Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.213	**Effective Date: 01/2018** **Revision Date: 01/2021**
Policy Name: Lumacaftor-Ivacaftor (Orkambi)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ☐ **Revised Policy***
- ✓ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2021 annual review: references reviewed and updated.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:**

Clinical Policy: Lumacaftor-Ivacaftor (Orkambi)

Reference Number: PA.CP.PHAR.213
Effective Date: 01/2018
Last Review Date: 01/2021

Coding Implications
Revision Log

Description
Lumacaftor/ivacaftor (Orkambi®) is a combination drug for cystic fibrosis (CF). Lumacaftor improves the conformational stability of F508del-cystic fibrosis transmembrane conductance regulator (CFTR), while ivacaftor is a CFTR potentiator.

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. Diagnosis of cystic fibrosis (CF);
2. Confirmation the member is homozygous for the *F508del* mutation in the *CFTR* gene;
3. Age ≥ 2 years;
4. Prescribed by or in consultation with a pulmonologist or cystic fibrosis specialist;
5. Documentation indicates member has baseline forced expiratory volume in 1 second (FEV1), unless member is unable to perform spirometry testing;
6. Orkambi is not prescribed concurrently with other ivacaftor-containing CFTR modulator combination products (e.g., Kalydeco, Symdeko, Trikafta);
7. Dose does not exceed one of the following (a, b, c, or d):
   a. Age 2 to 5 years weighing < 14 kg: lumacaftor 200 mg/ivacaftor 250 mg per day (2 packets per day);
   b. Age 2 to 5 years weighing ≥ 14 kg: lumacaftor 300 mg/ivacaftor 376 mg per day (2 packets per day);
   c. Age 6 to 11 years: lumacaftor 400 mg/ivacaftor 500 mg per day (4 tablets per day);
   d. Age ≥ 12 years: lumacaftor 800 mg/ivacaftor 500 mg per day (4 tablets per day).

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 OR the member continues to benefit from therapy based on the prescriber's assessment;
3. Orkambi is not prescribed concurrently with other ivacaftor-containing CFTR modulator combination products (e.g., Kalydeco, Symdeko, Trikafta);
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, or d):
    a. Age 2 to 5 years weighing < 14 kg: lumacaftor 200 mg/ivacaftor 250 mg per day (2 packets per day);
    b. Age 2 to 5 years weighing ≥ 14 kg: lumacaftor 300 mg/ivacaftor 376 mg per day (2 packets per day);
    c. Age 6 to 11 years: lumacaftor 400 mg/ivacaftor 500 mg per day (4 tablets per day);
    d. Age ≥ 12 years: lumacaftor 800 mg/ivacaftor 500 mg per day (4 tablets per day).

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

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACFLD: advanced cystic fibrosis lung disease
CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane conductance regulator
FDA: Food and Drug Administration
LCI: lung clearance index
MBW: multiple-breath washout
ppFEV1: percent predicted forced expiratory volume in 1 second

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Regarding the diagnostic criteria for CF of "genetic testing confirming the presence of two disease-causing mutations in CFTR gene," this is to ensure that whether heterozygous or homozygous, there are two disease-causing mutations in the CFTR gene, one from each parental allele.
- Most children can do spirometry by age 6, though some preschoolers are able to perform the test at a younger age. Some young children aren't able to take a deep enough breath and blow out hard and long enough for spirometry. Forced oscillometry is another way to test lung function in young children. This test measures how easily air flows in the lungs (resistance and compliance) with the use of a machine.
- The two most commonly reported parameters from multiple-breath washout (MBW) tests are the lung clearance index (LCI) and moment ratios (MRs). Measurements of LCI and MR are taken during the washout period. During the washout phase, subjects inhale gases that do not contain the test gas of interest. The principles of the washout are the same regardless of the test gas measured. The washout is stopped once the test gas reaches 1/40 of the initial gas concentration
- NHS Clinical Guidelines: Care of Children with Cystic Fibrosis: Normal ranges for LCI are device specific and still being established, but in general a value > 8.0 is above the normal range and > 10.0 is significantly abnormal.
- Cystic Fibrosis Foundation 2020 guidelines for advanced cystic fibrosis lung disease (ACFLD):
  - Define ACFLD as ppFEV1 < 40% when stable or referred for lung transplantation evaluation or previous intensive care unit (ICU) admission for respiratory failure, hypercarbia, daytime oxygen requirement at rest (excluding nocturnal use only), pulmonary hypertension, severe functional impairment from respiratory disease (New York Heart Association Class IV), six-minute walk test distance < 400m.
  - No recommendations on the start or continuation of CFTR modulator therapy with ACFLD guidelines.
  - Treatment recommendations included: lung transplantation, supplemental oxygen, continuous alternating inhaled antibiotics, and systemic corticosteroids
-

