Clinical Policy: Lumacaftor/Ivacaftor (Orkambi)

Reference Number: CP.PHAR.213
Effective Date: 05.01.16
Last Review Date: 02.18
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Orkambi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of CF;
2. Age ≥ 2 years;
3. Member is homozygous for the F508del mutation in the CFTR gene;
4. Dose does not exceed:
   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:
Medicaid – 6 months

Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed:
   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/day);
   d. Age ≥ 12 years: lumacaftor 800 mg/ivacaftor 500 mg per day (4 tablets/day).

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane conductance regulator
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
N/A

V. 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 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	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: <14 kg - lumacaftor 200 mg/ivacaftor 250 mg per day ≥ 14 kg - lumacaftor 300 mg/ivacaftor 376 mg per day

VI. 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

VII. References

1. Orkambi Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; August 2018. Available at http://www.orkambi.com. Accessed August 15, 2018.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.54 CF Treatments. Evidence of a "significant improvement in FEV1" to continue approval is replaced with "Demonstrated positive response (improvement, maintenance, decreased rate of progression/decline) to Orkambi therapy in one or more of the following areas: pulmonary function, quality of life, pulmonary exacerbations". Not having increased LFTs is removed as a discontinuation reason. Continuation approval period is extended from 6 to 12 months.	04.16	05.16
Age lowered to 6 years per PI – corresponding maximum dose added.	05.17	05.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Efficacy statement edited to indicate general positive response to therapy.		
1Q18 annual review: - Policies combined for Centene Medicaid and Commercial lines of business. - No significant changes from previous corporate approved policy - Commercial: Added age requirement per FDA labeling. Modified max dose criteria to be age-specific - References reviewed and updated.	10.26.17	02.18
No significant changes: updated age limit with corresponding dosing for pediatric patients down to 2 years of age per updated prescribing information.	09.26.18	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.