PRIOR AUTHORIZATION POLICY

POLICY: Cystic Fibrosis – Orkambi Prior Authorization Policy
- Orkambi™ (lumacaftor/ivacaftor tablets and oral granules – Vertex)

REVIEW DATE: 07/08/2020

OVERVIEW

Orkambi, a combination of lumacaftor and ivacaftor, is indicated for the treatment of cystic fibrosis (CF) in patients ≥ 2 years 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 CF 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 CF other than those homozygous for the F508del mutation. Orkambi contains a new 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 granules]), a CFTR potentiator that enhances chloride transport of CFTR on the cell surface. The F508del mutation in CFTR causes CF by limiting the amount of CFTR protein that reaches the epithelial cell surface.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Orkambi. 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 to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Cystic Fibrosis (CF), Homozygous for the F508del (Phe508del) Mutation in the Cystic Fibrosis Transmembrane Regulator (CFTR) Gene.** Approve for 3 years in a patient who meets the following criteria (A, B, and C):
   - **A)** Patient is homozygous for the F508del (Phe508del) mutation in the CFTR gene (meaning the patient has two copies of the F508del [Phe508del] mutation); AND
   - **B)** Patient is ≥ 2 years of age; AND
   - **C)** Orkambi is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of CF.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Orkambi is not recommended in the following situations:

1. **Cystic Fibrosis, <u>Heterozygous</u> 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, Symdeko, or Trikafta.** 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.

REFERENCES

1. Orkambi® [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; July 2019.
2. CF patient registry 2017. Available at: https://www.cff.org/Research/Researcher-Resources/Patient-Registry/2018-Patient-Registry-Annual-Data-Report.pdf. Accessed on June 23, 2020.
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. Ren CL, Morgan RL, Oermann C, et al. Cystic fibrosis foundation pulmonary guidelines: Use of CFTR modulator therapy in patients with cystic fibrosis. *Ann Am Thorac Soc*. 2018;15(3):271-280.