Pharmacy Medical Necessity Guidelines:
Cystic Fibrosis Medications

Effective: June 1, 2026

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: ☒ Tufts Health RITogether – A Rhode Island Medicaid Plan		**Fax Numbers:** RXUM: 617.673.0939	

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:

- **Alyftrek (vanzacaftor, tezacaftor, and deutivacaftor)**
  Treatment of cystic fibrosis (CF) in patients aged 6 years and older who have a clinical diagnosis of CF and who have at least one variant in the CFTR gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one variant in the CFTR gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein.
- **Kalydeco (ivacaftor)**
  Treatment of CF in patients age 1 month and older who have at least one mutation in the *CFTR* gene that is responsive to ivacaftor based on clinical and/or in vitro assay data. 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
- **Orkambi (lumacaftor/ivacaftor)**
  Treatment of CF in patients aged 1 year 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. 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. 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.
- **Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)**
  Treatment of CF in patients aged 2 years and older who have a clinical diagnosis of CF and who have at least one variant in the CFTR gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one variant in the CFTR gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein.

COVERAGE GUIDELINES

The plan may authorize coverage of a Cystic Fibrosis Medication when **ALL** of the following criteria are met:

Alyftrek

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

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

AND

4. Documentation that the patient has at least one variant in the CFTR gene that is either responsive to Alyftrek or results in production of CFTR protein

Kalydeco (ivacaftor)

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 1 months of age or older

AND

4. Documentation of a cystic fibrosis mutation test confirming one of the CFTR gene mutations responsive to Kalydeco

Orkambi (lumacaftor/ivacaftor)

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 1 year of age or older

AND

4. Documentation confirming the patient is homozygous for the Phe508del (F508del) mutation in the CFTR gene

Symdeko (tezacaftor/ivacaftor)

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

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

AND

4. Documentation of **one (1)** of the following:
    a. Patient is homozygous for the Phe508del (F508del) mutation in the CFTR gene
    b. Patient has at least one mutation in the CFTR gene that is responsive to Symdeko

Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 2 years of age or older

AND

4. Documentation that the patient has at least one variant in the CFTR gene that is either responsive to Trikafta or results in production of CFTR protein

LIMITATIONS

None

CODES

None

REFERENCES

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APPROVAL HISTORY

September 13, 2022: Reviewed by Pharmacy & Therapeutics Committee.

- July 11, 2023: Expanded age requirements of Kalydeco and Trikafta based on updated package labeling (effective August 1, 2023).
- May 14, 2024: No changes
- May 13, 2025: Added Alyftrek to the Medical Necessity Guideline (eff 6/1/25).
- May 12, 2026: Overview and criteria updated for Alyftrek and Trikafta based on updated package labeling for use in patients with at least one variant in the CFTR gene that is either response based on clinical and/or in vitro data or results in protein production (eff 6/1/26).

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