

UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

Program Number	2026 P 2180-9
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, 2/2025, 2/2026
Effective Date	5/1/2026

**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 clinical and/or *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 indicated mutation.

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 responsive mutations in the CFTR gene:\*

- (1) F508del mutation
- (2) A mutation that is responsive based on clinical data
- (3) A mutation that is responsive based on *in vitro* data
- (4) A mutation that is responsive based on extrapolated data

\*List of CFTR gene mutations responsive to Trikafta. A complete up to date list of responsive mutations can be referenced in the Trikafta Prescribing Information.

Based on clinical data\*\*

2789+5G→A	D1152H†	L206W†	R1066H†	S945L†
3272-26A→G	F508del†	L997F†	R117C†	T338I†
3849+10kbC→T	G85E†	M1101K†	R347H†	V232D†
A455E†	L1077P†	P5L†	R347P†	

Based on *in vitro* data‡

N1303K	F200I	I1139V	P574H	S1045Y
1507 1515del9	F311del	I125T	P67L	S108F
2183A→G	F311L	I1269N	P750L	S1118F
3141del9	F508C	I1366N	Q1291R	S1159F

<i>546insCTA</i>	<i>F508C; S1251N</i>	<i>I148N</i>	<i>Q1313K</i>	<i>S1159P</i>
<i>A1006E</i>	<i>F575Y</i>	<i>I148T</i>	<i>Q237E</i>	<i>S1235R</i>
<i>A1067P</i>	<i>F587I</i>	<i>I175V</i>	<i>Q237H</i>	<i>S1251N</i>
<i>A1067T</i>	<i>G1047R</i>	<i>I331N</i>	<i>Q359R</i>	<i>S1255P</i>
<i>A107G</i>	<i>G1061R</i>	<i>I336K</i>	<i>Q372H</i>	<i>S13F</i>
<i>A120T</i>	<i>G1069R</i>	<i>I502T</i>	<i>Q493R</i>	<i>S341P</i>
<i>A234D</i>	<i>G1123R</i>	<i>I506L</i>	<i>Q552P</i>	<i>S364P</i>
<i>A309D</i>	<i>G1244E</i>	<i>I556V</i>	<i>Q98R</i>	<i>S492F</i>
<i>A349V</i>	<i>G1247R</i>	<i>I601F</i>	<i>R1048G</i>	<i>S549I</i>
<i>A46D</i>	<i>G1249R</i>	<i>I618T</i>	<i>R1070Q</i>	<i>S549N</i>
<i>A554E</i>	<i>G126D</i>	<i>I807M</i>	<i>R1070W</i>	<i>S549R</i>
<i>A62P</i>	<i>G1349D</i>	<i>I980K</i>	<i>R1162L</i>	<i>S589N</i>
<i>C491R</i>	<i>G178E</i>	<i>K1060T</i>	<i>R117C; G576A; R668C</i>	<i>S737F</i>
<i>D110E</i>	<i>G178R</i>	<i>K162E</i>	<i>R117G</i>	<i>S912L</i>
<i>D110H</i>	<i>G194R</i>	<i>K464E</i>	<i>R117H</i>	<i>S977F</i>
<i>D1270N</i>	<i>G194V</i>	<i>L1011S</i>	<i>R117L</i>	<i>T1036N</i>
<i>D1445N</i>	<i>G27E</i>	<i>L1324P</i>	<i>R117P</i>	<i>T1053I</i>
<i>D192G</i>	<i>G27R</i>	<i>L1335P</i>	<i>R1283M</i>	<i>T1086I</i>
<i>D443Y</i>	<i>G314E</i>	<i>L137P</i>	<i>R1283S</i>	<i>T1246I</i>
<i>D443Y; G576A; R668C</i>	<i>G424S</i>	<i>L1480P</i>	<i>R170H</i>	<i>T1299I</i>
<i>D565G</i>	<i>G463V</i>	<i>L15P</i>	<i>R258G</i>	<i>T351I</i>
