Pharmacy Medical Necessity Guidelines: Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Potentiators: Kalydeco®, Orkambi™, Symdeko®, Trikafta™

Effective: January 18, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☒ Tufts Health Plan Commercial products – large group plans
☒ Tufts Health Plan Commercial products – small group and individual plans
☒ Tufts Health Freedom Plan products – large group plans
☒ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:

RXUM: 617.673.0988

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION (FDA)-APPROVED INDICATIONS

The cystic fibrosis transmembrane conductance regulator (CFTR) potentiators are indicated for:

- **Kalydeco (ivacaftor)**
  Treatment of cystic fibrosis (CF) in patients age 4 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data
- **Orkambi (lumacaftor/ivacaftor)**
  Treatment of CF in patients age 2 years and older who are homozygous for the F508del mutation in the CFTR gene.
  The efficacy and safety of Orkambi (lumacaftor/ivacaftor) have not been established in patients with CF other than those homozygous for the F80del mutation.
- **Symdeko (tezacaftor/ivacaftor)**
  Treatment of patients with CF aged 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.
- **Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)**
  Treatment of CF in patients aged 12 years and older who have at least one *F508del* mutation in the CFTR gene that is responsive based on in vitro data.

For Kalydeco (ivacaftor), Symdeko (tezacaftor/ivacaftor), and Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor), if the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use. For Orkambi (lumacaftor/ivacaftor), if he 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.

CF is caused by genetic mutations in the CFTR protein. The CFTR protein is present in the respiratory epithelium and plays an important role in the regulation of airway surface liquid. Genetic mutations in the protein result in abnormal airway secretions, chronic endobronchial infection, and progressive airway obstruction. The CFTR potentiators treat the underlying cause of CF by targeting the defective CFTR protein to help facilitate increased chloride transport. This class of medications has been shown to improve lung function, relieve CF symptoms, increase body weight, and decrease the risk of pulmonary exacerbations. Choice of specific CFTR potentiator for the treatment of CF is largely based dependent on the specific genetic mutation present.

COVERAGE GUIDELINES

Kalydeco (ivacaftor)

The plan may authorize coverage of Kalydeco (ivacaftor) tablets for Members when all of the following criteria are met:

1. Documented diagnosis of cystic fibrosis

AND

2. Genetic testing documenting the presence of a genetic mutation Kalydeco (ivacaftor) is indicated for per package labeling

AND

3. The Member is at least 6 years of age or older

The plan may authorize coverage of Kalydeco (ivacaftor) oral granules for Members when all of the following criteria are met:

1. Documented diagnosis of cystic fibrosis

AND

2. Genetic testing documenting the presence of a genetic mutation Kalydeco (ivacaftor) is indicated for per package labeling

AND

3. The Member must be age 4 months to less than 6 years of age

Orkambi (lumacaftor/ivacaftor)

The plan may authorize coverage of Orkambi (lumacaftor/ivacaftor) tablets for Members when all of the following criteria are met:

1. Documented diagnosis of cystic fibrosis

AND

2. Genetic testing documenting the Member is homozygous for the *F508del* mutation

AND

3. The Member is at least 6 years of age or older

The plan may authorize coverage of Orkambi (lumacaftor/ivacaftor) oral granules for Members when all of the following criteria are met:

1. Documented diagnosis of cystic fibrosis

AND

2. Genetic testing documenting the Member is homozygous for the *F508del* mutation

AND

3. The Member must be age 2 to 5 years of age

Symdeko (tezacaftor/ivacaftor)

The plan may authorize coverage of Symdeko (tezacaftor/ivacaftor) for Members when all of the following criteria are met:

1. Documented diagnosis of cystic fibrosis

AND

2. Genetic testing documenting one of the following:
    a. Member is homozygous for the *F508del* mutation
    b. Presence of a genetic mutation Symdeko (tezacaftor/ivacaftor) is indicated for per package labeling

AND

3. The Member must be at least 6 years of age or older

Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

The plan may authorize coverage of Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor) for Members when all of the following criteria are met:

1. Documented diagnosis of cystic fibrosis

AND

2. Genetic testing documenting at least one *F508del* mutation

AND

3. The Member must be at least 12 years of age or older

LIMITATIONS

1. The Plan will not cover Kalydeco, Orkambi, Symdeko, or Trikafta for any non-FDA approved indication(s).
2. CFTR potentiator combination therapy will not be approved. If a Member is switching therapies, Providers should submit documentation confirming the Member plans to discontinue treatment with the second agent.
3. The following quantity limitations apply:
    a. Kalydeco oral granules 56 units per 28 days
    b. Kalydeco tablets: 60 units per 30 days
    c. Orkambi tablets: 112 units per 28 days
    d. Orkambi oral granules: 56 units per 28 days
    e. Symdeko tablets: 56 units per 28 days
    f. Trikafta tablets: 84 units per 28 days

CODES

None

REFERENCES

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APPROVAL HISTORY

May 8, 2012: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. April 9, 2013: No changes
2. April 8, 2014: Added the newly approved mutations Kalydeco is indicated to treat.
3. January 13, 2015: Added the newly approved mutation R117H, Kalydeco is indicated to treat.
4. May 12, 2015: Added criteria for the newly approved oral granule dosage form indicated for age 2 to less than six years.
5. January 1, 2016: Administrative change to rebranded template applicable to Tufts Health Direct.
6. January 12, 2016: No changes
7. January 10, 2017: No changes. Effective 1/10/17, Medical Necessity Guideline applies to Tufts Health Together.
8. April 11, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether.
9. July 11, 2017: Updated genetic mutation requirements to be in line with expanded FDA-approved indication.
10. October 17, 2017: Administrative update of criterion #1 for both oral granules and tablet to ensure that additional specific genetic mutations are included in criteria as approved.
11. July 10, 2018: Changed name of Medical Necessity Guideline to "Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Potentiators: Kalydeco® (ivacaftor), Orkambi™ (lumacaftor/ivacaftor), Symdeko® (tezacaftor/ivacaftor)". Added existing coverage criteria for Orkambi (lumacaftor/ivacaftor) to the Medical Necessity Guideline. Added Symdeko (tezacaftor/ivacaftor) to the Medical Necessity Guideline. Added the following coverage limitation: CFTR potentiator combination therapy will not be approved. If a Member is switching therapies, Providers should submit documentation confirming the Member plans to discontinue treatment with the second agent.
12. September 18, 2018: Updated coverage criteria for Kalydeco oral granules based on updated indication for use in patients at least 12 months of age.
13. October 16, 2018: Added coverage criteria for Orkambi granules based on updated indication.
14. June 11, 2019: Updated coverage criteria for Kalydeco oral granules based on updated indication for use in patients at least 6 months of age.
15. August 13, 2019: Updated coverage criteria for Symdeko based on an updated indication for use in patients at least 6 years of age.
16. March 10, 2020: Added Trikafta to the Medical Necessity Guideline.
17. January 12, 2021: Updated age requirements of Kalydeco oral granules to allow coverage in members at least 4 months of age based on the expanded indication.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic. Provider Services