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

Reference Number: CP.PHAR.440
Effective Date: 12.01.19
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 both 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 CF in patients aged 2 years and older who have at least one *F508del* mutation in the *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.

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 health plans affiliated with Centene Corporation® 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 confirmed by all of the following (a, b, and c):
   a. Clinical symptoms consistent with CF in at least one organ system, or positive newborn screen or genetic testing for siblings of patients with CF;
   b. Evidence of CFTR dysfunction confirmed by one of the following (i or ii) (*see Appendix D*):
      i. Elevated sweat chloride ≥ 60 mmol/L;

ii. Genetic testing confirming the presence of two disease-causing mutations in CFTR gene, one from each parental allele;

c. Confirmation of one of the following (i or ii):
   i. Member has at least one *F508del* mutation in the CFTR gene;
   ii. Member has a mutation in the CFTR gene that is responsive to Trikafta based on clinical and/or *in vitro* data (*see Appendix E*);

2. Age ≥ 2 years;
3. Prescribed by or in consultation with a pulmonologist;
4. For age ≥ 6 years: Documentation of baseline percent predicted forced expiratory volume in 1 second (ppFEV1) performed within the last 90 days;
5. Trikafta is not prescribed concurrently with other CFTR modulators (e.g., Orkambi®, Kalydeco®, Symdeko®);
6. Dose does not exceed one of the following (a, b, c, d, or 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/tezcaftor 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 (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: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cystic Fibrosis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member meets one of the following (a or b):
   a. For age < 6 years: Member is responding positively to therapy (e.g., decreased number of pulmonary exacerbations, increase in body mass index (BMI), improvement in respiratory symptoms);
   b. For age ≥ 6 years: Member is responding positively to therapy as evidenced by stabilization or improvement (e.g., increase) in ppFEV1 from baseline;
3. Trikafta is not prescribed concurrently with other CFTR modulators (e.g., Orkambi, Kalydeco, Symdeko);
4. If request is for a dose increase, new dose does not exceed (a, b, c, d, or 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/tezcaftor 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 ≥ 30 kg (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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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. One of those two mutations must be an *F508del* mutation but does not necessarily require both.
- 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 Mutations that are Responsive to Trikafta				
Mutations 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*†	
Mutations responsive to Trikafta 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*
546insCTA	*F508C;S1251N*	*I148N*	*Q1313K*	*S1159F*
A1006E	*F575Y*	*I148T*	*Q237E*	*S1235R*
A1067P	*F587I*	*I175V*	*Q237H*	*S1251N*
A1067T	*G1047R*	*I331N*	*Q359R*	*S1255P*
A107G	*G1061R*	*I336K*	*Q372H*	*S13F*
A120T	*G1069R*	*I502T*	*Q493R*	*S341P*
A234D	*G1123R*	*I506L*	*Q552P*	*S364P*
A309D	*G1244E*	*I556V*	*Q98R*	*S492F*
A349V	*G1247R*	*I601F*	*R1048G*	*S549I*
A46D	*G1249R*	*I618T*	*R1070Q*	*S549N*
A554E	*G126D*	*I807M*	*R1070W*	*S549R*
A62P	*G1349D*	*I980K*	*R1162L*	*S589N*
C491R	*G178E*	*K1060T*	*R117C;G576A;R668C*	*S737F*
D110E	*G178R*	*K162E*	*R117G*	*S912L*
D110H	*G194R*	*K464E*	*R117H*	*S977F*
D1270N	*G194V*	*L1011S*	*R117L*	*T1036N*
D1445N	*G27E*	*L1324P*	*R117P*	*T1053I*
D192G	*G27R*	*L1335P*	*R1283M*	*T1086I*
D443Y	*G314E*	*L137P*	*R1283S*	*T1246I*

