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
Casirivimab/ Imdevimab (post-exposure prophylaxis of COVID-19 infection, ≥ 12 years)

of 6 October 2022

At its session on 6 October 2022, 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 Casirivimab/ Imdevimab as follows:

Casirivimab/ imdevimab

Resolution of: 6 October 2022
Entry into force on: 6 October 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 12 November 2021):

Ronapreve is indicated for prevention of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg.

Therapeutic indication of the resolution (resolution of 6 October 2022):

See therapeutic indication according to marketing authorisation

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

a) Adults and adolescents weighing at least 40 kg for post-exposure prophylaxis of COVID-19 following exposure to viral variants for which casirivimab/ imdevimab has insufficient efficacy.

Appropriate comparator therapy for post-exposure prophylaxis:

Monitoring wait-and-see approach

Extent and probability of the additional benefit of casirivimab/ imdevimab compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults and adolescents weighing at least 40 kg and without complete immunisation for post-exposure prophylaxis of COVID-19 after exposure to viral variants for which casirivimab/ imdevimab has sufficient efficacy.

Appropriate comparator therapy for post-exposure prophylaxis:

Monitoring wait-and-see approach

Extent and probability of the additional benefit of casirivimab/ imdevimab compared to the appropriate comparator therapy:

Hint for a minor additional benefit.

c) Adults and adolescents weighing at least 40 kg and with complete immunisation for post-exposure prophylaxis of COVID-19 after exposure to viral variants for which casirivimab/ imdevimab has sufficient efficacy.

Appropriate comparator therapy for post-exposure prophylaxis:

Monitoring wait-and-see approach

Extent and probability of the additional benefit of casirivimab/ imdevimab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults and adolescents weighing at least 40 kg for post-exposure prophylaxis of COVID-19 following exposure to viral variants for which casirivimab/ imdevimab has insufficient efficacy.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.

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

No suitable data submitted.

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-47) unless otherwise indicated.

b) Adults and adolescents weighing at least 40 kg and without complete immunisation for post-exposure prophylaxis of COVID-19 after exposure to viral variants for which casirivimab/ imdevimab has sufficient efficacy.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant differences for the benefit assessment.
Morbidity	↑	Advantages of hospitalisation due to COVID-19 (cohort B) and symptomatic SARS-CoV-2 infections.
Health-related quality of life	∅	No data available.
Side effects	↔	No relevant differences 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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

COV-2069 study: randomised, double-blind phase III study comparing casirivimab/ imdevimab vs placebo

Cohort A: SARS-CoV-2 negative at the start of the study, ≥ 12 years;

Cohort B: SARS-CoV-2 positive at the start of the study, ≥ 12 years

Mortality

COV-2069 study Endpoint	Casirivimab/ imdevimab		Placebo		Casirivimab/ imdevimab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
Overall mortality (until day 225)					
Cohort A (negative SARS-CoV-2 RT-qPCR test at the start of the study)	1174	3 (0.3)	1143	1 (0.1)	2.92 [0.30; 28.04]; 0.530

Cohort B (positive SARS-CoV-2 RT-qPCR test at the start of the study)	165	0 (0)	171	0 (0)	–

Morbidity

COV-2069 study Endpoint	**Casirivimab/ imdevimab**		**placebo**		**Casirivimab/ imdevimab vs placebo**
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a;] Absolute difference (AD)[2]
Symptomatic SARS-CoV-2 infection (broad definition)					
Cohort A (negative SARS-CoV-2 RT-qPCR test at the start of the study)	1174	15 (1.3)	1143	78 (6.8)	0.19 [0.11; 0.32]; < 0.001 AD: 5.5%
Cohort B (positive SARS-CoV-2 RT-qPCR test at the start of the study)	165	35 (21.2)	171	59 (34.5)	0.61 [0.43; 0.88]; 0.007 AD: 13.3%
Symptomatic SARS-CoV-2 infection (CDC definition; presented additionally)					
Cohort A (negative SARS-CoV-2 RT-qPCR test at the start of the study)	1174	9 (0.8)	1143	61 (5.3)	0.14 [0.07; 0.29]; < 0.001 AD: 4.5%
Cohort B (positive SARS-CoV-2 RT-qPCR test at the start of the study)	165	32 (19.4)	171	55 (32.2)	0.60 [0.41; 0.88]; 0.009 AD: 12.8%
Positive SARS-CoV-2 RT-qPCR test independent of symptoms (presented additionally)					
Cohort A (negative SARS-CoV-2 RT-qPCR test at the start of the study)	1174	56 (4.8)	1143	145 (12.7)	0.38 [0.28; 0.51]; < 0.001 AD: 7.9%
Cohort B	Not applicable				

[2] Only in the case of statistically significant results.

