

PRIOR AUTHORIZATION POLICY

- POLICY:** Cystic Fibrosis – Trikafta Prior Authorization Policy
- Trikafta® (elexacaftor/tezacaftor/ivacaftor tablets; ivacaftor tablets, co-packaged and elexacaftor/tezacaftor/ivacaftor oral granules; ivacaftor oral granules – Vertex)

REVIEW DATE: 04/10/2024

OVERVIEW

Trikafta is a combination of ivacaftor, a cystic fibrosis transmembrane regulator (CFTR) potentiator, tezacaftor, and elexacaftor. It is indicated for the **treatment of cystic fibrosis (CF)** in patients ≥ 2 years of age who:

- Have at least one F508del mutation in the CFTR gene; OR
- Have a mutation in the CFTR gene that is responsive to Trikafta based on *in vitro* data.¹

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation. Table 1 lists responsive CFTR mutations based on *in vitro* data in Fischer Rat Thyroid cells.

Table 1. List of CFTR Gene Mutations that are Responsive to Trikafta.¹

CFTR – Cystic Fibrosis Transmembrane Regulator.

Guidelines

Guidelines from the CF Foundation (2018) provide guidance on the use of CFTR therapy in patients with CF; Trikafta is not addressed.²

According to the CF Foundation (2017), CF is diagnosed when an individual has both a clinical presentation of CF and evidence of CFTR dysfunction.^{4,5} Clinical presentation of CF includes a positive newborn screening, signs and/or symptoms of CF, and/or family history of CF. To establish a diagnosis of CF, sweat chloride tests should be considered first, then CFTR genetic analysis (CFTR genotype), and then CFTR physiologic tests (nasal potential difference [NPD] or intestinal current measurement [ICM]). However, tests of CFTR function are not always done in this order. All individuals diagnosed with CF should have a sweat chloride test and CFTR genetic analysis performed.

In a patient with a sweat chloride test ≥ 60 mmol/L, CF diagnosis is established and in patients with a sweat chloride test < 30 mmol/L, a diagnosis of CF is unlikely.^{4,5} Rarely, patients with a sweat chloride < 30 mmol/L may be considered to have CF if alternatives are excluded and other confirmatory tests (genetic and physiologic testing) support CF. In patients with a sweat chloride test of ≥ 30 to < 60 mmol/L, CFTR genetic analysis is undertaken. If the genetic analysis identifies two CF-causing CFTR mutations, CF is diagnosed, if no CFTR mutations are identified, a diagnosis of CF is unlikely. In patients with a CFTR genotype that is undefined or of varying clinical consequence, full gene CFTR sequencing (if not already performed) or CFTR physiologic testing is performed (NPD or ICM). If only one CFTR variant is identified on limited analysis, full gene CFTR sequencing be performed. CF is possible if both alleles possess CF-causing, undefined, or mutation of varying clinical consequence mutations; CF is unlikely if only no CF-causing mutations are found. If results of the NPD or ICM show CFTR dysfunction, CF is diagnosed; when testing is unavailable or equivocal, the diagnosis of CF is not resolved, and when results of the physiologic testing show CFTR function is preserved, a diagnosis of CF is considered unlikely. It is recommended that patients with challenging diagnoses be evaluated at an accredited CF Foundation Care Center.

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POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Trikafta. All approvals are provided for 1 year unless otherwise noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Trikafta as well as the monitoring required for adverse events and long-term efficacy, approval requires Trikafta to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Trikafta is recommended in those who meet the following criteria:

