### Orkambi

**Description**

Orkambi (lumacaftor/ivacaftor)

**Background**

Orkambi (lumacaftor/ivacaftor) is used for the treatment of cystic fibrosis (CF) in patients who have two copies of the F508del mutation in their CFTR gene. Having two copies of this mutation (one inherited from each parent) is the leading cause of CF. Orkambi is a transmembrane conductance regulator (CFTR) potentiator which causes the production of an abnormal protein that disrupts how water and chloride are transported in the body (1-2).

CF is a serious genetic disorder that results in the formation of thick mucus that builds up in the lungs, digestive tract and other parts of the body leading to severe respiratory and digestive problems, as well as other complications such as infections and diabetes (1).

**Regulatory Status**

FDA-approved indication: Orkambi is a combination of lumacaftor and ivacaftor, a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator, indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who are homozygous for the F508del mutation in the CFTR gene. If the patient’s genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene (1).

**Limitations of Use:**
The efficacy and safety of Orkambi have not been established in patients with CF other than those homozygous for the *F508del* mutation. Orkambi should not be used in patients other than those who have two copies of the *F508del* mutation in their CFTR gene (1).

Orkambi may cause worsening of liver function, including hepatic encephalopathy, in patients with advanced liver disease and should be used with caution and only if the benefits are expected to outweigh the risks. If Orkambi is used in these patients, they should be closely monitored after the initiation of treatment and the dose should be reduced (1).

Transaminases (ALT or AST) should be assessed prior to initiating Orkambi, every 3 months during the first year of treatment, and annually thereafter. Patients who develop increased transaminase levels should be closely monitored until the abnormalities resolve. Dosing should be interrupted in patients with ALT or AST of greater than 5 times the upper limit of normal (1).

Respiratory events may be observed in patients during initiation of Orkambi. These events can be serious, particularly in patients with advanced lung disease. Clinical experience in patients with ppFEV₁<40 is limited, and additional monitoring of these patients is recommended during initiation of therapy (1).

Based on the clinical studies that were done for Orkambi patients who meet any of the following exclusion criteria were not eligible to for the study. Any of the following abnormal laboratory values at screening: (1)

1. Hemoglobin <10 g/dL
2. Abnormal liver function defined as any 3 or more of the following: ≥3 × upper limit of normal (ULN) aspartate aminotransferase (AST), ≥3 × ULN alanine aminotransferase (ALT), ≥3 × ULN gamma-glutamyl transpeptidase (GGT), ≥3 × ULN alkaline phosphatase
3. Abnormal renal function defined as glomerular filtration rate ≤50 mL/min/1.73 m².

The safety and efficacy of Orkambi in patients less than 2 years of age have not been established (1).
Orkambi may be considered **medically necessary** for the treatment of cystic fibrosis (CF) in patients age 2 years and older and if the conditions indicated below are met.

Orkambi is considered **investigational** in patients under the age of 2 and for all other indications.

**Prior-Approval Requirements**

**Age**

2 years of age and older

**Diagnosis**

Patient must have the following:

- Cystic fibrosis (CF)

  **AND ALL** of the following:
  1. Homozygous for F508del mutation in the cystic fibrosis transmembrane regulator (CFTR) gene confirmed by FDA approved CF mutation test
  2. Pretreatment percent predicted forced expiratory volume (ppFEV) must be provided
  3. Hemoglobin must be greater than or equal to \( \geq 10\)g/dL
  4. eGFR must be greater than or equal to \( \geq 50\)ml/min
  5. Baseline levels of ALT, AST and bilirubin must not be greater than 3x the upper limit of normal
  6. Must be prescribed by a pulmonologist, or gastroenterologist
  7. **NO** dual therapy with another a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator

**Prior – Approval Renewal Requirements**

**Age**

2 years of age and older

**Diagnosis**

Patient must have the following:

- Cystic fibrosis (CF)
AND ALL of the following:
1. Stable or improvement of ppFEV₁ from baseline
2. Annual testing of ALT, AST and bilirubin levels after the first year of therapy
3. NO dual therapy with another a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

Quantity 336 tablets per 84 days OR
180 packets per 90 days

Duration 6 months

Prior – Approval Renewal Limits

Quantity 336 tablets per 84 days OR
180 packets per 90 days

Duration 12 months

Rationale

Summary
Orkambi is a potentiator of the CFTR protein and is effective only in cystic fibrosis patients who are homozygous for the F508del mutation in the CFTR gene. Cystic fibrosis is caused by mutations in a gene that encodes for a protein called cystic fibrosis transmembrane regulator (CFTR) which regulates chloride and water transport in the body. The defect results in the formation of thick mucus that builds up in the lungs, digestive tract and other parts of the body. Orkambi is not effective in patients who are not homozygous for the F508del mutation in the CFTR gene. Orkambi is indicated for patients 2 years of age and older (1-2).
Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Orkambi while maintaining optimal therapeutic outcomes.

References

Policy History

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<thead>
<tr>
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<tbody>
<tr>
<td>July 2015</td>
<td>Addition to PA</td>
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<tr>
<td>July 2015</td>
<td>Removal of not to be used concurrently with other medications for cystic fibrosis and the addition of no dual therapy with another a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator Change of quantity limits from 360/ 90 days to 336/ 84 days due to packaging</td>
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<tr>
<td>September 2015</td>
<td>Annual Review</td>
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<td>December 2015</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>March 2016</td>
<td>Annual review Policy number changed from 5.13.06 to 5.45.06</td>
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<td>Annual editorial review and reference update.</td>
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<tr>
<td>October 2016</td>
<td>Change to new age of 6 yrs. and older</td>
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<td>March 2017</td>
<td>Annual editorial review and reference update.</td>
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### Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.