Gemeinsamer Bundesausschuss

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

Resolution of: 15 August 2019 Valid until: 01 10 2021
Entry into force on: 15 August 2019
Federal Gazette, BAnz AT 09 09 2019 B2

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)

Abbreviations used:
BMI: Body Mass Index; CF: cystic fibrosis; FEV_1%: 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

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