Premier Health Plan

# POLICY AND PROCEDURE



| | |
|---|---|
| **POLICY TITLE:** | **Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), and Symdeko (tezacaftor/ivacaftor)** |
| **DEPARTMENT:** | **Clinical Pharmacy Services- Utilization Management** |
| **ORIGINAL DATE:** | ***April 2012 (as adopted from UPMC Health Plan)*** |

**Last P & T Committee Approval Date:** *September 2018*

**Product Applicability:** *mark all applicable products below:*

| | |
|---|---|
| **COMMERCIAL** | [ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x ] All |
| **OTHER** | [ x ] Self-funded/ASO |

## PURPOSE

The purpose of this policy is to define the prior authorization process for Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), and Symdeko (tezacaftor/ivacaftor).

Kalydeco (ivacaftor) is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator that is indicated for the treatment of cystic fibrosis (CF) in patients aged 12 months and older who have one mutation in the CFTR gene that is responsive to Kalydeco potentiation based on clinical and/or in vitro assay data. If the patient's genotype is unknown, a FDA- cleared CF mutation test should be used to detect the presence of *F508del* mutation on both alleles of the *CFTR* gene.

- Limitations of Use: Not effective in patients with CF who are homozygous for the F508del mutation of the CFTR gene.

Orkambi (lumacaftor/ivacaftor) is indicated for the Treatment of cystic fibrosis (CF) in patients 6 years and older who are homozygous for the F508del mutation in the transmembrane conductance regulator (CFTR) gene. If the patient's genotype is unknown, a FDA- cleared CF mutation test should be used to detect the presence of *F508del* mutation on both alleles of the *CFTR* gene.

- Limitations of Use: The efficacy and safety of lumacaftor/ivacaftor have not been established in patients with CF other than those homozygous for the F508del mutation.

evolent HEALTH

Symdeko (tazacaftor/ivacaftor) is indicated for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor. If the patient's genotype is unknown, a FDA- cleared CF mutation test should be used to detect the presence of *F508del* mutation on both alleles of the *CFTR* gene.

- Limitations of Use: The efficacy and safety of tezacaftor/ivacaftor have not been established in patients with CF other than those homozygous for the F508del mutation or a mutation that is suspected to be responsive to tezacaftor/ivacaftor.

## DEFINITIONS

**FEV1** – Forced expiratory volume in 1 second

**Percent predicted FEV1** – percent of the predicted FEV1 value for persons of the same age, sex and height

## POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.002 Pharmacy and Therapeutics Committee and RX.003-Prior Authorization Process.

The drugs, Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), and Symdeko (tezacaftor/ivacaftor), are subject to the prior authorization process.

## PROCEDURE

**Initial Authorization Criteria:**

*Must meet all of the criteria listed under the respective product:*

1. **Kalydeco (ivacaftor):**
   - Must be prescribed by a cystic fibrosis specialist
   - Must be age 12 months or older
   - Must have a diagnosis of cystic fibrosis
   - Must submit a baseline percent of predicted FEV1

  - For patients ≤ 6 years of age, must submit appropriate baseline pulmonary monitoring/testing
- Must have at least one mutation in the *CFTR* gene that is responsive to Kalydeco based on clinical and/or in vitro assay data (see table below from prescribing information)

| Table 3: List of *CFTR* Gene Mutations that Produce CFTR Protein and are Responsive to KALYDECO | | | | | |
|---|---|---|---|---|---|
| *E56K* | *G178R* | *S549R* | *S977F* | *F1074L* | *2789+5G→A* |
| *P67L* | *E193K* | *G551D* | *F1052V* | *D1152H* | *3272-26A→G* |
| *R74W* | *L206W* | *G551S* | *K1060T* | *G1244E* | *3849+10kbC→T* |
| *D110E* | *R347H* | *D579G* | *A1067T* | *S1251N* | |
| *D110H* | *R352Q* | *711+3A→G* | *G1069R* | *S1255P* | |
| *R117C* | *A455E* | *E831X* | *R1070Q* | *D1270N* | |
| *R117H* | *S549N* | *S945L* | *R1070W* | *G1349D* | |

- Must have a baseline AST/ALT less than 3 times the upper limit of normal for the reference range

**2. Orkambi (lumacaftor/ivacaftor):**

- Must be prescribed by a cystic fibrosis specialist
- Must have a diagnosis of cystic fibrosis
- Must be 6 years of age or older
- Must have a homozygous F508del mutation in the transmembrane conductance regulator gene.
  - Documentation of lab result confirming mutation is required
- Must submit a baseline percent of predicted FEV1
- Must have a baseline bilirubin and AST/ALT less than 3 times the upper limit of normal for the reference range
- Must identify and submit documentation of one or more of the following disease markers that is anticipated to benefit from lumacaftor/ivacaftor treatment:
  - Decline in predicted FEV1
  - Frequent cystic fibrosis exacerbations
  - Poor nutritional status or low weight

**3. Symdeko (tezacaftor/ivacaftor):**

- Must be prescribed by a cystic fibrosis specialist
- Must have a diagnosis of cystic fibrosis
- Must be 12 years of age or older
- Must have a homozygous F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or at least one mutation that is responsive to Symdeko (see table)
  - Documentation of lab result confirming mutation is required

| Table 4: List of *CFTR* Gene Mutations that Produce CFTR Protein and are Responsive to SYMDEKO | | | | | |
|---|---|---|---|---|---|
| *E56K* | *R117C* | *A455E* | *S945L* | *R1070W* | *3272-26A→G* |
| *P67L* | *E193K* | *F508del** | *S977F* | *F1074L* | *3849+10kbC→T* |
| *R74W* | *L206W* | *D579G* | *F1052V* | *D1152H* | |
| *D110E* | *R347H* | *711+3A→G* | *K1060T* | *D1270N* | |
| *D110H* | *R352Q* | *E831X* | *A1067T* | *2789+5G→A* | |
| *A patient must have two copies of the *F508del* mutation or at least one copy of a responsive mutation presented in Table 4 to be indicated. | | | | | |

