

Clinical Policy: Elexacaftor/Ivacaftor/Tezacaftor; Ivacaftor (Trikafta)

Reference Number: PA.CP.PHAR.440

Effective Date: 01/2020

Last Review Date: 07/2026

Description

Elexacaftor/ivacaftor/tezacaftor (Trikafta[®]) is a triple combination drug for cystic fibrosis (CF).

- Elexacaftor and tezacaftor bind to different sites on the cystic fibrosis transmembrane conductance regulator (CFTR) protein and have an additive effect in facilitating the cellular processing and trafficking of select mutant forms of CFTR (including F508del-CFTR) to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone.
- Ivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface.
- The combined effect of elexacaftor, tezacaftor, and ivacaftor is increased quantity and function of CFTR at the cell surface, resulting in increased CFTR activity as measured by CFTR mediated chloride transport in vitro and by sweat chloride in patients with CF.

FDA Approved Indication(s)

Trikafta is indicated for the treatment of cystic fibrosis (CF) in adult and pediatric patients aged 2 years and older who have a clinical diagnosis of CF and who have at least one variant in the CFTR gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein. If the patient's genotype is unknown, an FDA-cleared CF genetic test should be used to

confirm the presence of at least one variant in the CFTR gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness[®] that Trikafta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. Cystic Fibrosis (must meet all):**

1. Diagnosis of CF;
2. Age $\geq$ 2 years;
3. Prescribed by or in consultation with a pulmonologist or cystic fibrosis specialist;
4. Documentation indicates member has baseline forced expiratory volume in 1 second (FEV1), unless member is unable to perform spirometry testing;
5. Confirmation of one of the following (a or b):
 - a. Member has at least one *one variant in the CFTR gene that is responsive based on clinical and/or in vitro data (see Appendix E)*;

- b. Documentation of at least one variant in the CFTR gene that results in the production of CFTR protein;
- 6. Trikafta is not prescribed concurrently with other CFTR modulators (e.g., Alyftrek[®], Orkambi[®], Kalydeco[®], Symdeko[®]);
- 7. Dose does not exceed (a-e):
 - a. Age 2 to < 6 years and weight < 14 kg (both i and ii):
 - i. Elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 119.5 mg per day;
 - ii. One packet (elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg) of oral granules and one packet (ivacaftor 59.5 mg) of oral granules per day;
 - b. Age 2 to < 6 years and weight ≥ 14 kg (both i and ii):
 - i. Elexacaftor 100 mg/tezacaftor 50 mg/ ivacaftor 150 mg per day;
 - ii. One packet (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) oral granules and one packet (ivacaftor 75 mg) oral granules per day;
 - c. Age 6 to < 12 years and weight < 30 kg (both i and ii):
 - i. Elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 150 mg per day;
 - ii. 2 tablets (elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg) and 1 tablet (ivacaftor 75 mg) per day;
 - d. Age 6 to < 12 years and weight ≥ 30 kg, or age ≥ 12 years (both i and ii):
 - i. Elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day;
 - ii. 2 tablets (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) and 1 tablet (ivacaftor 150 mg) per day.
 - e. Age ≥ 12 years (both i and ii):
 - i. Elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day;
 - ii. 2 tablets (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) and 1 tablet (ivacaftor 150 mg) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Cystic Fibrosis (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is benefiting from Trikafta based on the prescriber's assessment;
3. Trikafta is not prescribed concurrently with other CFTR modulators (e.g., Alyftrek, Orkambi, Kalydeco, Symdeko);
4. If request is for a dose increase, new dose does not exceed (a-e):
 - a. Age 2 to < 6 years and weight < 14 kg (both i and ii):
 - i. Elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 119.5 mg per day;
 - ii. One packet (elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg) of oral granules and one packet (ivacaftor 59.5 mg) of oral granules per day;
 - b. Age 2 to < 6 years and weight ≥ 14 kg (both i and ii):

- i. Elexacaftor 100 mg/tezacaftor 50 mg/ ivacaftor 150 mg per day;
- ii. One packet (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) of oral granules and one packet (ivacaftor 75 mg) of oral granules per day;
- c. Age 6 to < 12 years and weight < 30 kg (both i and ii):
 - i. Elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 150 mg per day;
 - ii. 2 tablets (elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg) and 1 tablet (ivacaftor 75 mg) per day;
- d. Age 6 to < 12 years and weight $\geq$ 30 kg, or age $\geq$ 12 years (both i and ii):
 - i. Elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day;
 - ii. 2 tablets (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) and 1 tablet (ivacaftor 150 mg) per day.
- e. Age $\geq$ 12 years (both i and ii):
 - i. Elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day;
 - ii. 2 tablets (elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) and 1 tablet (ivacaftor 150 mg) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACFLD: advanced cystic fibrosis lung disease

