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: 05/03/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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]

3141del9	F1016S	G628R	L320V	R170H	S737F
546insCTA	F1052V	G85E	L346P	R258G	S912L
A1006E	F1074L	G970D	L453S	R31L	S945L
A1067T	F1099L	H1054D	L967S	R334L	S977F
A120T	F191V	H1085P	L997F	R334Q	T1036N
A234D	F311del	H1085R	M1101K	R347H	T1053I
A349V	F311L	H1375P	M152V	R347L	T338I
A455E	F508C	H139R	M265R	R347P	V1153E

A46D	F508C;S1251N	H199Y	M952I	R352Q	V1240G
A554E	F508del	H939R	M952T	R352W	V1293G
D110E	F575Y	I1027T	P205S	R553Q	V201M
D110H	G1061R	I1139V	P574H	R668C	V232D
D1152H	G1069R	I1269N	P5L	R74Q	V456A
D1270N	G1244E	I1366N	P67L	R74W	V456F
D192G	G1249R	I148T	Q1291R	R74W;D1270N	V562I
D443Y	G126D	I175V	Q237E	R74W;V201M	V754M
D443Y;G576A;R668C	G1349D	I336K	Q237H	R74W;V201M;D1270N	W1098C
D579G	G178E	I502T	Q359R	R751L	W1282R
D614G	G178R	I601F	Q98R	R75Q	W361R
D836Y	G194R	I618T	R1066H	R792G	Y1014C
D924N	G194V	I807M	R1070Q	R933G	Y1032C
D979V	G27R	I980K	R1070W	S1159F	Y109N
E116K	G314E	K1060T	R1162L	S1159P	Y161D
E193K	G463V	L1077P	R117C	S1251N	Y161S
E403D	G480C	L1324P	R117G	S1255P	S737F
E474K	G551D	L1335P	R117H	S13F	S912L
E56K	G551S	L1480P	R117L	S341P	S945L
E588V	G576A	L15P	R117P	S364P	S977F
E60K	G576A;R668C	L165S	R1283M	S492F	
E822K	G622D	L206W	R1283S	S549N	

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]

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.

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is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Cystic Fibrosis (CF).** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   A) Patient is ≥ 2 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 COVERED

- **Trikafta® (elexacaftor/tezacaftor/ivacaftor tablets; ivacaftor tablets, co-packaged and elexacaftor/tezacaftor/ivacaftor oral granules; ivacaftor oral granules – Vertex)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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.

REFERENCES

1. Trikafta® tablets [prescribing information]. Cambridge, MA: Vertex; April 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/29/2022
Early Annual Revision	Trikafta oral granules were added to the policy. **Cystic Fibrosis:** The age criterion was changed to ≥ 2 years of age based on the new indication for Trikafta.	05/03/2023