

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
Ivacaftor/ Tezacaftor/ Elexacaftor (new therapeutic
indication: cystic fibrosis, combination regimen with
ivacaftor, 6 to 11 years (heterozygous for F508del and other
or unknown mutations))

of 4 August 2022

At its session on 4 August 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. **In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Ivacaftor/ Tezacaftor/ Elexacaftor in accordance with the resolution of 4 August 2022:**

Ivacaftor/ Tezacaftor/ Elexacaftor

Resolution of: 4 August 2022
Entry into force on: 4 August 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 7 January 2022):

Kaftrio is indicated in a combination regimen with ivacaftor for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

Therapeutic indication of the resolution (resolution of 4 August 2022):

Kaftrio is indicated in a combination regimen with ivacaftor for the treatment of cystic fibrosis in children aged 6 to 11 years, who are heterozygous for the F508del mutation in the CFTR gene and carry a mutation on the second allele, which is not a minimal function, gating (including R117H) or residual function mutation, or the mutation on the second allele is unknown (other mutations).

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

Children aged 6 to 11 years with cystic fibrosis, who are heterozygous for the F508del mutation in the CFTR gene and carry a mutation on the second allele, which is not a minimal function, no gating (including R117H) and no residual function mutation, or the mutation on the second allele is unknown (other mutations)

Appropriate comparator therapy for Ivacaftor/ Tezacaftor/ Elexacaftor in combination with Ivacaftor:

Best supportive care

Best Supportive Care (BSC) is defined as the therapy that ensures the best possible, patient-individual optimised, supportive treatment to alleviate symptoms and improve the quality of life (in particular antibiotics for pulmonary infections, mucolytics, pancreatic enzymes for pancreatic insufficiency, physiotherapy (as defined in the Remedies Directive), making full use of all possible dietary measures).

Extent and probability of the additional benefit of Ivacaftor/ Tezacaftor/ Elexacaftor in combination with ivacaftor compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

Children aged 6 to 11 years with cystic fibrosis, who are heterozygous for the F508del mutation in the CFTR gene and carry a mutation on the second allele, which is not a minimal function, no gating (including R117H) and no residual function mutation, or the mutation on the second allele is unknown (other mutations)

No data are available to allow an assessment of the additional benefit.

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		

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

Children aged 6 to 11 years with cystic fibrosis, who are heterozygous for the F508del mutation in the CFTR gene and carry a mutation on the second allele, which is not a minimal function, no gating (including R117H) and no residual function mutation, or the mutation on the second allele is unknown (other mutations)

approx. 56 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 Kaftrio (combination of active ingredients: ivacaftor/tezacaftor/ elexacaftor) at the following publicly accessible link (last access: 17 May 2022):

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

Treatment with ivacaftor/ tezacaftor/ elexacaftor should only be initiated and monitored by doctors experienced in treating children with cystic fibrosis.

4. Treatment costs

Annual treatment costs:

Children aged 6 to 11 years with cystic fibrosis, who are heterozygous for the F508del mutation in the CFTR gene and show a mutation on the second allele, which is not a minimal function, no gating (including R117H) and no residual function mutation, or the mutation on the second allele is unknown (other mutations)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ivacaftor/ tezacaftor/ elexacaftor	€ 156,562.19
+ ivacaftor	€ 82,914.18 - € 82,970.63
Total:	€ 239,476.37 - € 239,532.81
+ best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2022)

Costs for additionally required SHI services: not applicable

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 4 August 2022.

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

Berlin, 4 August 2022

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

Prof. Hecken