UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2021 P 2180-4
Program	Prior Authorization/Medical Necessity
Medication	Trikafta® (elexacaftor/tezacaftor/ivacaftor)
P&T Approval Date	11/2019, 11/2020, 3/2021, 7/2021
Effective Date	9/1/2021; Oxford only: 10/1/2021

1. Background:

Trikafta is a combination of elexacaftor, tezacaftor, and ivacaftor, indicated for the treatment of patients with cystic fibrosis (CF) age 6 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or a mutation in the CFTR gene that is responsive based on *in vitro* data.

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 or a mutation that is responsive based on *in vitro* data.

Members will be required to meet the coverage criteria below.

2. Coverage Criteria[a]:

A. Initial Authorization

1. Trikafta will be approved based upon **all** of the following criteria:

a. Diagnosis of cystic fibrosis (CF)

-AND-

b. Submission of laboratory results documenting that the patient has at least **one** of the following mutations in the CFTR gene:
(1) F508del mutation
(2) A mutation that is responsive based on *in vitro* data[1]*

*List of *CFTR* gene mutations that are responsive to Trikafta					
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	*F508del **	*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*	*S737F*	

* *F508del* is a responsive *CFTR* mutation based on both clinical and *in vitro* data *[see Clinical Studies (14)]*.

† Complex/compound mutations where a single allele of the *CFTR* gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

-AND-

c. The patient is ≥ 6 years of age

-AND-

d. Prescribed by or in consultation with a specialist affiliated with a CF care center

Authorization will be issued for 6 months.

B. <u>Reauthorization</u>

1. Trikafta will be approved based on **<u>both</u>** of the following criteria:

a. Provider attests that the patient has achieved a clinically meaningful response while on Trikafta therapy to **<u>one</u>** of the following:

(1) Lung function as demonstrated by percent predicted expiratory volume in 1 second ($ppFEV_1$)
(2) Body mass index (BMI)
(3) Pulmonary exacerbations
(4) Quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score

-AND-

b. Prescribed by or in consultation with a specialist affiliated with a CF care center

Authorization will be issued for 24 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Trikafta [package insert]. Cambridge, MA: Vertex Pharmaceuticals, Inc.; June 2021.

Program	Prior Authorization/Medical Necessity – Trikafta (elexacaftor/tezacaftor/ivacaftor)
Change Control	
11/2019	New program
11/2020	Annual review. Updated reference.
3/2021	Updated criteria due to expanded indication approved for additional mutations.
7/2021	Updated criteria due to expanded indication approved for patients 6 years and older.