Lumacaftor/ ivacaftor (new therapeutic indication: cystic fibrosis, homozygous F508del mutation in CFTR gene, ≥ 1 to < 2 years)

Resolution of: 18 January 2024 valid until: unlimited
Entry into force on: 18 January 2024
Federal Gazette, BAnz AT 23 02 2024 B2

New therapeutic indication (according to the marketing authorisation of 4 July 2023):

Orkambi granules are indicated for the treatment of cystic fibrosis (CF) in patients aged 1 year and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

Therapeutic indication of the resolution (resolution of 18 January 2024):

Orkambi granules are indicated for the treatment of cystic fibrosis (CF) in children aged 1 to <2 years who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

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

Children with cystic fibrosis aged 1 to <2 years who are homozygous for the F508del mutation in the CFTR gene

Appropriate comparator therapy:

− Best supportive care

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

Hint for a non-quantifiable additional benefit

Study results according to endpoints:[1]

Children with cystic fibrosis aged 1 to <2 years who are homozygous for the F508del mutation in the CFTR gene

1 Data from the dossier of the pharmaceutical company, unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant differences for the benefit assessment with transfer of evidence of the results from older patients with homozygous F508del mutation
Morbidity	↑	Advantage with transfer of evidence of the results from older patients with homozygous F508del mutation
Health-related quality of life	↔	No relevant differences for the benefit assessment with transfer of evidence of the results from older patients with homozygous F508del mutation
Side effects	↔	No relevant differences for the benefit assessment with transfer of evidence of the results from older patients with homozygous F508del mutation
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		

VX16-809-122 study Part B: single-arm, open-label study of lumacaftor/ ivacaftor + BSC over 24 weeks

Mortality

Endpoint	LUMA/ IVA + BSC	
	N	Patients with event n (%)
Overall mortality	46	0 (0)

Morbidity

Endpoint	LUMA/ IVA + BSC	
	N	Patients with event until week 24; n (%)
Pulmonary exacerbation	46	9 (19.6)
Hospitalisation for pulmonary exacerbation	46	3 (6.5)

Endpoint	LUMA/ IVA + BSC			
	N	Values at the start of study MV (SD)	Values at week 24 MV (SD)	Mean change at week 24 MV (SD)
Ratio of body weight to body height (age-related z-score)	38	0.79 (0.77)	0.79 (0.87)	0.04 (0.53)
Sweat chloride concentration ([mmol/l], absolute change) *(presented additionally)*	24	104.2 (7.7)	73.1 (13.9)	-29.1 (13.5)

Health-related quality of life

No data on health-related quality of life were collected.

Side effects

Endpoint	LUMA/ IVA + BSC	
	N	Patients with event n (%)
Adverse events (AEs)	46	44 (95.7)
Serious AEs (SAEs)	46	5 (10.9)
Severe AEs (grade 3 or 4)	46	2 (4.3)
Discontinuation due to AEs	46	1 (2.2)

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

Children with cystic fibrosis aged 1 to <2 years who are homozygous for the F508del mutation in the CFTR gene

approx. 50 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: lumacaftor/ ivacaftor) at the following publicly accessible link (last access: 18 October 2023):

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

Treatment with lumacaftor/ ivacaftor should only be initiated and monitored by doctors experienced in the therapy of children with cystic fibrosis.

4. Treatment costs

Annual treatment costs:

Children with cystic fibrosis aged 1 to <2 years who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Lumacaftor/ ivacaftor	€ 147,785.37
+ 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: 1 January 2024

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 with cystic fibrosis aged 1 to <2 years who are homozygous for the F508del mutation in the CFTR gene

No medicinal product with new active ingredients that can be used in a combination therapy that 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.