Cystic Fibrosis Agents
(Kalydeco, Orkambi, and Symdeko)

**BENEFIT APPLICATION**

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

**DESCRIPTION**

The intent of the Cystic Fibrosis Agent Policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies for Kalydeco (ivacaftor) and Orkambi (ivacaftor/lumacaftor), and Symdeko (tezacaftor/ivacaftor).

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**

Kalydeco is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 6 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data.

Orkambi (lumacaftor/ivacaftor) is approved by the FDA for the treatment of CF in patients age 2 years and older that are homozygous for the F508del mutation in 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.

Symdeko is a combination of tezacaftor and ivacaftor, indicated for the treatment of patients with cystic fibrosis (CF) aged 6 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 based on in vitro data and/or clinical evidence.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

All other indications are considered experimental/investigational and are not a covered benefit.
POLICY

Required Documentation
The following information is necessary to initiate the prior authorization review:

- Genetic testing report confirming the presence of the appropriate CFTR gene mutation
- Submission of medical records (e.g., chart notes, laboratory values, pulmonary function tests, CFQ-R score) documenting clinical benefit from therapy

Criteria for Initial Approval

I. Kalydeco (ivacaftor) may be considered medically necessary for the treatment of cystic fibrosis when all of the following criteria are met:

- Genetic testing was conducted to detect a mutation in the CFTR gene.
- The patient is at least 6 months of age
- Kalydeco will not be used in combination with Orkambi or Symdeko

Initial approval will be for 6 months.

II. Orkambi (lumacaftor/ivacaftor) may be considered medically necessary for the treatment of cystic fibrosis when all of the following criteria are met:

- The patient is at least 2 years of age
- Genetic testing was conducted to detect a mutation in the CFTR gene
- The patient is positive for the F508del mutation on both alleles of the CFTR gene
- The patient will not be using Orkambi in combination with Kalydeco or Symdeko

Initial approval will be for 6 months.

III. Symdeko (tezacaftor/ivacaftor) may be considered medically necessary for the treatment of cystic fibrosis when all of the following criteria are met:

- Genetic testing was conducted to detect a mutation in the CFTR gene.
- The member is at least 6 years of age
- Symdeko will not be used in combination with Kalydeco or Orkambi

Initial approval will be for 6 months.

IV. Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), and Symdeko (tezacaftor/ivacaftor) are considered not medically necessary for patients who do not meet the criteria set forth above.

Continuation of Therapy

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All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria and achieve a clinically meaningful response as demonstrated by any of the following:

- Improvement in percent predicted forced expiratory volume in 1 second (ppFEV₁) from baseline
- Increased body mass index (BMI)
- Decreased pulmonary exacerbations
- Improvement in quality of life from baseline as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score

**Approval** will be for 12 months.

**Quantity Limits Apply:**
- Kalydeco 56 tablets/28 days
- Kalydeco Pak 56 packets/28 days
- Orkambi 112 tablets/28 days
- Symdeko 56 tablets/28 days

**PROCEDURES AND BILLING CODES**

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- No applicable codes

**REFERENCES**


*Some content reprinted from CVSHealth

**POLICY HISTORY**

**Policy #:** 05.01.39  
**Original Effective Date:** May 2012  
**Reviewed:** January 2019  
**Revised:** June 2019  
**Current Effective Date:** TBD