ILLINOIS DEPARTMENT OF Healthcare and Family Services

Orkambi® (lumacaftor-ivacaftor tablet) – Prior Authorization Criteria

Orkambi® is FDA approved for the treatment of cystic fibrosis (CF) in patients 12 years of age and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.[1] The F508del is the most common CFTR mutation, with approximately 45% of patients with CF being homozygous for this allele.[2] The CFTR protein is a chloride channel present at the surface of epithelial cells in multiple organs. The F508del CTFR mutation results in protein misfolding that causes a defect in cellular processing and trafficking and targets the protein for degradation, which results in a reduction in the quantity of CFTR at the cell surface. The small amount of F508del CFTR that reaches the cell surface is less stable and has defective gating activity.[1]

Orkambi is a combination product that contains lumacaftor and ivacaftor. Lumacaftor improves the conformational stability of the F508del CFTR protein, increasing the processing and trafficking of mature protein to the cell surface.[1] Ivacaftor is a CFTR potentiator that increases the fraction of time that the CFTR channels are open.[2] The combination of lumacaftor with ivacaftor has been associated with a greater increase in chloride ion transport in epithelial cell CFTR protein resulting in improved regulation of salt and water balance in various tissues including the lung.[2] Clinical studies have demonstrated a positive impact on forced expiratory volume (FEV1), pulmonary exacerbations, and body mass index (BMI).[2]

Initial Approval Criteria

An initial approval for a period of 3 months may be granted if the following criteria are met:

1. Participant is ≥ 12 years of age and < 66 years of age.
2. Participant has a diagnosis of CF with documentation of homozygous F508del CFTR gene mutation on FDA approved CF mutation test.
3. Prescriber is board certified in subspecialty of Pulmonary Disease or Pediatric Pulmonology or provides a consultation report from a board certified pulmonologist who has seen the patient within the past 3 months and recommended treatment with Orkambi.
4. If appropriate, participant is receiving and/or has had adequate trials of the following medications:
    - Dornase alfa
    - Hypertonic saline
    - Inhaled or oral antibiotics
5. Baseline liver function (ALT/AST) and bilirubin tests are provided.
6. Baseline FEV1 is provided and is between ≥40% and ≤90% of predicted normal for age, sex, and height.
7. Number of exacerbations and/or hospitalizations in the past 12 months is provided.
8. Documentation of baseline comprehensive eye examination, including cataract screening, in pediatric participants is provided.
9. Participant is not taking **contraindicated** medications or herbal supplements such as:

- Anti-infectives: rifampin or rifabutin
- Seizure medications: phenobarbital, carbamazepine, or phenytoin
- Sedatives/Anxiolytics: triazolam or midazolam
- Immunosuppressants: cyclosporine, everolimus, sirolimus, or tacrolimus
- Herbal supplement: St John's wort (Hypericum perforatum)

10. In the opinion of the prescriber, the patient (parent or guardian, if patient is a minor) is able to make appropriate decisions about treatment and comply with dosing and other instructions.
11. Goals of therapy are provided.

Renewal Criteria

Additional approvals, beyond the initial 3 month approval, may be granted for 3 months at a time if the following criteria continue to be met:

1. Adherence to Orkambi® therapy is confirmed through pharmacy claims review. Repeated noncompliance may result in denial of the renewal request.
2. Response to therapy is documented and submitted by the prescriber (e.g. improved FEV1, weight gain, decreased exacerbations, improved quality of life demonstrated on CFQ-R Respiratory Domain Score, etc.).
3. Number of exacerbations and/or hospitalizations since initiating Orkambi therapy is provided by the prescriber.
4. Documentation of continued use of standard therapies previously initiated, if appropriate/tolerated, is provided by the prescriber.
5. Liver function (ALT/AST) and bilirubin tests are provided by the prescriber with each renewal during the first year of treatment and annually thereafter.
6. Documentation of annual comprehensive eye examination, including cataract screening, in pediatric participants is provided.
7. Participant is not taking contraindicated medications or herbal supplements such as:

    - Anti-infectives: rifampin or rifabutin
    - Seizure medications: phenobarbital, carbamazepine, or phenytoin
    - Sedatives/Anxiolytics: triazolam or midazolam
    - Immunosuppressants: cyclosporine, everolimus, sirolimus, or tacrolimus
    - Herbal supplement: St John's wort (Hypericum perforatum)

8. If Orkambi® therapy is discontinued by or with the knowledge of the prescriber, notification of reason for discontinuation will be provided.

References

1. Orkambi (ivacaftor) package insert. Boston, MA: Vertex Pharmaceuticals; July 2015.

2. Wainwright, C.E., Elborn, J.S., Ramsey, B.W., et al. Lumacaftor–Ivacaftor in Patients with Cystic Fibrosis Homozygous for Phe508del CFTR. *N Engl J Med*. 2015, May 17;1-12. doi: 10.1056/NEJMoa1409547