

UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

Program Number	2024 P 2180-7
Program	Prior Authorization/Medical Necessity
Medication	Trikafta® (elexacaftor/tezacaftor/ivacaftor)
P&T Approval Date	11/2019, 11/2020, 3/2021, 7/2021, 7/2022, 6/2023, 6/2024
Effective Date	9/1/2024

**1. Background:**

Trikafta is a combination of elexacaftor, tezacaftor, and ivacaftor, indicated for the treatment of patients with cystic fibrosis (CF) in patients aged 2 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<sup>a</sup>:**

**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<sup>1\*</sup>

<sup>a</sup>List of *CFTR* gene mutations that are responsive to Trikafta

<i>3141del9</i>	<i>E822K</i>	<i>G1069R</i>	<i>L967S</i>	<i>R117L</i>	<i>S912L</i>
<i>546insCTA</i>	<i>F191V</i>	<i>G1244E</i>	<i>L997F</i>	<i>R117P</i>	<i>S945L</i>
<i>A46D</i>	<i>F311del</i>	<i>G1249R</i>	<i>L1077P</i>	<i>R170H</i>	<i>S977F</i>
<i>A120T</i>	<i>F311L</i>	<i>G1349D</i>	<i>L1324P</i>	<i>R258G</i>	<i>S1159F</i>
<i>A234D</i>	<i>F508C</i>	<i>H139R</i>	<i>L1335P</i>	<i>R334L</i>	<i>S1159P</i>
<i>A349V</i>	<i>F508C;S1251N †</i>	<i>H199Y</i>	<i>L1480P</i>	<i>R334Q</i>	<i>S1251N</i>
<i>A455E</i>	<i>F508del *</i>	<i>H939R</i>	<i>M152V</i>	<i>R347H</i>	<i>S1255P</i>

<i>A554E</i>	<i>F575Y</i>	<i>H1054D</i>	<i>M265R</i>	<i>R347L</i>	<i>T338I</i>
<i>A1006E</i>	<i>F1016S</i>	<i>H1085P</i>	<i>M952I</i>	<i>R347P</i>	<i>T1036N</i>
<i>A1067T</i>	<i>F1052V</i>	<i>H1085R</i>	<i>M952T</i>	<i>R352Q</i>	<i>T1053I</i>
<i>D110E</i>	<i>F1074L</i>	<i>H1375P</i>	<i>M1101K</i>	<i>R352W</i>	<i>V201M</i>
<i>D110H</i>	<i>F1099L</i>	<i>I148T</i>	<i>P5L</i>	<i>R553Q</i>	<i>V232D</i>
<i>D192G</i>	<i>G27R</i>	<i>I175V</i>	<i>P67L</i>	<i>R668C</i>	<i>V456A</i>
<i>D443Y</i>	<i>G85E</i>	<i>I336K</i>	<i>P205S</i>	<i>R751L</i>	<i>V456F</i>
<i>D443Y;G576A;R668C †</i>	<i>G126D</i>	<i>I502T</i>	<i>P574H</i>	<i>R792G</i>	<i>V562I</i>
<i>D579G</i>	<i>G178E</i>	<i>I601F</i>	<i>Q98R</i>	<i>R933G</i>	<i>V754M</i>
<i>D614G</i>	<i>G178R</i>	<i>I618T</i>	<i>Q237E</i>	<i>R1066H</i>	<i>V1153E</i>
<i>D836Y</i>	<i>G194R</i>	<i>I807M</i>	<i>Q237H</i>	<i>R1070Q</i>	<i>V1240G</i>
<i>D924N</i>	<i>G194V</i>	<i>I980K</i>	<i>Q359R</i>	<i>R1070W</i>	<i>V1293G</i>
<i>D979V</i>	<i>G314E</i>	<i>I1027T</i>	<i>Q1291R</i>	<i>R1162L</i>	<i>W361R</i>
<i>D1152H</i>	<i>G463V</i>	<i>I1139V</i>	<i>R31L</i>	<i>R1283M</i>	<i>W1098C</i>
<i>D1270N</i>	<i>G480C</i>	<i>I1269N</i>	<i>R74Q</i>	<i>R1283S</i>	<i>W1282R</i>
<i>E56K</i>	<i>G551D</i>	<i>I1366N</i>	<i>R74W</i>	<i>S13F</i>	<i>Y109N</i>
<i>E60K</i>	<i>G551S</i>	<i>K1060T</i>	<i>R74W;D1270N †</i>	<i>S341P</i>	<i>Y161D</i>
<i>E92K</i>	<i>G576A</i>	<i>L15P</i>	<i>R74W;V201M †</i>	<i>S364P</i>	<i>Y161S</i>
<i>E116K</i>	<i>G576A;R668C †</i>	<i>L165S</i>	<i>R74W;V201M;D1270N †</i>	<i>S492F</i>	<i>Y563N</i>
<i>E193K</i>	<i>G622D</i>	<i>L206W</i>	<i>R75Q</i>	<i>S549N</i>	<i>Y1014C</i>
<i>E403D</i>	<i>G628R</i>	<i>L320V</i>	<i>R117C</i>	<i>S549R</i>	<i>Y1032C</i>
<i>E474K</i>	<i>G970D</i>	<i>L346P</i>	<i>R117G</i>	<i>S589N</i>	
<i>E588V</i>	<i>G1061R</i>	<i>L453S</i>	<i>R117H</i>	<i>S737F</i>	
* <i>F508del</i> is a responsive <i>CFTR</i> mutation based on both clinical and <i>in vitro</i> data.					
† Complex/compound mutations where a single allele of the <i>CFTR</i> gene has multiple mutations; these exist independent of the presence of mutations on the other allele.					

**-AND-**

c. The patient is  $\geq 2$  years of age

**-AND-**

d. Prescribed by or in consultation with a provider who specializes in the treatment of CF

**Authorization will be issued for 12 months.**

**B. Reauthorization**

1. **Trikafta** will be approved based on the following criterion:

a. Documentation of positive clinical response to Trikafta therapy (e.g., improved lung function, stable lung function)

**Authorization will be issued for 12 months.**

<sup>a</sup> 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.; August 2023.

Program	Prior Authorization/Medical Necessity – Trikafta (elexacaftor/tezacaftor/ivacaftor)
<b>Change Control</b>	
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.
7/2022	Annual review with no change to coverage criteria. Updated reauthorization duration to 12 months and reference.
6/2023	Updated criteria due to expanded indication approved for patients two years and older. Updated prescriber requirement, simplified reauthorization criteria, and updated reference.
6/2024	Annual review. Increased initial authorization approval duration to 12

	months. Removed prescriber requirement from reauthorization criteria. Updated reference.
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