List of CFTR Gene Mutations that are Responsive to Trikafta				
D443Y;G576A;R668C	*G424S*	*L1480P*	*R170H*	*T1299I*
D565G	*G463V*	*L15P*	*R258G*	*T351I*
D579G	*G480C*	*L165S*	*R297Q*	*V1153E*
D614G	*G480S*	*L320V*	*R31C*	*V1240G*
D836Y	*G551A*	*L333F*	*R31L*	*V1293G*
D924N	*G551D*	*L333H*	*R334L*	*V201M*
D979V	*G551S*	*L346P*	*R334Q*	*V392G*
D993Y	*G576A*	*L441P*	*R347L*	*V456A*
E116K	*G576A;R668C*	*L453S*	*R352Q*	*V456F*
E116Q	*G622D*	*L619S*	*R352W*	*V562I*
E193K	*G628R*	*L967S*	*R516S*	*V603F*
E292K	*G970D*	*M1137V*	*R553Q*	*V754M*
E403D	*G970S*	*M150K*	*R555G*	*W1098C*
E474K	*H1054D*	*M152V*	*R668C*	*W1282R*
E56K	*H1085P*	*M265R*	*R709Q*	*W361R*
E588V	*H1085R*	*M952I*	*R74Q*	*Y1014C*
E60K	*H1375P*	*M952T*	*R74W*	*Y1032C*
E822K	*H139R*	*N1088D*	*R74W;D1270N*	*Y109N*
E92K	*H199Y*	*N1303I*	*R74W;V201M*	*Y161D*
F1016S	*H620P*	*N186K*	*R74W;V201M;D1270N*	*Y161S*
F1052V	*H620Q*	*N187K*	*R751L*	*Y301C*
F1074L	*H939R*	*N418S*	*R75L*	*Y563N*
F1099L	*H939R;H949L*	*P140S*	*R75Q*	
F1107L	*I1027T*	*P205S*	*R792G*	
F191V	*I105N*	*P499A*	*R933G*	
Mutations responsive to Trikafta based on extrapolation from Trial 5[§]				
4005+2T→C	*2789+2insA*	*3849+40A→G*	*5T;TG13*	
1341G→A	*296+28A→G*	*3849+4A→G*	*621+3A→G*	
1898+3A→G	*3041-15T→G*	*3850-3T→G*	*711+3A→G*	
2752-26A→G	*3600G→A*	*5T;TG12*	*E831X*	

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

[†] 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CF	Pediatric patients age 2 to less than 6 years weighing less than 14 kg:	Age 2 to 6 years weighing less than 14 kg:

