PRIOR AUTHORIZATION POLICY

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

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OVERVIEW

Trikafta is a combination of ivacaftor, a cystic fibrosis transmembrane regulator (CFTR) potentiator, tezacaftor, and elexacaftor indicated for the **treatment of cystic fibrosis (CF)** in patients ≥ 12 years of age who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive 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 indicating that Trikafta increases chloride transport to ≥ 10% of normal over baseline.

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

3141del9	A349V	D110E	D579G	D1152H	G576A;R668C
E822K	F508C;S1251N	F1074L	G178E	G463V	R74W;V201M;D1270N
G1069R	H199Y	H1375P	I601F	I1139V	S492F
L967S	L1480P	M1101K	Q98R	R31L	Y563N
R117L	R334Q	R352W	R933G	R1283M	E193K
S912L	S1251N	V201M	V754M	W1098C	G622D
546insCTA	A455E	D110H	D614G	D1270N	L206W
F191V	F508del	F1099L	G178R	G480C	R75Q
G1244E	H939R	I148T	I618T	I1269N	S549N
L997F	M152V	P5L	Q237E	R74Q	Y1014C
R117P	R347H	R553Q	R1066H	R1283S	E403D
S945L	S1255P	V232D	V1153E	W1282R	G628R
A46D	A554E	D192G	D836Y	E56K	L320V
F311del	F575Y	G27R	G194R	G551D	R117C
G1249R	H1054D	I175V	I807M	I1366N	S549R
L1077P	M265R	P67L	Q237H	R74W	Y1032C
R170H	R347L	R668C	R1070Q	S13F	E474K
S977F	T338I	V456A	V1240G	Y109N	G970D
A120T	A1006E	D443Y	D924N	E60K	L346P
F311L	F1016S	G85E	G194V	G551S	R117G
G1349D	H1085P	I336K	I980K	R74W;D1270N	S589N
L1324P	M952I	P205S	Q359R	S341P	E588V
R258G	R347P	R751L	R1070W	Y161D	G1061R
S1159F	T1036N	V456F	V1293G	E92K	L453S
A234D	A1067T	D443Y;G576A;R668C	D979V	G576A	R117H
F508C	F1052V	G126D	G314E	L15P	S737F
H139R	H1085R	I502T	I1027T	R74W;V201M	L165S
L1335P	M952T	P574H	Q1291R	S364P	K1060T
R334L	R352Q	R792G	R1162L	Y161S	
S1159P	T1053I	V562I	W361R	E116K	

CFTR – Cystic Fibrosis Transmembrane Regulator.

Elexacaftor is a new chemical entity. Ivacaftor is also available as Kalydeco® (tablets and oral granules) and as part of the co-formulated Orkambi® (lumacaftor/ivacaftor tablets and oral granules).[2,3] Tezacaftor

and ivacaftor are part of the co-formulated product, Symdeko® (tezacaftor/ivacaftor tablets; ivacaftor tablets).[4]

Both elexacaftor and tezacaftor bind to different sites of the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of F508del-CFTR to increase the amount of CFTR protein delivered to the cell surface compared with either molecule alone.[1] Ivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface. The combined effect of the three drugs is increased quantity and function of F508del-CFTR at the cell surface, resulting in increased CFTR activity as measured by CFTR mediated chloride transport.

Guidelines

Guidelines from the CF Foundation (2018) provide guidance on the use of CFTR therapy in patients with CF; Trikafta is not addressed.[5]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Trikafta. All approvals are provided for 3 years 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 Indications

1. **Cystic Fibrosis (CF).** Approve for 3 years if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 12 years of age; AND
   - **B)** Patient has at least one copy of one of the following mutations in the cystic fibrosis conductance regulator gene: 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) 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), Patients 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, Kalydeco, and Symdeko. Tezacaftor, another component of Trikafta is also contained in Symdeko.

3. 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 Pharmaceuticals, Inc; December 2020.
2. Kalydeco® tablets and oral granules [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; September 2020.
3. Orkambi® tablets and oral granules [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; July 2019.
4. Symdeko® tablets [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; December 2019.
5. 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.