<i>D579G</i>	<i>G480C</i>	<i>L165S</i>	<i>R297Q</i>	<i>V1153E</i>
<i>D614G</i>	<i>G480S</i>	<i>L320V</i>	<i>R31C</i>	<i>V1240G</i>
<i>D836Y</i>	<i>G551A</i>	<i>L333F</i>	<i>R31L</i>	<i>V1293G</i>
<i>D924N</i>	<i>G551D</i>	<i>L333H</i>	<i>R334L</i>	<i>V201M</i>
<i>D979V</i>	<i>G551S</i>	<i>L346P</i>	<i>R334Q</i>	<i>V392G</i>
<i>D993Y</i>	<i>G576A</i>	<i>L441P</i>	<i>R347L</i>	<i>V456A</i>
<i>E116K</i>	<i>G576A; R668C</i>	<i>L453S</i>	<i>R352Q</i>	<i>V456F</i>
<i>E116Q</i>	<i>G622D</i>	<i>L619S</i>	<i>R352W</i>	<i>V562I</i>
<i>E193K</i>	<i>G628R</i>	<i>L967S</i>	<i>R516S</i>	<i>V603F</i>
<i>E292K</i>	<i>G970D</i>	<i>M1137V</i>	<i>R553Q</i>	<i>V754M</i>
<i>E474K</i>	<i>H1054D</i>	<i>M152V</i>	<i>R668C</i>	<i>W1282R</i>
<i>E56K</i>	<i>H1085P</i>	<i>M265R</i>	<i>R709Q</i>	<i>W361R</i>
<i>E588V</i>	<i>H1085R</i>	<i>M952I</i>	<i>R74Q</i>	<i>Y1014C</i>
<i>E60K</i>	<i>H1375P</i>	<i>M952T</i>	<i>R74W</i>	<i>Y1032C</i>
<i>E92K</i>	<i>H199Y</i>	<i>N1303I</i>	<i>R74W; V201M</i>	<i>Y161D</i>
<i>F1016S</i>	<i>H620P</i>	<i>N186K</i>	<i>R74W; V201M; D1270N</i>	<i>Y161S</i>
<i>F1052V</i>	<i>H620Q</i>	<i>N187K</i>	<i>R751L</i>	<i>Y301C</i>
<i>F1074L</i>	<i>H939R</i>	<i>N418S</i>	<i>R75L</i>	<i>Y563N</i>
<i>F1099L</i>	<i>H939R; H949L</i>	<i>P140S</i>	<i>R75Q</i>	
<i>F1107L</i>	<i>I1027T</i>	<i>P205S</i>	<i>R792G</i>	
<i>F191V</i>	<i>I105N</i>	<i>P499A</i>	<i>R933G</i>	
Based on extrapolation from Trial 5 <sup>s</sup>				
<i>4005+2T→C</i>	<i>2789+2insA</i>	<i>3849+40A→G</i>	<i>5T; TG13</i>	
<i>1341G→A</i>	<i>296+28A→G</i>	<i>3849+4A→G</i>	<i>621+3A→G</i>	
<i>1898+3A→G</i>	<i>3041-15T→G</i>	<i>3850-3T→G</i>	<i>711+3A→G</i>	
<i>2752-26A→G</i>	<i>3600G→A</i>	<i>5T; TG12</i>	<i>E831X</i>	

\*\* Clinical data obtained from Trials 1 (NCT03525444), 2 (NCT03525548), and 5 (NCT05274269).  
 † This mutation is also predicted to be responsive by FRT assay.  
 ‡ The N1303K mutation is predicted to be responsive by HBE assay. All other mutations predicted to be responsive with in vitro data are supported by FRT assay.  
 § Efficacy is extrapolated from Trial 5 to non-canonical splice mutations because clinical trials in all mutations of this subgroup are infeasible and these mutations are not amenable to interrogation by FRT system.

-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.; September 2025.

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.
2/2025	Updated list of CFTR responsive gene mutations. Updated background and reference.
2/2026	Annual review. No changes to coverage criteria. Updated reference.