FDA-Approved Indication

- 1. Cystic Fibrosis (CF).** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
 - A)** Patient is ≥ 2 years of age; AND
 - B)** Patient has at least ONE of the following mutations in the cystic fibrosis conductance regulator gene that is considered to be a pathogenic or likely pathogenic variant: F508del, 3141del9, E822K, G1069R, L967S, R117L, S912L, 546insCTA, F191V, G1244E, L997F, R117P, S945L, A46D, F311del, G1249R, L1077P, R170H, S977F, A120T, F311L, G1349D, L1324P, R258G, S1159F, A234D, F508C, H139R, L1335P, R334L, S1159P, A349V, F508C;S1251N, H199Y, L1480P, R334Q, S1251N, A455E, H939R, M152V, R347H, S1255P, A554E, F575Y, H1054D, M265R, R347L, T338I, A1006E, F1016S, H1085P, M952I, R347P, T1036N, A1067T, F1052V, H1085R, M952T, R352Q, T1053I, D110E, F1074L, H1375P, M1101K, R352W, V201M, D110H, F1099L, I148T, P5L, R553Q, V232D, D192G, G27R, I175V, P67L, R668C, V456A, D443Y, G85E, I336K, P205S, R751L, V456F, D443Y;G576A;R668C, G126D, I502T, P574H, R792G, V562I, D579G, G178E, I601F, Q98R, R933G, V754M, D614G, G178R, I618T, Q237E, R1066H, V1153E, D836Y, G194R, I807M, Q237H, R1070Q, V1240G, D924N, G194V, I980K, Q359R, R1070W, V1293G, D979V, G314E, I1027T, Q1291R, R1162L, W361R, D1152H, G463V, I1139V, R31L, R1283M, W1098C, D1270N, G480C, I1269N, R74Q, R1283S, W1282R, E56K, G551D, I1366N, R74W, S13F, Y109N, E60K, G551S, K1060T, R74W;D1270N, S341P, Y161D, E92K, G576A, L15P, R74W;V201M, S364P, Y161S, E116K, G576A;R668C, L165S, R74W;V201M;D1270N, S492F, Y563N, E193K, G622D, L206W, R75Q, S549N, Y1014C, E403D, G628R, L320V, R117C, S549R, Y1032C, E474K, G970D, L346P, R117G, S589N, E588V, G1061R, L453S, R117H, or S737F; AND
 - C)** Patient meets at least ONE of the following (i, ii, or iii):
 - i.** Positive cystic fibrosis newborn screening test; OR
 - ii.** Family of cystic fibrosis; OR
 - iii.** Clinical presentation consistent with signs and symptoms of cystic fibrosis; AND
Note: Examples of clinical presentation of cystic fibrosis include but are not limited to meconium ileus, sino-pulmonary symptoms (e.g., persistent cough, wheezing, pulmonary function tests consistent with obstructive airway disease, excess sputum production), bronchiectasis, sinusitis, failure to thrive, pancreatic insufficiency.
 - D)** Patient has evidence of abnormal cystic fibrosis transmembrane conductance regulator function as demonstrated by at least ONE of the following (i, ii, or iii):
 - i.** Elevated sweat chloride test; OR
 - ii.** Two cystic fibrosis-causing cystic fibrosis transmembrane conductance regulator mutations; OR

- iii. Abnormal nasal potential difference; AND
- E) The medication is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of CF.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Trikafta is not recommended in the following situations:

1. **Cystic Fibrosis (CF), Patient with Unknown Cystic Fibrosis Transmembrane Regulator (CFTR) Gene Mutation.** An FDA-cleared CF mutation test should be used to detect the presence of the CFTR mutation prior to use of Trikafta.¹
2. **Combination Therapy with Orkambi, Kalydeco, or Symdeko.** Trikafta contains ivacaftor which is a component of Orkambi (lumacaftor/ivacaftor tablets and oral granules), Kalydeco (tablets and oral granules), and Symdeko (tezacaftor/ivacaftor tablets; ivacaftor tablets). Tezacaftor, another component of Trikafta is also contained in Symdeko.
3. **Infertility.** Trikafta is indicated for the treatment of cystic fibrosis in a patient ≥ 2 years of age who has at least one F508del mutation in the CFTR gene, or has a mutation in the CFTR gene that is responsive to Trikafta based on *in vitro* data.¹ **Note:** A patient with a diagnosis of cystic fibrosis should be reviewed using criteria for the FDA-approved indication, above.
4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Trikafta® tablets [prescribing information]. Cambridge, MA: Vertex; August 2023.
2. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Foundation Pulmonary Guidelines: Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. *Ann Am Thorac Soc.* 2018;15(3):271-280.
3. Farrell PM, White TB, Ren CL, et al. Diagnosis of cystic fibrosis: consensus guidelines from the cystic fibrosis foundation. *J Pediatr.* 2017;181S:S4-S15.
4. Farrell PM, White TB, Howenstine MS, et al. Diagnosis of cystic fibrosis in screened populations. *J Pediatr.* 2017;181S:S33-S44.