [Andrés et al.,1994])

h. For the additionally presented endpoint Hospitalisation due to heart failure, there is an effect modification by the age characteristic (HR [95% CI]): < 75 years: 0.81 [0.71; 0.92], p value: 0.002; ≥ 75 years 1.08 [0.89; 1.31], p value: 0.477. See page 34 IQWiG dossier assessment (A21-120).

AD: absolute difference; EQ-5D: European Quality of Life Questionnaire - 5 Dimensions; ESRD: end-stage kidney disease; HR: hazard ratio; n. d.: no data available; KCCQ: Kansas City Cardiomyopathy Questionnaire; CI: confidence interval; LOCF: last observation carried forward; n: number of patients with (at least 1) event; N: number of patients evaluated; n.a.: not achieved; OSS: overall summary score; RCT: randomised

controlled trial; RR: relative risk; TSS: total symptom score; VAS: visual analogue scale; vs: versus

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

Adults with symptomatic, chronic heart failure with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy

approx. 74,600 to 530,000 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 Verquvo (active ingredient: vericiguat) at the following publicly accessible link (last access: 21 December 2021):

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

4. Treatment costs

Annual treatment costs:

Adults with symptomatic, chronic heart failure with reduced ejection fraction who are stabilised after a recent decompensation event requiring IV therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Vericiguat	€ 1,593.33
+ 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: 15 February 2022)

Costs for additionally required SHI services: not applicable