Clinical Policy: Lumacaftor-Ivacaftor (Orkambi)
Reference Number: ERX.SPMN.79
Effective Date: 07/16
Last Review Date: 06/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that lumacaftor-ivacaftor (Orkambi™) is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Cystic Fibrosis (CF) (must meet all):
      1. Age ≥12 years;
      2. Diagnosis of CF;
      3. Member is homozygous for the F508del mutation in the CFTR gene;
      4. Prescribed dose of Orkambi does not exceed lumacaftor 800 mg / ivacaftor 500 mg per day.

      Approval duration: 6 months

   B. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.

II. Continued Approval
   A. Cystic Fibrosis (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
      2. Member continues to respond positively to Orkambi therapy in one or more of the following areas: pulmonary function, quality of life, pulmonary exacerbations.

      Approval duration: 12 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
      2. Refer to ERX.SPMN.16 - 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. In vitro responses do not necessarily correspond to in vivo pharmacodynamic response or clinical benefit.

Formulations:
Orkambi is a film-coated tablet for oral administration containing 200 mg of lumacaftor and 125 mg of ivacaftor.

FDA Approved Indication:
Orkambi is a combination of lumacaftor and ivacaftor oral formulation indicated for:
- Treatment of CF in patients age 12 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

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<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
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References

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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