COV-2069 study Endpoint	Casirivimab/ imdevimab		placebo		Casirivimab/ imdevimab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]; Absolute difference (AD)[2]
(positive SARS-CoV-2 RT-qPCR test at the start of the study)					
Hospitalisation due to COVID-19 (until day 29)					
Cohort A (negative SARS-CoV-2 RT-qPCR test at the start of the study)	1174	0 (0)	1143	1 (0.1)	0.32 [0.01; 7.96][b]; 0.369
Cohort B (positive SARS-CoV-2 RT-qPCR test at the start of the study)	165	0 (0)	171	4 (2.3)	-[c]; 0.049 AD: 2.3%

Health-related quality of life

No endpoints of the quality of life category were assessed.

Side effects

COV-2069 study Endpoint	Casirivimab/ imdevimab		placebo		Casirivimab/ imdevimab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
AEs (presented additionally)					
No usable data available[d]					
SAEs					
No usable data available[d]					
Severe AEs[e]					

COV-2069 study Endpoint	Casirivimab/ imdevimab		placebo		Casirivimab/ imdevimab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
No usable data available[d]					
Discontinuation due to AEs					
Cohort A (negative SARS-CoV-2 RT-qPCR test at the start of the study)	1439	0	1428	0	–
Cohort B (positive SARS-CoV-2 RT-qPCR test at the start of the study)	165	0	170	0	–

a: IQWiG's own calculation, unconditional exact test (CSZ method according to Andrés et al, 1994).
b: IQWiG's own calculation, asymptotic
c: Discrepancy between p value (exact) and CI (asymptotic) due to different calculation methods; no presentation of effect estimate and CI, as not informative.
d: The pharmaceutical company does not provide any information on the events which it classifies as disease-related.
e: Severe AEs are operationalised as CTCAE grade ≥ 3.

Abbreviations used:
CTCAE: Common Terminology Criteria for Adverse Events; CI: confidence interval; n: number of subjects with (at least 1) event; N: number of subjects evaluated; RCT: randomised controlled trial; RR: relative risk; RT-qPCR: quantitative reverse transcriptase polymerase chain reaction; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus Type 2; SAE: serious adverse event; AE: adverse event; vs: versus

c) Adults and adolescents weighing at least 40 kg and with complete immunisation for post-exposure prophylaxis of COVID-19 after exposure to viral variants for which casirivimab/ imdevimab has sufficient efficacy.

Summary of results for relevant clinical endpoints

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No suitable data submitted.

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

Adults and adolescents weighing at least 40 kg for post-exposure prophylaxis of COVID-19 following exposure to viral variants for which casirivimab/ imdevimab has insufficient efficacy. (Patient population a)

0 patients

Adults and adolescents weighing at least 40 kg for post-exposure prophylaxis of COVID-19 following exposure to viral variants for which casirivimab/ imdevimab has sufficient efficacy. (Patient populations b + c)

0 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 Ronapreve (combination of active ingredients: casirivimab/ imdevimab) at the following publicly accessible link (last access: 2 September 2022):

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

The decision to use casirivimab/ imdevimab for treatment shall take into account the evidence on the characteristics of the circulating SARS CoV-2 viruses, including regional or geographical differences, and the available information on their sensitivity patterns to casirivimab/ imdevimab.

For casirivimab/ imdevimab, no sufficient efficacy could be demonstrated against variants of the Omicron virus[3] circulating alone in Germany at the time of the decision using *in vitro* neutralisation tests.

4. Treatment costs

Annual treatment costs:

Adults and adolescents weighing at least 40 kg for post-exposure prophylaxis of COVID-19. (Patient population a - c)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Casirivimab/ imdevimab	incalculable
Appropriate comparator therapy:	
Monitoring wait-and-see approach	incalculable

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 6 October 2022.

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

Berlin, 6 October 2022

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

Prof. Hecken

[3] RKI weekly situation report on the coronavirus disease-2019 (COVID-19) (15.09.2022)