Cystic Fibrosis Agents (Oral)

WA.PHAR.48 Effective: June 1, 2021

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: https://pharmacy.envolvehealth.com/content/dam/centene/envolve-pharmacy-solutions/pdfs/PDL/FORMULARY-CoordinatedCare_Washington.pdf

Background:

Cystic fibrosis (CF) occurs from mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene resulting in dysfunctional transport of electrolytes across epithelial linings. Chloride transport is most affected resulting in thick mucus build-up in the lungs, digestive tract, and other organ systems. Although many CFTR gene mutations can lead to CF, *F508del* is most common. Homozygous *F508del* CFTR mutations account for up to 50% of CF cases. CFTR modulators target specific changes on the CFTR gene and have demonstrated improved clinical outcomes associated with CF including increased FEV1, weight gain, symptom reduction, and decreased pulmonary exacerbations.

Medical necessity

Drug	Medical Necessity
ivacaftor **(KALYDECO)** lumacaftor/ivacaftor **(ORKAMBI)** Tezacaftor/ivacaftor and ivacaftor **(SYMDEKO)** Elexacaftor/tezacaftor/ivacaftor and ivacaftor **(TRIKAFTA)**	**Cystic Fibrosis Agents** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
ivacaftor **(KALYDECO)** lumacaftor/ivacaftor **(ORKAMBI)** Tezacaftor/ivacaftor and ivacaftor **(SYMDEKO)**	KALYDECO, ORKAMBI, SYMDEKO, and TRIKAFTA may be authorized when **ALL** the following criteria are met: 1. Diagnosis of cystic fibrosis; **AND** 2. Documentation of one of the following CFTR gene mutations:

Elexacaftor/tezacaftor/ivacaftor and ivacaftor **(TRIKAFTA)**	a. At least one responsive mutation (See product labeling) for Kalydeco, Symdeko, or Trikafta; **OR** b. Homozygous *F508del* CFTR mutation (2 copies) for Orkambi or Symdeko; **OR** c. At least one *F508del* CFTR mutation for Trikafta; **AND** 3. Patient is at least: a. 1 months of age for Kalydeco; **OR** b. 1 years of age for Orkambi: **OR** c. 6 years of age for Symdeko: **OR** d. 2 years of age for Trikafta; **AND** 4. Patient has baseline body mass index, percent predicted FEV1 and liver function tests; **AND** 5. Patient does not have severe hepatic impairment (Child-Pugh Class C); **AND** 6. Baseline ophthalmic examination was performed to monitor lens opacities/cataracts in pediatric patients (not required in adults 18 or older); **AND** 7. Not taken simultaneously with a strong CYP3A4 inducer (See Table 1); **AND** 8. Prescribed by or in consultation with a provider who specializes in the treatment of cystic fibrosis. If all the above criteria are met, the request will be **approved for 6 months.** If all criteria are not met, but there are circumstances supported by clinical judgement and documentation, requests may be approved by a clinical reviewer on a case-by-case basis up to initial authorization duration.
Drug	**Transitioning to TRIKAFTA (Initial Approval)**
Elexacaftor/tezacaftor/ivacaftor and ivacaftor **(TRIKAFTA)**	If patient is currently stable on Kalydeco, Symdeko or Orkambi, a request to transition to Trikafta may be approved if all the following conditions are met: 1. The patient meets initial approval criteria above; **AND** 2. The request for Trikafta will not be effective until at least 85% of patient's current supply of Kayldeco, Symdeko or Orkambi has been depleted (based on pharmacy claims data) If all the above criteria are met, the request will be **approved for 6 months**
Drug	**Criteria (Reauthorization)**
ivacaftor **(KALYDECO)** lumacaftor/ivacaftor **(ORKAMBI)** Tezacaftor/ivacaftor and ivacaftor **(SYMDEKO)**	CFTR modulators may be reauthorized when all the following are met: 1. Documentation of liver function tests within the last 6 months 2. Patient demonstrates disease response as indicated by at least one of the following: a. Improvement of FEV1 over baseline; **OR** b. Decreased pulmonary exacerbations or infections; **OR**

Elexacaftor/tezacaftor/ivacaftor and ivacaftor **(TRIKAFTA)**	c. Decreased hospitalizations; **OR** d. Increase in weight or growth; **OR** e. Decrease in the decline of lung function If **ALL** of the above criteria are met, the request may be **reauthorized for 12 months** If all criteria are not met, but there are circumstances supported by clinical judgement and documentation, requests may be approved by a clinical reviewer on a case-by-case basis up to the reauthorization duration.

Dosage and quantity limits:

Drug Name	How Supplied	Dose and Quantity Limits
ivacaftor (KALYDECO)	• 150 mg tablet • 25 mg packet • 50 mg packet • 75 mg packet	• Tablets: One tablet twice daily*; 60 tablets (1 bottle) per 30-days • Granule packets: One packet twice daily*; 56 packets (1 carton) per 28 days
lumacaftor/ivacaftor (ORKAMBI)	• 100 mg/125 mg tablet • 200 mg/125 mg tablet • 100 mg/125 mg packet • 150 mg/188 mg packet	• Tablets: Two tablets twice daily*; 112 tablets (1 box) per 28 days • Granules: One packet twice daily; 56 packets (1 carton) per 28days
Tezacaftor/ivacaftor and ivacaftor (SYMDEKO)	• Kit: 50 mg/75 mg tablet plus 75 mg ivacaftor tablet • Kit: 100 mg/150 mg tablet plus 150 mg ivacaftor tablet	• Tablets: One tablet twice daily*; 56 tablets (1 carton) per 28days
Elexacaftor/tezacaftor/ivacaftor and ivacaftor (TRIKAFTA)	• Tablet Kit: 100 mg/50 mg/75 mg fixed-dose tablet plus 150 mg ivacaftor tablet • Tablet Kit: 50 mg/25 mg/37.5 mg fixed-dose tablet plus 75 mg ivacaftor tablet • Granules Kit: 100 mg/50 mg/75 mg granule packet plus 75 mg ivacaftor granule packet • Granules Kit: 80 mg/40 mg/50 mg granule packet plus 59.5 mg ivacaftor granule packet	• Tablet: Two fixed-dose tablets daily and one ivacaftor tablet nightly*; 84 tablets (1 carton) per 28 days. • Granules: One granule packet in the morning and one ivacaftor granule packet nightly; 56 granules (1 carton) per 28 days

*Dose should be reduced with concurrent use of moderate to strong CYP3A4 inhibitors or hepatic insufficiency (refer to specific package inserts)

Appendix:

Table 1: Strong CYP3A4 Inducers

Carbamazepine	Phenobarbital	Phenytoin	Rifabutin	Rifampin	St. John's Wort

References:

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3. SYMDECO [prescribing information]. Boston, MA: Vertex Pharmaceuticals incorporated; December 2019
4. TRIKAFTA [prescribing information]. Boston, MA: Vertex Pharmaceuticals incorporated; November 2020.
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History

Date	Action and Summary of Changes
6/1/2021	New Policy
12/16/2020	Approved by DUR Board
08/12/2021	• Formatting updates • Minimum age for Trikafta has been updated to reflect new FDA label expansion • "How supplied" section for Trikafta updated with new kit tabletpack
09/29/2023	Version 2 Updates: 1. Updated medical necessity language 2. Updated age indication for Kalydeco, Orkambi and Trikafta 3. Added Trikafta granules to dosage and quantity limits