CF: cystic fibrosis

CFF: Cystic Fibrosis Foundation

CFTR: cystic fibrosis transmembrane conductance regulator

FDA: Food and Drug Administration

LCI: lung clearance index

ppFEV1: percent predicted forced expiratory volume in 1 second

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): None reported
- Boxed warning(s): Drug-induced liver injury and liver failure

Appendix D: General Information

- The Cystic Fibrosis Foundation (CFF) Mutation Analysis Program (MAP) available here: <https://www.cff.org/medical-professionals/mutation-analysis-program>. The MAP is a free and confidential genetic testing program for people with a strongly suspected or confirmed diagnosis of CF.
- Regarding the diagnostic criteria for CF:
 - The Cystic Fibrosis Foundation (CFF) guidelines state that CFTR dysfunction needs to be confirmed with an elevated sweat chloride ≥ 60 mmol/L.
 - “Genetic testing confirming the presence of two disease-causing mutations in CFTR gene” is used to ensure that whether heterozygous or homozygous, there are two disease-causing mutations in the CFTR gene, one from each parental allele.
- Most children can do spirometry by age 6, though some preschoolers are able to perform the test at a younger age. Some young children aren’t able to take a deep enough breath and blow out hard and long enough for spirometry.

Appendix E: CFTR Gene Mutations that are Responsive to Trikafta

List of CFTR Gene Variants that are Responsive to Trikafta				
Variants responsive to Trikafta 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 [†]	
Variants responsive to Trikafta based on in vitro data [‡]				
1140-1151dup N1303K	E264V F200I	H620P I1139V	N396Y P574H	S1251N S1045Y
1461insGAT 1507 1515del9	E282D F311del	H620Q I125T	N418S P67L	S1255P S108F
1507 1515del9 2183A→G	E292K F311L	H939R I1269N	N900K P750L	S13F S1118F
3141del92055del9	E384K F508C	H939R;H949L I1366N	P1013H Q1291R	S13P S1159F
2183A→G 546insCTA	E403D F508C;S1251N	H954P I148N	P1013L Q1313K	S158N S1159F
2851A/G A1006E	E474K F575Y	I1023R I148T	P1021L Q237E	S182R S1235R
293A→G A1067P	E527G F587I	I1027T I175V	P1021T Q237H	S18I S1251N
3007del6 A1067T	E56K G1047R	I105N I331N	P111L Q359R	S18N S1255P
3132T→G A107G	E588V G1061R	I1139V I336K	P1372T Q372H	S308P S13F
3141del9 A120T	E60K G1069R	I1203V I502T	P140S Q493R	S341P S341P
3143del9 A234D	E822K G1123R	I1234L I506L	P205S Q552P	S364P S364P
314del9 A309D	E92K G1244E	I1234V del6aa I556V	P439S Q98R	S434P S492F

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3331del6 A349V	F1016S G1247R	I125T I601F	P499A R1048G	S492F S549I
3410T→C A46D	F1052V G1249R	I1269N I618T	P574H R1070Q	S50P S549N
3523A→G A554E	F1074L G126D	I1366N I807M	P67L R1070W	S519G S549R
3601A→C A62P	F1078S G1349D	I1366T I980K	P750L R1162L	S531P S589N
3761T→G C491R	F1099L G178E	I148L K1060T	P798S R117C;G576 A;R668C	S549I S737F
3791C/T D110E	F1107L G178R	I148N K162E	P988R R117G	S549N S912L
3850G→A D110H	F191V G194R	I148T K464E	Q1012P R117H	S549R S977F
3978G→C D1270N	F200I G194V	I175V L1011S	Q1209P R117L	S557F T1036N
546insCTA D1445N	F311del G27E	I331N L1324P	Q1291H R117P	S589I T1053I
548insTAC D192G	F311L G27R	I336K L1335P	Q1291R R1283M	S589N T1086I
A1006E D443Y	F312del G314E	I336L L137P	Q1313K R1283S	S624R T1246I
A1025D D443Y;G576A;R6 68C	F433L G424S	I444S L1480P	Q1352H R170H	S686Y T1299I
A1067P D565G	F508C G463V	I497S L15P	Q151K R258G	S737F T351I
A1067T D579G	F508C;S1251N G480C	I502T L165S	Q179K R297Q	S821G V1153E
A1067V D614G	F508del;R1438 W G480S	I506L L320V	Q237E R31C	S898R V1240G
A107G D836Y	F575Y G551A	I506V L333F	Q237H R31L	S912L V1293G
A1081V D924N	F587I G551D	I506V;D1168G L333H	Q237P R334L	S912L;G1244 V V201M
A1087P D979V	F587L G551S	I521S L346P	Q30P R334Q	S912T V392G
A120T D993Y	F693L(TTG) G576A	I530N L441P	Q359K/T360 K R347L	S955P V456A
A1319E E116K	F87L G576A;R668C	I556V L453S	Q359R R352Q	S977F V456F
A1374D E116Q	F932S G622D	I586V L619S	Q372H R352W	S977F;R1438 W V562I
A141D E193K	G1047D G628R	I601F L967S	Q493L R516S	T1036N V603F
A1466S E292K	G1047R G970D	I618N M1137V	Q493R R553Q	T1053I V754M