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CF	Adults and pediatric patients age 12 years and older: two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) PO Q12H Pediatric patients age 6 through 11 years: two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) PO Q12H Pediatric patients age 2 through 5 years and weighing < 14 kg: one packet of granules (each containing lumacaftor 100 mg/ivacaftor 125 mg) PO Q12H	Adults and pediatric patients age 12 years and older: lumacaftor 800 mg/ivacaftor 500 mg per day Pediatric patients age 6 through 11 years: lumacaftor 400 mg/ivacaftor 500 mg per day Pediatric patients age 2 through 5:

Indication	Dosing Regimen	Maximum Dose
	Pediatric patients age 2 through 5 years and weighing ≥ 14 kg: one packet of granules (each containing lumacaftor 150 mg/ivacaftor 188 mg) PO Q12H	<14 kg - lumacaftor 200 mg/ivacaftor 250 mg per day ≥ 14 kg - lumacaftor 300 mg/ivacaftor 376 mg per day

V. Product Availability

- Tablets: lumacaftor 100 mg and ivacaftor 125 mg, lumacaftor 200 mg and ivacaftor 125 mg
- Oral granules: lumacaftor 100 mg and ivacaftor 125 mg, lumacaftor 150 mg and ivacaftor 188 mg

VI. References

1. Orkambi Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; July 2019. Available at http://www.orkambi.com. Accessed November 9, 2020.
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. 2013; 187(7): 680-689.
3. Farrell PM, White TB, Ren CL et al. Diagnosis of cystic fibrosis: Consensus guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017; 181S: S4-15.
4. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Foundation pulmonary guidelines: Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. Ann Am Thorac Soc. 2018; 15(3): 271-280.
5. Davies J, Sheridan P, Lee P, et al. Effect of ivacaftor on lung function in subjects with CF who have the G551D-CFTR mutation and mild lung disease: a comparison of lung clearance index (LCI) vs. spirometry. Journal of Cystic Fibrosis. 2012;11(1):S15.
6. Alexander S, Alshafi K, Al-Yaghchi C, et al. Clinical Guidelines: Care of Children with Cystic Fibrosis. Royal Brompton and Harefield NHS. 2020;(8):22-23.
7. Kapnadak SG, Dimango E, Hadjiliadis D, et al. Cystic Fibrosis Foundation consensus guidelines for the care of individuals with advanced cystic fibrosis lung disease. J Cyst Fibros. 2020 May;19(3):344-354.

Reviews, Revisions, and Approvals	Date	Approval Date
References reviewed and updated.	02/18	
1Q 2019 annual review: updated age limit with corresponding dosing for pediatric patients down to 2 years of age per updated prescribing information; references reviewed and updated.	01/19	
1Q 2020 annual review: added the following criteria to initial approval: prescriber requirement of pulmonologist or cystic fibrosis specialist, requirement for baseline FEV1 unless unable to perform spirometry, requirement that Orkambi not be prescribed concurrently with other ivacaftor-containing CFTR modulator combination products; added the	01/2020	

Reviews, Revisions, and Approvals	Date	Approval Date
following to continued therapy criteria: not prescribed concurrently with other CFTR modulators; references reviewed and updated.		
1Q 2021 annual review: references reviewed and updated.	01/2021	