# Clinical Policy: Lumacaftor-Ivacaftor (Orkambi)

Reference Number: PA.CP.PHAR.213
Effective Date: 01/18
Last Review Date: 07/18

Coding Implications
Revision Log

**Description**
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for lumacaftor-ivacaftor (Orkambi™).

**FDA Approved Indication(s)**
Orkambi is indicated for the treatment of 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.

Limitation(s) of use: The efficacy and safety of Orkambi have not been established in patients with CF other than those homozygous for the F508del mutation.

**Policy/Criteria**
It is the policy of Pennsylvania Health and Wellness that Orkambi is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Cystic Fibrosis** (must meet all)**:**

1. Age ≥ 2 years;
2. Diagnosis of cystic fibrosis (CF);
3. Member is homozygous for the *F508del* mutation in the *CFTR* gene;
4. Prescribed total daily dose of Orkambi does not exceed:
   a. Ages 6 through 11 years: lumacaftor 400 mg/ivacaftor 500 mg (4 tablets);
   b. Ages 12 years and older: lumacaftor 800 mg/ivacaftor 500 mg (4 tablets).

**Approval duration: 6 months**

**B. Other diagnoses/indications:** Refer to PA.CP.PMN.53

**II. Continued Approval**

**A. Cystic Fibrosis** (must meet all)**:**

1. Currently, receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g.: stable or improved pulmonary function, improved quality of life, reduced hospitalization);
3. Prescribed total daily dose of Orkambi does not exceed:
   a. Ages 6 through 11 years: lumacaftor 400 mg/ivacaftor 500 mg (4 tablets);
   b. Ages 12 years and older: lumacaftor 800 mg/ivacaftor 500 mg (4 tablets).

**Approval duration: 12 months**

**B. Other diagnoses/indications** (1 or 2)**:**

1. Currently, receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   **Approval duration: Duration of request or 6 months (whichever is less);** or

2. Refer to PA.CP.PMN.53

**Background**

*Description/Mechanism of Action:*

The cystic fibrosis transmembrane conductance regulator (CFTR) protein is a chloride channel present at the surface of epithelial cells in multiple organs. The *F508del* mutation results in protein misfolding, causing a defect in cellular processing and trafficking that targets the protein for degradation and therefore reduces the quantity of CFTR at the cell surface. The small amount of F508del-CFTR that reaches the cell surface is less stable and has low channel-open probability (defective gating activity) compared to wild-type CFTR protein. Lumacaftor improves the conformational stability of F508del-CFTR, resulting in increased processing and trafficking of mature protein to the cell surface. Ivacaftor is a CFTR potentiator that facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein at the cell surface. *In vitro* studies have demonstrated that both lumacaftor and ivacaftor act directly on the CFTR protein in primary human bronchial epithelial cultures and other cell lines harboring the *F508del*-CFTR mutation to increase the quantity, stability, and function of F508del-CFTR at the cell surface, resulting in increased chloride ion transport.

*Formulations:*

Orkambi: Oral tablet

- 200 mg of lumacaftor and 125 mg of ivacaftor
- 100 mg of lumacaftor and 125 mg of ivacaftor
- .

**Appendices**

**Appendix A: Abbreviation Key**

CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane conductance regulator

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| N/A | |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| References reviewed and updated. | 02/18 | |

**References**

1. Orkambi Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; September 2016. Available at http://www.orkambi.com. Accessed October 26, 2017.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines: Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med.* April 1, 2013; 187(7): 680-689.