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<i>A155P E403D</i>	<i>G1061R G970S</i>	<i>I618T M150K</i>	<i>Q552P R555G</i>	<i>T1057R W1098C</i>
<i>A234D E474K</i>	<i>G1069R H1054D</i>	<i>I807M M152V</i>	<i>Q98P R668C</i>	<i>T1086A W1282R</i>
<i>A234V E56K</i>	<i>G1123R H1085P</i>	<i>I86M M265R</i>	<i>Q98R R709Q</i>	<i>T1086I W361R</i>
<i>A238V E588V</i>	<i>G1173S H1085R</i>	<i>I980K M952I</i>	<i>R1048G R74Q</i>	<i>T1246I Y1014C</i>
<i>A309D E60K</i>	<i>G1237V H1375P</i>	<i>K1060T M952T</i>	<i>R1066G R74W</i>	<i>T1299I Y1032C</i>
<i>A349V E822K</i>	<i>G1244E H139R</i>	<i>K162E N1088D</i>	<i>R1070P R74W;D1270 N</i>	<i>T1299K Y109N</i>
<i>A357T E92K</i>	<i>G1244R H199Y</i>	<i>K464E N1303I</i>	<i>R1070Q R74W;V201M</i>	<i>T351I Y161D</i>
<i>A455V F1016S</i>	<i>G1247R H620P</i>	<i>K464N N186K</i>	<i>R1070W R74W;V201M ;D1270N</i>	<i>T351S Y161S</i>
<i>A457T F1052V</i>	<i>G1249E H620Q</i>	<i>K522E N187K</i>	<i>R1162L R751L</i>	<i>T351S;R851L Y301C</i>
<i>A462P F1074L</i>	<i>G1249R H939R</i>	<i>K522Q N418S</i>	<i>R1162Q R75L</i>	<i>T388M Y563N</i>
<i>A46D F1099L</i>	<i>G1265V H939R;H949L</i>	<i>K951E P140S</i>	<i>R117C;G576 A;R668C R75Q</i>	<i>T465I</i>
<i>A534E F1107L</i>	<i>G126D I1027T</i>	<i>L1011S P205S</i>	<i>R117G R792G</i>	<i>T501A</i>
<i>A554E F191V</i>	<i>G1298V I105N</i>	<i>L102R;F1016S P499A</i>	<i>R117H R933G</i>	<i>T582S</i>
<i>A62P</i>	<i>G149R;G576A;R 668C</i>	<i>L1227S</i>	<i>R117L;L997F</i>	<i>T990I</i>
<i>A872E</i>	<i>G178E</i>	<i>L1324P</i>	<i>R117P</i>	<i>V1008D</i>
<i>c.1367_1369dupT TG</i>	<i>G178R</i>	<i>L1335P</i>	<i>R1239S</i>	<i>V1010D</i>
<i>C225R</i>	<i>G194R</i>	<i>L137P</i>	<i>R1283G</i>	<i>V1153E</i>
<i>C491R</i>	<i>G194V</i>	<i>L1388P</i>	<i>R1283M</i>	<i>V11I</i>
<i>C590Y</i>	<i>G213E</i>	<i>L1480P</i>	<i>R1283S</i>	<i>V1240G</i>
<i>C866Y</i>	<i>G213E;R668C</i>	<i>L159S</i>	<i>R1438W</i>	<i>V1293G</i>
<i>D110E</i>	<i>G213V</i>	<i>L15P</i>	<i>R170H</i>	<i>V1293I</i>
<i>D110H</i>	<i>G226R</i>	<i>L15P;L1253F</i>	<i>R248K</i>	<i>V1415F</i>
<i>D110N</i>	<i>G239R</i>	<i>L165S</i>	<i>R258G</i>	<i>V201M</i>
<i>D1152A</i>	<i>G253R</i>	<i>L167R</i>	<i>R297Q</i>	<i>V232A</i>
<i>D1270N</i>	<i>G27E</i>	<i>L210P</i>	<i>R31C</i>	<i>V317A</i>
<i>D1270Y</i>	<i>G27R</i>	<i>L293P</i>	<i>R31L</i>	<i>V322M</i>
<i>D1312G</i>	<i>G314E</i>	<i>L320V</i>	<i>R334L</i>	<i>V392G</i>
<i>D1377H</i>	<i>G314R</i>	<i>L327P</i>	<i>R334Q</i>	<i>V456A</i>