- Must have a trial, failure, contraindication or intolerance to Orkambi
- Must submit a baseline percent of predicted $FEV_1$
- Must have a baseline AST/ALT less than 3 times the upper limit of normal for the reference range
- Must identify and submit documentation of one or more of the following disease markers that is anticipated to benefit from tezacaftor/ivacaftor treatment:
    - Decline in predicted FEV1
    - Frequent cystic fibrosis exacerbations
    - Poor nutritional status or low weight

**Reauthorization Criteria:**

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon the following:

- Chart documentation showing that the member has benefited from Kalydeco, Orkambi, or Symdeko therapy
    - For Orkambi and Symdeko:
        - Must include documentation of benefit in at least one of the disease markers that was identified in initial authorization:
            - Stabilization or improvement in FEV1
            - Decrease in cystic fibrosis exacerbations
            - Improved nutritional status or weight gain
        - Must document that LFTs are being monitored
- Clinical rationale from provider to support continuation of therapy
- Chart documentation of the member's current percent predicted FEV1 must be submitted

**Limitations:**

| Length of Authorization (if above criteria met) | |
|---|---|
| Initial Authorization | Up to 6 months |
| Reauthorization | Up to 1 year |
| **Quantity Level Limit** | |

| | |
|---|---|
| Kalydeco | 60 tablets/packets per 30 days |
| Orkambi 200mg/125mg | 120 tablets per 30 days (ages 12 years and older) |
| Orkambi 100mg/125mg | 120 tablets per 30 days (age 6 through 11 years) |
| Symdeko | 1 box per 28 days |

If the established criteria are not met, the request is referred to a Medical Director for review.

## REFERENCES

1. Kalydeco [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals Incorporated; August 2018.
2. Symdeko [prescribing information]. Boston, MA: Vertex Pharmaceuticals Incorporated; February 2018.
3. Ramsey WB, Davie J, McElvaney G, et al. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. N Engl J Med 2011;365:1663-72
4. Welsh MJ, Ramsey BW, Accurso FJ et al. Cystic Fibrosis. In: Scriver CR, Beaudet AR, Sly W et al, eds. The metabolic and molecular basis of inherited disease. 8th ed. New York: McGraw-Hill, 2001:521-88
5. Yu H, Burton B, Huang C, et al. Ivacaftor potentiation of multiple CFTR channels with gating mutations. J Cyst Fibros 2012;11:237-245
6. Orkambi [prescribing information]. Boston, MA: Vertex Pharmaceuticals: September 2016.
7. Cystic Fibrosis Foundation. (2015). Orkambi. Retrieved from: http://www.cff.org/research/ClinicalResearch/FAQs/CombinedKalydeco-VX-809/
8. Wainwright CE, Elborn JS, Ramsey BW, et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. DOI:10.1056/NEJmoa1409547
9. Boyle MP, Bell SC, Konstan MW, et al. A CFTR corrector (lumacaftor) and a CFTR potentiator (ivacaftor) for treatment of patients with cystic fibrosis who have a phe508del CFTR mutation: a phase 2 randomised controlled trial. Lancet Respir Med 2014;2:527-38
10. Elborn, et al. Efficacy and safety of lumacaftor/ ivacaftor combination therapy in patients with cystic fibrosis homozygous for Phe508del CFTR by pulmonary function subgroup: a pooled analysis. Lancet
Respir Med. 2016;4(8):617-26.
11. Rosenfeld M, et al. Pharmacokinetics and safety of lumacaftor in combination with ivacaftor in patients aged 6-11 years with CF who are homozygous for F508del-CFTR. Pediatr Pulmonol. 2014;49(S38):287. Poster Session Abstract No. 203. Presented: North American Cystic Fibrosis Conference, Atlanta, GA, October 2014.
12. Milla CE, et al. Results from an open-label phase 3 study evaluating the safety, tolerability, and pharmacodynamics of combination lumacaftor/ivacaftor (LUM/IVA) therapy in children aged 6 through 11 years with cystic fibrosis (CF) homozygous for the F508del-CFTR mutation. Presented: European Cystic Fibrosis Conference, Basel, Switzerland , June 8-11, 2016.
13. Taylor-Cousar J, Munck A, McKone E, et al. Tezacaftor-Ivacaftor in Patients with Cystic Fibrosis Homozygous for Phe508del. N Engl J Med. 2017; 377(21): 2013-2023.
14. Rowe S, Daines C, Ringshausen F, et al. Tezacaftor-Ivacaftor in Residual-Function Heterozygotes with Cystic Fibrosis. N Engl J Med. 2017; 377(21):2024-2035.
15. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Pulmonary Clinical Practice Guidelines for Maintenance of Lung Health. Am J Respir Crit Care Med. 2013; 187(7): 680-689.

## RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

## REVIEW HISTORY

| DESCRIPTION OF REVIEW / REVISION | DATE APPROVED |
|---|---|
| *Annual review* | *02/16, 02/17, 02/18* |
| *Criteria update* | *12/16, 10/17, 09/18* |
| *Addition of Symdeko* | *05/18* |