Clinical Policy: Lumacaftor-Ivacaftor (Orkambi)

Reference Number: CP.PHAR.213
Effective Date: 05/16
Last Review Date: 05/17

Coding Implications
Revision Log

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

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

Policy/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. Age ≥ 6 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 CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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

1. Currently, receiving medication via Centene benefit or member has previously met all initial approval criteria;
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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to CP.PHAR.57 - Global Biopharm Policy.

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

FDA Approved Indications:
Orkambi is a combination of lumacaftor and ivacaftor/oral tablet formulation indicated for:

- Treatment of CF in patients age 6 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.
  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.

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
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. Efficacy statement edited to indicate general positive response to therapy.	05/17	05/17

References

1. Orkambi Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; September 2016. Available at http://pi.vrtx.com/files/uspi_lumacaftor_ivacaftor.pdf. Accessed May 1, 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.

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.

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.

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