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<i>D1445N</i>	<i>G424S</i>	<i>L32P</i>	<i>R347L</i>	<i>V456F</i>
<i>D192G</i>	<i>G437D</i>	<i>L333F</i>	<i>R352Q</i>	<i>V520I</i>
<i>D192N</i>	<i>G461R</i>	<i>L333H</i>	<i>R352W</i>	<i>V562I</i>
<i>D373N</i>	<i>G461V</i>	<i>L346P</i>	<i>R516S</i>	<i>V562I;A1006E</i>
<i>D426N</i>	<i>G463V</i>	<i>L441P</i>	<i>R553Q</i>	<i>V562L</i>
<i>D443Y</i>	<i>G480C</i>	<i>L453S</i>	<i>R555G</i>	<i>V591A</i>
<i>D443Y;G576A;R668C</i>	<i>G480D</i>	<i>L467F</i>	<i>R600S</i>	<i>V603F</i>
<i>D529G</i>	<i>G480S</i>	<i>L558F</i>	<i>R668C</i>	<i>V754M</i>
<i>D565G</i>	<i>G500D</i>	<i>L619S</i>	<i>R709Q</i>	<i>V920L</i>
<i>D567N</i>	<i>G545R</i>	<i>L633P</i>	<i>R74Q</i>	<i>V920M</i>
<i>D579G</i>	<i>G551A</i>	<i>L636P</i>	<i>R74Q;R297Q</i>	<i>V93D</i>
<i>D58H</i>	<i>G551D</i>	<i>L88S</i>	<i>R74Q;V201M;D1270N</i>	<i>W1098C</i>
<i>D58V</i>	<i>G551R</i>	<i>L927P</i>	<i>R74W</i>	<i>W1282G</i>
<i>D614G</i>	<i>G551S</i>	<i>L967F;L1096R</i>	<i>R74W;D1270N</i>	<i>W1282R</i>
<i>D651H</i>	<i>G576A</i>	<i>L967S</i>	<i>R74W;R1070W;D1270N</i>	<i>W202C</i>
<i>D651N</i>	<i>G576A;R668C</i>	<i>L973F</i>	<i>R74W;S945L</i>	<i>W361R</i>
<i>D806G</i>	<i>G576A;S1359Y</i>	<i>M1137R</i>	<i>R74W;V201M</i>	<i>W496R</i>
<i>D836Y</i>	<i>G622D</i>	<i>M1137V</i>	<i>R74W;V201M;D1270N</i>	<i>Y1014C</i>
<i>D924N</i>	<i>G622V</i>	<i>M1210K</i>	<i>R74W;V201M;L997F</i>	<i>Y1032C</i>
<i>D979A</i>	<i>G628A</i>	<i>M150K</i>	<i>R751L</i>	<i>Y1032N</i>
<i>D979V</i>	<i>G628R</i>	<i>M150R</i>	<i>R75L</i>	<i>Y1073C</i>
<i>D985H</i>	<i>G930E</i>	<i>M152L</i>	<i>R75Q</i>	<i>Y1092H</i>
<i>D985Y</i>	<i>G970D</i>	<i>M152V</i>	<i>R75Q;L1065P</i>	<i>Y109H</i>
<i>D993A</i>	<i>G970S</i>	<i>M265R</i>	<i>R75Q;N1088D</i>	<i>Y109N</i>
<i>D993G</i>	<i>G970V</i>	<i>M348K</i>	<i>R75Q;S549N</i>	<i>Y122C</i>
<i>D993Y</i>	<i>H1054D</i>	<i>M394L</i>	<i>R792G</i>	<i>Y1381H</i>
<i>E1104K</i>	<i>H1079P</i>	<i>M469V</i>	<i>R792Q</i>	<i>Y161C</i>
<i>E1104V</i>	<i>H1085P</i>	<i>M498I</i>	<i>R810G</i>	<i>Y161D</i>
<i>E1126K</i>	<i>H1085R</i>	<i>M952I</i>	<i>R851L</i>	<i>Y161S</i>
<i>E116K</i>	<i>H1375N</i>	<i>M952T</i>	<i>R933G</i>	<i>Y301C</i>
<i>E116Q</i>	<i>H1375P</i>	<i>M961L</i>	<i>S1045Y</i>	<i>Y563N</i>
<i>E1221V</i>	<i>H139L</i>	<i>N1088D</i>	<i>S108F</i>	<i>Y89C</i>
<i>E1228K</i>	<i>H139R</i>	<i>N1195T</i>	<i>S1118F</i>	<i>Y913S</i>
<i>E1409K</i>	<i>H146R</i>	<i>N1303I</i>	<i>S1159F</i>	<i>Y919C</i>
<i>E1433K</i>	<i>H199Q</i>	<i>N1303K</i>	<i>S1159P</i>	
<i>E193K</i>	<i>H199Y</i>	<i>N186K</i>	<i>S1188L</i>	
<i>E217G</i>	<i>H609L</i>	<i>N187K</i>	<i>S1235R</i>	