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

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

1. Trikafta Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; December 2024. Available at: https://pi.vrtx.com/files/uspi_elexacaftor_tezacaftor_ivacaftor.pdf. Accessed January 16, 2025.
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.
3. Farrell PM, White TB, Ren CL, et al. Diagnosis of cystic fibrosis: consensus guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017 Feb;181S:S4-S15.e1.
4. Goss CH, Burns JL. Exacerbations in cystic fibrosis. 1: Epidemiology and pathogenesis. Thorax. 2007;62(4):360–367.
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6. Kapnadak SG, Dimango E, Hadjiliadis D, et al. Cystic Fibrosis Foundation consensus guidelines for the care of individuals with advanced cystic fibrosis lung disease. J Cyst Fibros. 2020 May;19(3):344-354.
7. Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Pulmonary Clinical Practice Guidelines Committee. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. Am J Respir Crit Care Med. 2013 Apr 1;187(7):680-9.
8. Cystic Fibrosis Foundation: Clinical Care Guidelines. Available at: https://www.cff.org/medical-professionals/clinical-care-guidelines. Accessed May 17, 2024.
9. Alexander S, Alshafi K, Al-Yaghchi C, et al. Clinical Guidelines: Care of Children with Cystic Fibrosis. Royal Brompton and Harefield NHS. 2020;(8):22-23.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: Finalized line of businesses on policy to include HIM per SDC and prior clinical guidance; for initial approval: added comprehensive diagnostic criteria to confirm CF diagnosis (e.g., clinical symptoms in at least one organ, positive newborn screen, siblings genetic testing, and evidence of CFTR dysfunction confirmed by sweat chloride or genetic testing); added in vitro testing demonstrates a baseline chloride transport < 10% of wild type CFTR; added requirement for lack of responsiveness to other CFTR modulators; added for members currently using another CFTR modulator switching to Trikafta must show increase in chloride transport of < 10% over baseline; added positive response after at least 12 weeks of therapy of a) stabilization in ppFEV1 in lieu of an increase is acceptable if baseline was ≥ 70% and b) chloride transport ≥ 10% since baseline; modified initial approval duration to 4 months with reauthorization for 12 months; added Appendix D.	12.17.19	02.20
Clarify continuation of therapy requires an increase in chloride transport of 10% or greater.	02.11.20	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised initial approval criteria: revised the requirement for evidence of clinical severity as defined by an average sweat chloride from > 86 mmol/L to > 60 mmol/L; removed in vitro testing requirement demonstrating a baseline chloride transport < 10% of wild type CFTR; removed requirement for lack of responsiveness to other CFTR modulators; removed for members currently using another CFTR modulator switching to Trikafta to show increase in chloride transport of < 10% over baseline; removed positive response requirement after at least 12 weeks of therapy to show chloride transport ≥ 10% since baseline requirement; revised Appendix D.	04.22.20	08.20
1Q 2021 annual review: references to HIM.PHAR.21 revised to HIM.PA.154; RT4: based on the updated FDA-labeled indication and gene mutations responsive to Trikafta, added diagnosis criteria option for member to have a mutation in the CFTR gene that is responsive to Trikafta, in addition to the previous requirement of member having one *F508del* mutation in the CFTR gene, with a reference to new addition of Appendix E; references reviewed and updated.	01.19.21	02.21
RT4: revised to include pediatric expansion and new dose strength.	06.15.21	
1Q 2022 annual review: added legacy Wellcare line of business (WCG.CP.PHAR.440 to be retired); for legacy WCG: revised the requirement for evidence of clinical severity as defined by an average sweat chloride from > 86 mmol/L to > 60 mmol/L; removed in vitro testing requirement demonstrating a baseline chloride transport < 10% of wild type CFTR; removed requirement for lack of responsiveness to other CFTR modulators; removed for members currently using another CFTR modulator switching to Trikafta to show increase in chloride transport of < 10% over baseline; removed positive response requirement after at least 12 weeks of therapy to show chloride transport ≥ 10% since baseline requirement; references reviewed and updated.	10.22.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.26.22	
1Q 2023 annual review: removed "if member has received at least 12 weeks of therapy" for ppFEV1 criteria in the continuation of therapy section to align with approach in other CF policies; consolidated Legacy Wellcare initial approval duration from 12 months to 6 months consistent with standard Medicaid initial approval duration; updated appendix D; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	10.07.22	02.23
RT4: revised criteria to include pediatric expansion and new granule formulation; revised initial approval criteria requiring chart notes for pulmonary function test: added "for age > 2 years" for ppFEV1, added alternative option for ppFEV1 for age < 6 years to allow for LCI ≥	05.04.23	06.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
7.4, and revised continuation criteria to include stabilization in LCI if baseline was ≥ 7.4; updated Appendix D to include information on LCI; references reviewed and updated.		
3Q23 annual review: no significant changes after comprehensive review completed as part of the RT4 review in June 2023.	05.10.23	08.23
Revised initial approval criteria: removed "for age 2 > years" and "ppFEV1 that is between 40 – 90%" in criteria stating documentation of member's ppFEV1; revised "chart notes that indicate pulmonary function tests" to "documentation of one of the following pulmonary function tests"; for continued therapy criteria: revised criteria from "stabilization in ppFEV1 if baseline was ≥ 70%, or increase in ppFEV1 if baseline was <70%" to "stabilization or improvement in ppFEV1" and revised "stabilization in LCI if baseline was ≥ 7.4" to "stabilization or decrease in LCI from baseline"; revised Appendix D to remove information on advanced Cystic Fibrosis disease.	01.11.24	02.24
3Q 2024 annual review: for continued therapy, clarified positive response as an "improvement" (e.g., decrease) of LCL and improvement of ppFEV1 as an "increase from baseline"; for Appendix D, updated LCI supplemental information; references reviewed and updated.	05.09.24	08.24
Removed lung clearance index from criteria to align with competitor analysis and standard of care; for initial approval criteria, updated approval duration from 4 months to 6 months. RT4: added new indication to criteria for non-F508del mutation responsive to Trikafta based on clinical data; for Appendix E, updated list of CFTR gene mutations responsive to Trikafta per prescriber information.	01.16.25	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering

benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.