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
Isavuconazole (new therapeutic indication: aspergillosis, ≥ 1 to ≤ 17 years)

of 20 March 2025

At its session on 20 March 2025, 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 Isavuconazole in accordance with the resolution of 4 May 2016.

Isavuconazole

Resolution of: 20 March 2025
Entry into force on: 20 March 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 22 August 2024):

CRESEMBA is indicated in patients from 1 year of age and older for the treatment of

- invasive aspergillosis
- mucormycosis in patients for whom amphotericin B is inappropriate

Therapeutic indication of the resolution (resolution of 20 March 2025):

CRESEMBA is indicated in children and adolescents from 1 year of age and older for the treatment of invasive aspergillosis.

1. Extent of the additional benefit and significance of the evidence

Isavuconazole is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The G-BA determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Children and adolescents aged 1 to ≤ 17 years with invasive aspergillosis

Extent of the additional benefit and significance of the evidence of isavuconazole:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Children and adolescents aged 1 to ≤ 17 years with invasive aspergillosis

There are no assessable data.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	∅	No data available.
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 ∅: No data available. n.a.: not assessable		

9766-CL-0107 study: Uncontrolled phase II study

Mortality

Endpoint	Isavuconazole			
	IA proven or probable		IFD possible	
	N	*Patients with event n (%)*	N	*Patients with event n (%)*
Deaths on day 42[a)]	12	1 (8.3)	16	1 (6.3)

[1] Data from the dossier assessment of the G-BA (published on 2. January 2025), unless otherwise indicated.

Morbidity

Endpoint	Isavuconazole			
	IA proven or probable		IFD possible	
	N	*Patients with event n (%)*	N	*Patients with event n (%)*
Clinical response according to the principal investigator's assessment of EOT				
Success[b)]	n.a.			
Failure[c)]	n.a.			
Not assessable [d)]	n.a.			

Health-related quality of life

Data on health-related quality of life were not collected.

Side effects

Endpoint **MedDRA system organ classes/ preferred terms/ AEs of special interest**	**Isavuconazole**			
	IA proven or probable		**IFD possible**	
	N	*Patients with event n (%)*	N	*Patients with event n (%)*
Total adverse events (presented additionally)	12	11 (91.7)	16	15 (93.8)
Severe AEs[e)]	12	6 (50.0)	16	9 (56.3)
Serious adverse events (SAE)	12	9 (75.0)	16	9 (56.3)
Therapy discontinuation due to adverse events	12	2 (16.7)	16	1 (6.3)
Severe adverse events according to MedDRA (with an incidence ≥ 10%; SOC)				
Blood and lymphatic system disorders	12	1 (8.3)	16	2 (12.5)
Infections and infestations	12	1 (8.3)	16	7 (43.8)
Musculoskeletal and connective tissue disorders	12	1 (8.3)	16	2 (12.5)
Renal and urinary disorders	12	0	16	2 (12.5)

Respiratory, thoracic and mediastinal disorders	12	3 (25.0)	16	3 (18.8)
Vascular disorders	12	1 (8.3)	16	2 (12.5)
SAEs according to MedDRA (with an incidence ≥ 10%; SOC)				
Blood and lymphatic system disorders	12	2 (16.7)	16	0
Gastrointestinal disorders	12	2 (16.7)	16	1 (6.3)
Infections and infestations	12	2 (16.7)	16	8 (50.0)
Musculoskeletal and connective tissue disorders	12	2 (16.7)	16	1 (6.3)
Respiratory, thoracic and mediastinal disorders	12	2 (16.7)	16	1 (6.3)
Blood and lymphatic system disorders	12	2 (16.7)	16	0
Gastrointestinal disorders	12	2 (16.7)	16	1 (6.3)
Infections and infestations	12	2 (16.7)	16	8 (50.0)

a. Primary endpoint of the 9766-CL-0107 study
b. In SAP and the eCRF, a distinction was made between "complete" and "partial" success. This distinction is not made in the presentation of results.
c. In the SAP and eCRF, a distinction was made between "stable symptoms and findings" and "progression of symptoms and findings". This distinction is not made in the presentation of results.
d. One subject in each of these groups was not categorised by this endpoint. It is unclear why these subjects were not assigned to the "Not evaluable" category, which according to SAP includes "No assessment or no clinical signs or symptoms at the start of the study".
e. The study's own criteria were used for severity grading.

Abbreviations used:

eCRF: electronic case report form; EOT: end of treatment; FAS: full analysis set; IA: invasive aspergillosis; IA: invasive aspergillosis; IFD: invasive fungal disease; MedDRA: Medical Dictionary for Regulatory Activities; SAE: serious adverse event; SAP: statistical analysis plan

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

Children and adolescents aged 1 to ≤ 17 years with invasive aspergillosis

Approx. 40 to 215 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 Cresemba (active ingredient: isavuconazole) at the following publicly accessible link (last access: 10 February 2025):

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

4. Treatment costs

Annual treatment costs:

Children and adolescents aged 1 to ≤ 17 years with invasive aspergillosis

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Isavuconazole	€ 45,656.81 - € 165,053.00

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 March 2025)

Costs for additionally required SHI services: not applicable

5. Designation of 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:

Children and adolescents aged 1 to ≤ 17 years with invasive aspergillosis

- No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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 20 March 2025.

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

Berlin, 20 March 2025

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

Prof. Hecken