* Clinical data obtained from Trials 1, 2, and 5.

† This variant is also predicted to be responsive by FRT assay.

‡ The N1303k variant is predicted to be responsive by HBE assay. All other variants predicted to be responsive with in vitro data are supported by FRT assay.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CF	Pediatric patients age 2 to less than 6 years weighing less than 14 kg: • <u>Morning dose</u>: One packet (containing elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg oral granules) • <u>Evening dose</u>: One packet (containing ivacaftor 59.5 mg oral granules)	Age 2 to 6 years weighing less than 14 kg: elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 119.5 mg per day
	Pediatric patients age 2 to less than 6 years weighing 14 kg or more: • <u>Morning dose</u>: One packet (containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg oral granules) • <u>Evening dose</u>: One packet (containing ivacaftor 75 mg oral granules)	Age 2 to 6 years weighing 14 kg or more and pediatric patients, or age 6 years to less than 12 years weighing less than 30 kg: elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 150 mg per day
	Pediatric patients age 6 years to less than 12 years weighing less than 30 kg: • <u>Morning dose</u>: 2 tablets (each containing elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg) • <u>Evening dose</u>: 1 tablet of ivacaftor 75 mg	
	Adults and pediatric patients age 12 years and older: • <u>Morning dose</u>: 2 tablets (each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) • <u>Evening dose</u>: 1 tablet of ivacaftor 150 mg Morning and evening dose should be taken approximately 12 hours apart with fat-containing food	Adults, pediatric patients age 12 years and older, or pediatric patients age 6 years to less than 12 years weighing 30 kg or more: elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day

VI. Product Availability

- Tablets: co-packaged fixed dose combination containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg and ivacaftor 150 mg; co-packaged fixed dose combination containing elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg and ivacaftor 75 mg

- Unit-dose packets containing oral granules: fixed dose combination containing elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg co-packaged with ivacaftor 75 mg; fixed dose combination containing elexacaftor 80 mg, tezacaftor 40 mg, ivacaftor 60 mg co-packaged with ivacaftor 59.5 mg

VII. References

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Reviews, Revisions, and Approvals	Date
Policy created	01/2020
1Q 2021 annual review: no significant changes; references reviewed and updated.	01/2021
1Q 2022 annual review: include pediatric expansion and new dose strength; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; updated appendix D; references reviewed and updated.	01/2023
3Q 2023 annual review: revised criteria to include pediatric expansion and new granule formulation; updated Appendix D to include information on LCI; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; for Appendix D, updated LCI supplemental information; references reviewed and updated.	07/2024
3Q 2025 annual review: RT4: added new indication to criteria for non-F508del mutation responsive to Trikafta based on clinical data; for	07/2025

CLINICAL POLICY

Elexacaftor/Ivacaftor/Tezacaftor; Ivacaftor



Reviews, Revisions, and Approvals	Date
Appendix E, updated list of CFTR gene mutations responsive to Trikafta per prescriber information; added Alyftrek to list of CFTR modulator concurrent exclusion criteria; references reviewed and updated.	
3Q 2026 annual review: RT4: updated FDA approved indication to patients who have at least one variant in the <i>CFTR</i> gene that is either responsive based on clinical and/or in vitro data or results in production of CFTR protein; updated Appendix E with list of <i>CFTR</i> gene variants that are responsive to Trikafta per prescribing information; for initial therapy, updated duration from 6 months to 12 months for chronic therapy; references reviewed and updated.	07/2026