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Vericiguat (cardiac failure) –

Addendum to Commission A21-120[1]

Addendum

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List of abbreviations

Abbreviation	Meaning
CHF	chronic heart failure
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
i.v.	intravenous

1 Background

On 25 January 2022, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A21-120 (Vericiguat – Benefit assessment according to §35a Social Code Book V) [1].

The commissioned order comprises an assessment of the data on the outcome of all-cause hospitalization from the VICTORIA study.

The responsibility for the present assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

The randomized controlled trial VICTORIA was used for the benefit assessment of vericiguat in patients with symptomatic chronic heart failure (CHF) with reduced ejection fraction who were stabilized after a recent decompensation event which required intravenous (i.v.) therapy. Said study compared vericiguat with placebo, each in combination with individualized CHF therapy.

A detailed description of the VICTORIA study can be found in dossier assessment A21-120 [1].

All-cause hospitalization was not a planned outcome in the VICTORIA study. Consequently, the pharmaceutical company (hereinafter "company") did not submit any results on this outcome in its dossier [2]. Following the oral hearing [3], the company subsequently submitted corresponding results. However, the company did not provide any information on this outcome's operationalization. Hence, the exact criteria (e.g. on the duration of hospitalization) for inclusion of hospitalizations in the outcome are unclear. In addition, information is missing on the reasons for hospitalization, particularly for non-cardiovascular hospitalizations. Depending on the context of care, the outcome of all-cause hospitalization may also include less relevant events leading to hospitalization (e.g. elective procedures). The subsequently submitted analyses of the outcome of all-cause hospitalization are therefore unsuitable for the benefit assessment.

Below, the outcome of all-cause hospitalization is assessed as commissioned.

Risk of bias on the outcome level

The risk of bias on the outcome level for the outcome of all-cause hospitalization was rated as low.

Results

Table 1 summarizes the results regarding the outcome of all-cause hospitalization for the comparison of vericiguat + optimized standard therapy versus placebo + optimized standard therapy for symptomatic CHF in patients with reduced ejection fraction who are stabilized after a recent decompensation event requiring i.v. therapy.

Table 1: Results (all-cause hospitalization) – RCT, direct comparison: vericiguat + optimized standard therapy vs. placebo + optimized standard therapy

Study Outcome category Outcome	Vericiguat + optimized standard therapy		Placebo + optimized standard therapy		Vericiguat + optimized standard therapy vs. placebo + optimized standard therapy
	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]
VICTORIA					
Morbidity					
All-cause hospitalization	2158	13.5 [12.2; 14.9] 1092 (50.6)	2158	11.2 [10.2; 12.7] 1158 (53.7)	0.91 [0.83; 0.98]; 0.019
Heart failure	2158	– 445 (20.6)	2158	– 497 (23.0)	–[b]
Myocardial infarction	2158	– 26 (1.2)	2158	– 24 (1.1)	–[b]
Stroke	2158	– 18 (0.8)	2158	– 20 (0.9)	–[b]
Other cardiovascular event	2158	– 205 (9.5)	2158	– 240 (11.1)	–[b]
Noncardiovascular	2158	– 398 (18.4)	2158	– 377 (17.5)	–[b]

a. HR [95% CI] based on Cox regression model with treatment as a covariable, stratified by region and ancestry; p-value based on two-sided logrank test stratified by region and ancestry.
b. No calculation of the effect estimations. The presented events do not represent the outcome exhaustively. Only events that are relevant for the formation of the composite outcome are presented.

CI: confidence interval; HR: hazard ratio; n: number of patients with (at least 1) event; N: number of analysed patients; RCT: randomized controlled trial

A statistically significant difference in favour of vericiguat + optimized standard therapy was found for the outcome of all-cause hospitalization.

Subgroups and other effect modifiers

The following subgroup characteristics were taken into account in dossier assessment A21-120:

- age (< 75 years versus ≥ 75 years)
- sex (male versus female)
- severity of heart failure (New York Heart Association class I/II vs. III/IV)

Regarding the outcome of all-cause hospitalization, none of these characteristics exhibit any statistically significant interaction between treatment and subgroup characteristic (p-value < 0.05).

2.1 Summary

The data subsequently submitted by the company in the commenting procedure have not changed the conclusion on the added benefit of vericiguat from dossier assessment A21-120.

The following Table 2 shows the result of the benefit assessment of vericiguat, taking into account dossier assessment A21-120 and the present addendum.

Table 2: Vericiguat – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adults with symptomatic chronic heart failure with reduced ejection fraction who are stabilized after a recent decompensation event requiring intravenous therapy	Optimized standard therapy for the treatment of symptomatic chronic heart failure and underlying medical conditions, e.g. hypertension, cardiac arrhythmia, coronary heart disease, diabetes mellitus, hypercholesterolaemia and the concomitant symptoms	▪ Age < 75 years: hint of a non-quantifiable added benefit. ▪ Age ≥ 75 years: added benefit not proven.
a. Presented is the respective ACT specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The G-BA decides on the added benefit.

3 References

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Vericiguat (Herzinsuffizienz) – Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2021 [Accessed: 15.12.2021]. URL: https://www.iqwig.de/download/a21-120_vericiguat_nutzenbewertung-35a-sgb-v_v1-0.pdf.

2. Bayer Vital. Vericiguat (VERQUVO); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2021 [Accessed: 10.01.2022]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/738/#dossier.

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