MEDICAL MUTUAL®

Drug Policy

Policy:	Orkambi (lumacaftor/ivacaftor)	Annual Review Date: 10/19/2023 Last Revised Date: 10/19/2023

OVERVIEW

Orkambi, a combination of lumacaftor and ivacaftor, is indicated for the treatment of **cystic fibrosis** in patients ≥ 1 year of age who are homozygous for the F508del mutation in the cystic fibrosis transmembrane regulator (CFTR) gene.[1]

If the patient's genotype is unknown, an FDA-cleared cystic fibrosis mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene. The efficacy and safety of Orkambi have not been established in patients with cystic fibrosis other than those homozygous for the F508del mutation. Orkambi contains a unique chemical entity, lumacaftor, which is a CFTR corrector that increases trafficking of F508del CFTR to the cell surface, and ivacaftor (the same active ingredient contained in Kalydeco® [ivacaftor tablets and oral granules]), a CFTR potentiator that enhances chloride transport of CFTR on the cell surface. The F508del mutation in CFTR causes cystic fibrosis by limiting the amount of CFTR protein that reaches the epithelial cell surface.

POLICY STATEMENT

This policy involves the use of Orkambi. Prior authorization is recommended for pharmacy benefit coverage of Orkambi. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Orkambi as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Orkambi be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Orkambi is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Cystic Fibrosis (CF)**
   Criteria. *Patient must meet the following criteria*

   For initial therapy, approve in patients who meet the following criteria (a, b, and c):
   For continuation of therapy, approve in patients who meet the following criteria (c):
   a) Patient is ≥ 1 year of age; AND
   b) According to the results of an FDA-cleared CF mutation test, patient is homozygous for the F508del (Phe508del) mutation in the CFTR gene (meaning the patient has two copies of the F508del [Phe508del] mutation); AND
   c) Prescribed by or in consultation with a pulmonologist or physician who specializes in the treatment of CF.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Orkambi has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Cystic Fibrosis, Heterozygous for the F508del (Phe508del) Mutation in the CFTR Gene.** Orkambi is not indicated for patients with only one copy of the F508del mutation in the CFTR gene.[1] Patients who are heterozygous for the F508del mutation and have one of the following mutations are potential candidates for Kalydeco therapy: G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D, or R117H.

2. **Combination Therapy with Kalydeco (ivacaftor tablets and oral granules), Symdeko (tezacaftor/ivacaftor; ivacaftor tablets, co-packaged), or Trikafta (elexacaftor/tezacaftor/ivacaftor tablets; ivacaftor tablets, co-packaged).** Orkambi contains ivacaftor, the active agent in Kalydeco and therefore is not indicated in combination with Kalydeco. Symdeko and Trikafta contain ivacaftor and are therefore not indicated in combination with Orkambi.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or

performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Orkambi® [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; July 2019.
2. CF patient registry annual data report. Available at: https://www.cff.org/2014-Annual-Data-Report.pdf. Accessed on13 August 2018.
3. Wainwright CE, Elborn JS, Ramsey G, et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for F508del CFTR. *N Engl J Med.* 2015; 373:220-231.
4. Milla, Carlos E., et al. "Lumacaftor/Ivacaftor in Patients Aged 6â€ " 11 Years with Cystic Fibrosis and Homozygous for F508del-CFTR." *American Journal of Respiratory and Critical Care Medicine*, vol. 195, no. 7, 2017, pp. 912–920., doi:10.1164/rccm.201608-1754oc.
5. Institute for Clinical and Economic Review (ICER). Modulator Treatments for Cystic Fibrosis: Effectiveness and Value. May 3, 2018.
6. Lumacaftor/ivacaftor. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 16 August 2019. Accessed on 18 August 2019.
7. Orkambi® tablets and oral granules [prescribing information]. Cambridge, MA: Vertex; September 2022.