

Resolution



Gemeinsamer
Bundesausschuss

**of the Federal Joint Committee (G-BA) on an
Amendment of the Pharmaceuticals Directive
(AM-RL):**

**Annex XII– Resolutions on the Benefit
Assessment of Medicinal Products with New
Active Ingredients According to Section 35a
SGB V**

**Lumacaftor/ivacaftor (new therapeutic
indication: cystic fibrosis, patients aged 2–5
years)**

of 15 August 2019

At its session on 15 August 2019, the Federal Joint Committee (G-BA) resolved to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (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 on DD 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 lumacaftor/ivacaftor in accordance with the resolution of 2 August 2018:

Lumacaftor/ivacaftor

Resolution of: 15 August 2019
Entry into force on: 15 August 2019
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 15 January 2019):

Orkambi® granules are indicated for the treatment of cystic fibrosis (CF) in children aged 2 years and older who are homozygous for the *F508del* mutation in the *CFTR* gene.

The present resolution relates exclusively to the newly approved therapeutic indication of 15 January 2019 (i.e. children from 2 to 5 years of age with cystic fibrosis who are homozygous for the F508del mutation in the CFTR gene).

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

Patients aged 2 to 5 years with cystic fibrosis who are homozygous for the *F508del* mutation.

Appropriate comparator therapy:

- 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 quality of life (especially antibiotics for pulmonary infections, mucolytics, pancreatic enzymes for pancreatic insufficiency, physiotherapy (in the sense of the HeilmittelRichtlinie (Remedies Directive)), under exhaustion of all possible dietary measures).

Extent and probability of the additional benefit of lumacaftor/ivacaftor compared with best supportive care:

Hint for a non-quantifiable additional benefit.

Study results according to endpoints:¹

Patients aged 2 to 5 years with cystic fibrosis who are homozygous for the F508del mutation.

VX15-809-115 study: lumacaftor/ivacaftor (LUM/IVA)

Endpoint category	LUM/IVA
Mortality	
No deaths occurred.	

Endpoint category Endpoint	LUM/IVA				
	Baseline		Absolute change to Week 24		Mean change from baseline to week 24
	N	MV (SD)	N	MV (SD)	MD (SD) [95% CI] p value
Morbidity					
Absolute change in FEV ₁ [%]	17	83.1 (10.8)	12	86.1 (10.1)	0.5 (11.6) [-20.2; 18.5] p = 0.883
Absolute change in LCI _{2,5}	24	9.01 (1.94)	21	8.31 (1.52)	-0.58 (1.16) [-1.17; 0.02] p = 0.056
Absolute change in BMI [kg/m ²]	60	15.98 (1.03)	57	16.26 (0.98)	0.27 (0.75) [0.07; 0.47] p = 0.009
Absolute change in BMI z-score < 20 years	60	0.17 (0.80)	57	0.45 (0.76)	0.29 (0.57) [0.14; 0.45] p < 0.001

¹ Data from the dossier unless otherwise indicated.

Endpoint category Endpoint	LUM/IVA	
	N	Events nE/patient years
Morbidity		
Pulmonary exacerbations	60	25/29
Hospitalisations because of CF	60	4/29

Endpoint category	LUM/IVA
Health-related quality of life	
not collected	

Endpoint category Endpoint	LUM/IVA	
	N	Number of patients with event n (%)
Side effects		
AEs overall	60	59 (98.3)
SAE	60	4 (6.7)
Serious AEs (≥ Grade 3)	60	5 (8.3)
Therapy discontinuations because of AEs	60	3 (5.0)
<p>Abbreviations used: BMI: Body Mass Index; CF: cystic fibrosis; FEV₁%: Percent value of the predicted, forced one-second volume; CI: Confidence interval; LCI: lung clearance index; LUM/IVA: Lumacaftor/ivacaftor; MV: Mean; MD: Mean difference; n: Number of patients with (at least one) event; N: Number of patients evaluated; nE: number of events; PE: pulmonary exacerbations, SD: standard deviation; (S)AE: (serious) adverse event; vs: versus</p>		

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

Patients aged 2 to 5 years with cystic fibrosis who are homozygous for the *F508del* mutation.

Approx. 280 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 Orkambi® (active ingredient combination: lumacaftor/ivacaftor) at the following publicly accessible link (last access: 24 June 2019):

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

Treatment with lumacaftor/ivacaftor should only be initiated and monitored by specialists who are experienced in the treatment of patients with cystic fibrosis.

4. Treatment costs

Annual treatment costs:

Patients aged 2 to 5 years with cystic fibrosis who are homozygous for the *F508del* mutation.

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Lumacaftor/ivacaftor	€ 152,687.32
Best supportive care	different for each individual patient
Appropriate comparator therapy:	
Best supportive care	different for each individual patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2019)

Costs for additionally required SHI services: not applicable

II. Entry into force

1. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 15 August 2019.
2. The period of validity of the resolution is limited to 1 October 2021.

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

Berlin, 15 August 2019

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

Prof Hecken

Resolution has been repealed